Journal of ENT masterclass ISSN 2047-959X

Journal of

ENT MASTERCLASS®

Year Book 2016

Volume 9 Number 1

JOURNAL OF ENT MASTERCLASS®

Volume 9 Issue 1 December 2016

Contents

JOURNAL OF ENT MASTERCLASS®

Welcome to Volume 9 Issue 1 of Journal of ENT Masterclass® 2016

This volume arrives in my second year as the Chairman of the Editorial Board of the Journal of ENT Masterclass®. Taking this role last year made me realise the magnitude of hard work that had been taken in the past years and I am very pleased that we have continued with the previous successes. The 8th Journal of ENT Masterclass® was very well received by the ENT fraternity in UK and the free subscription has been extended to all the members of ENT-UK following its official accreditation by our national body.

This year, we have expanded the Editorial Board with the addition of Professor Zhiqiang Gao and Professor Shusheng Gong from China. To keep with the growing body of scientific knowledge and improve on the editorial scrutiny, new co-editors for each of the four sections have joined the board. Andrea Thirwall and Hasnaa Ismail-Koch have taken the role of editing the Paediatric Section from Michael Kuo, to whom we are extremely grateful for producing outstanding articles for volume 8. Michael had to step down because of his extensive commitments. Ricard Simo will be joined by Ian Nixon as a Head & Neck Section co-editor, Charlie Huins joins Richard Irving in Otology and Alwyn D'Souza joins Shahzada Ahmed in Rhinology and Facial Plastics. The Rhinology Section has always encompassed Facial Plastics articles and we have incorporated this in the title.

The quality of articles remains of a very high standard and we hope to keep this resource free for all ENT surgeons in UK and abroad. To this end, the journal has also been distributed in symbolic numbers to some overseas countries like Germany, India, Saudi Arabia and China.

On the other front, over the last 12 months the ENT Masterclass® platform has continued to expand its academic profile. Within UK, the National Audiology & Balance Masterclass was well received, as was the Masterclass for General Practitioners.

To cater for the high international demands, ENT Masterclass® China was held in Beijing and Hong Kong with over 600 delegates. For Europe, Berlin hosted a very well attended 2-day Masterclass with delegates from all corners of the continent. In April 2017, the ENT Masterclass® Academic Travelling Club is planning a substantive event in Cape Town with Professor Johan Fagan and his team.

We continue to support online resources and are very pleased that the 4th Edition of the Cybertextbook with over 400 surgical videos still remains a very popular part of the website: www.entmasterclass.com.

The free ENT Masterclass educational resources have expanded beyond our expectation when it started as a revision course in Doncaster in 2005. It is all down to the generous and selfless contributions from UK and international faculty, and the continuing support and interest of the ENT community. Once again we hope that we continue to provide a free educational value that is accessible to all.

Mr Hesham Saleh, FRCS (ORL, H&N)
Consultant Rhinologist/Facial Plastic Surgeon
Charing Cross and Royal Brompton Hospitals, London.
Chairman, Editorial Board, Journal of ENT Masterclass®.

December 2016.

Intracranial complications of suppurative ear disease

James E.F. Howard and **Matthew S. Rollin**
ENT Department, St Mary's Hospital, Imperial College NHS Trust, London.

Correspondence:
James E.F. Howard
ENT Department, St Mary's Hospital, Imperial College NHS Trust, London.
Email: howard@doctors.org.uk

Abstract
Intracranial complications of suppurating ear disease are typically caused by spread of infection to surrounding areas. This can be direct, local or to distant areas via haematogenous spread. The pattern of disease has changed in developed countries in recent years with these now being more frequently seen as a complication of AOM in young children with only rare cases presenting in adults and complicating chronic ear disease. Before the antibiotic era, acute otitis media (AOM) commonly resulted in intracranial complications, with mortality of 75% or more being reported. In advanced health systems intracranial complications can be seen in approximately 3%[1] with published mortality rates now approximately 5%[2]. Although this represents a huge advance, it should be noted that this is still 1 patient in 20.

J ENT Masterclass 2016; 9 (1): 4 - 8.

Key words
Intra cranial, suppurative ear disease, complications

Pathogenesis
Infection spreading beyond the mucoperiosteum and bony walls of the middle ear and mastoid exits via a number of routes. These are vascular, through thrombophlebitis of small valveless venules, following bone erosion or via pre-existing pathways, such as the oval and round windows, IAM, endolymphatic duct and sac, dehiscent tegmen, around the jugular bulb or through fracture lines.

Diagnosis and investigation
In their early stages, intracranial complications can be surprisingly silent. Typical symptoms are fever & headache. Clinical mastoiditis is not a prerequisite for development of an intracranial complication: many patients have only clinical signs of AOM, which may include a discharging ear. Despite the irritation of adjacent structures, disequilibrium and hearing loss are rare as presenting symptoms of intracranial complications.

Imaging is recommended as a first-line diagnostic modality in all cases. CT should be contrast-enhanced. CT has the advantage over MR that images can be acquired quickly, raising the possibility of a feed-and-sleep scan in a young child, and light sedation in an older child. Contrast-enhanced MRI has a higher sensitivity for fluid collections, parenchymal oedema, and vascular complications. For presence and propagation of thrombi, MR is superior to CT, but MR venography is best.

Pus or tissue samples for microbiology are very important for empirical antibiotic therapy. If surgical intervention is planned, then pus can be retrieved from the middle ear via a myringotomy in order to identify the causative organism. Intracranial infection can often be diagnosed from culturing cerebrospinal fluid (CSF) obtained via lumbar puncture, but cross-sectional imaging is mandatory first, in order to examine for the possibility of a space-occupying lesion.

Meningitis
A degree of meningitis may co-exist with other complications of AOM however isolated meningitis is relatively uncommon. Congenital anomalies or acquired injuries of the temporal bone, which provide a more ready passage to the meninges, will increase the likelihood of meningitis as a complication of AOM[3,4]. This includes dural exposure in previous mastoid surgery. Middle ear injury complicated by infection may lead to acute suppurative labyrinthitis, which can then easily lead on into meningitis.

Meningitis as a complication of AOM can be a challenging diagnosis, as the symptoms of headache, vomiting and severe fever are non-specific. Signs such as photophobia and seizures are less common in older children and adults. Infants may present with convulsions. Nuchal rigidity and conscious level are not considered reliable signs early in the disease course. Kernig's and Brudzinski's signs can suggest meningeal irritation, but are not considered reliable in young children. Lumbar puncture (LP) is usually required to provide a definitive diagnosis via CSF chemistry and culture, but raised intracranial pressure (ICP) may make this procedure perilous, and imaging is usually considered mandatory before LP is undertaken. Analysis of obtained CSF will show cloudy fluid, >1000 cells per ml, elevated protein, reduced glucose, and organisms. Myringotomy may provide an alternative and less hazardous route to identification of the causative organism. If the suppurating disease is acute and limited to the middle ear, the mainstay of treatment is intravenous antibiotic therapy and further surgery is unlikely to be necessary. If the suppurating disease extends to the mastoid or is chronic in nature, mastoid exploration may be required when the patient's condition allows. If such intervention is contemplated, CT and MR are recommended in order to investigate for further intracranial complications. It has been reported that meningitis is more frequently lethal when secondary to chronic otitis media, as opposed to the acute form. Patients with meningitis usually require high-dependency care, a prolonged course of intravenous antibiotic therapy, and involvement of several clinical teams.

Extradural abscess
This is an abscess between the dura and the endosteum of the cranial vault more commonly located in the posterior rather than the middle cranial fossa. An extradural abscess closely associated with the sigmoid sinus is termed a peri-sinus abscess. Symptoms are a spiking fever and headache despite appropriate antibiotic therapy, deep pain in the mastoid region and otorrhoea[5]. Extradural abscess is frequently associated with other complications of acute infection, such as a brain abscess or dural sinus thrombosis (Fig 1). Localised meningitis is expected, and the involved dura can thicken in response to the intense inflammatory stimulus (this is termed pachymeningitis). Treatment is surgical drainage via mastoidectomy combined with antimicrobial therapy. Wide mastoid exposure is recommended, maximising access before addressing the area adjacent to the abscess[6].

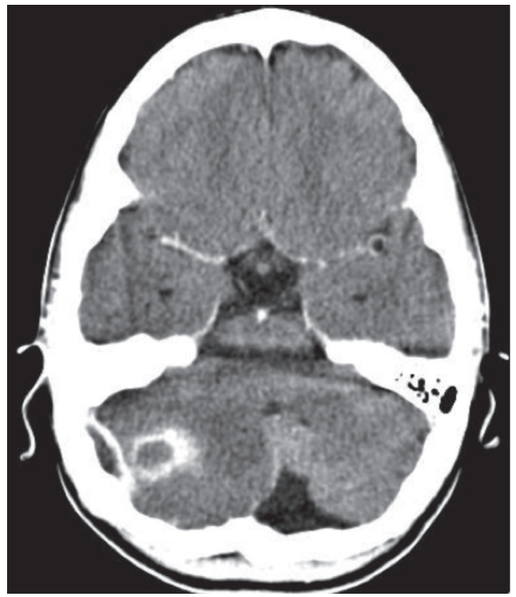


Figure 1: *Contrast enhanced CT on soft tissue setting demonstrating an extradural abscess, Cerebellar abscess and surrounding cerebellar oedema.*

Empirical antimicrobial regimens are targeted against traditional AOM organisms. A typical regimen is: Metronidazole with Ceftriaxone or Cefotaxime. Ceftazidime may be substituted where there is a suspicion of involvement with pseudomonas (for example in the context of chronic ear disease). Vancomycin can be used for coverage of MRSA although achieves only low concentrations in the central nervous system[7,8], therefore Rifampicin may be added for its superior CNS penetration[7,9].

Antimicrobial therapy is usually continued for 6 weeks (8 if slow progress), with a repeat MRI at 4-6 weeks, or earlier if there is clinical deterioration.

Subdural empyema
This is a serious complication with infection between the dura and the arachnoid. The majority of such infections develop secondary to trauma or neurosurgery, but in the context of otitis, infection is typically transmitted by extension of disease through an emissary vein or other breach in the dura, and it may also develop secondary to meningitis and localised osteitis[2]. Pus in the subdural space spreads rapidlay resulting in progressive thrombophlebitis, encephalitis, raised ICP and cortical infarction causing focal neurology and seizures. The majority of cases occur in the second decade of life, and more commonly in males[6].

Headache is universal, and the typical patient will also be unwell, febrile and vomiting. Later signs include worsening fever, nuchal rigidity, focal neurology and fluctuating consciousness. Paralysis of contralateral conjugate gaze may result in deviation of the eyes towards the side of the lesion. The presence of focal neurology and declining consciousness in the context of otitis media demands decisive action. Empyema localised to the posterior fossa may show fewer localising signs, but will produce signs of meningeal irritation and raised ICP[6].

Early in the disease course, radiological signs may be subtle, particularly with unenhanced CT and contrast-enhanced scans are recommended. MRI is more sensitive than CT for the presence of subdural pus and oedema of adjacent brain parenchyma.

Lumbar puncture is contraindicated in the presence of clear subdural empyema owing to raised ICP. An apparently-reassuring scan early in the disease course may lead to consideration of LP as a diagnostic test, and in the case of bacterial meningitis without empyema this would represent correct management. Therefore, if LP is considered as a diagnostic modality, it should be performed as soon as possible after a scan demonstrates no evidence of raised ICP.

Treatment of subdural empyema is emergent neurosurgical drainage, washout and empirical antibiotic therapy (see "Extradural abscess" section for appropriate agents). Percentage chance of survival correlates with conscious level at the time of surgical intervention[6]. If acute mastoiditis is present, treatment is wide exploration of the mastoid and clearance of infected material. Patients will often require high-dependency care and joint management with neurosurgery.

Dural venous thromboses

Sigmoid sinus thrombosis can arise via spread through emissary veins or as a result of venous endothelium irritation secondary to osteitis in acute infection, which is more likely if there is bone erosion from chronic infection or cholesteatoma. For this reason it is more common in older children and young adults than in young children. Inflamed and partially-necrotic endothelium attracts platelets, fibrin and red cells, and a mural thrombus forms. It is estimated to occur in 3-12% of cases of acute mastoiditis with complete clinical recovery in 76-84% of cases[1,10]. Forty-three percent of cases of sigmoid thrombosis occur without the presence of clinical mastoiditis[2], possibly secondary to initial thrombus of the jugular bulb, however 100% of septic lateral sinus thrombi are associated with infection in the mastoid. Occlusion of the dominant sinus can result in raised ICP secondary to decreased CSF reabsorption via the sagittal sinus arachnoid villi (see section on otitic hydrocephalus).

The most common causative organisms are beta haemolytic streptococcus group A, streptococcus pneumonia, staphylococcus aureus, pseudomonas aeruginosa and anaerobes[5,11]. In a review of paediatric cases Au *et al.* (2013) reported no growth in more than 50% of cases with positive cultures being usually a single organism[11].

Presentation is headache and vomiting, a spiking fever, neck pain and torticollis, seizures, and there may be progressive anaemia in infection with haemolytic streptococcus[12]. Lemierre's syndrome occurs when septic emboli break from an infected thrombus, leading to distant septic foci most commonly in the lung.

Thrombophlebitis of the mastoid emissary veins will cause oedema and tenderness of the mastoid tip, which is known as Griesinger's sign. Raised ICP can cause bilateral papilloedema, and there can be loss of visual acuity[12].

Imaging (enhanced CT or MR) may reveal a "delta sign", whereby the empty triangle of the thrombosed vessel is surrounded by a rim of enhancing sinus-wall tissue. MRI is the diagnostic modality of choice, and MR angiography can be used to assess venous flow. If a dominant sinus is affected the secondary hydrocephalus may be visible on imaging. Lumbar puncture is recommended in all cases after imaging has excluded cerebral abscess or space-occupying lesion. CSF pressure is often raised, and has a normal composition in two-thirds of cases.

Primary treatment is with antibiotics and surgery. Patients should be managed jointly with neurology and haematology, and subject to serial imaging. Steroid drugs and carbonic anhydrase inhibitors such as Acetazolamide can be used to reduce CSF pressure.

Anticoagulation

The use of anticoagulation is controversial and debated it is however regarded as safe and its use is increasing[1]. Reported risks include the release of septic emboli and post-operative haemorrhage[13]. In their review of 190 cases, 113 (59%) of whom were anticoagulated, Wong *et al.* (2015) report bleeding complications in only 8 patients[1]. None resulted in haemodyamic instability.

Advice is best sought from haematology in the case of a stable thrombus, as there may be a local protocol. Anticoagulation should be considered if there are neurological changes, persistent fever, if there are embolic events or evidence of thrombus extension[14,15].

There is no evidence from the literature that anticoagulation improves the rate of sinus recanalization[1,11,16]). Wong et al. (2015) reported rates of partial or complete recanalisation of 83% and 82% for the anticoagulated and non-anticoagulated cohorts respectively (total n=63)[1].

Anticoagulation may be associated with improved neurological outcome. De Weber et al. (2001) retrospectively analysed 160 children with cerebral sinus thrombosis of all origins and found a neurological morbidity rate of 21.5% in the non-anticoagulated cohort, and 0% in the anticoagulated cohort[17]. A meta-analysis of 2 randomised controlled trials investigating anticoagulation in acute cerebral venous thrombosis suggested that anticoagulation may be associated with decreased mortality or dependency[18]. Consistent with this the general consensus for acute cerebral venous thrombosis management is for anticoagulation[19].

Surgery

A small minority of cases in the literature are treated without surgery although this is not standard management. Au et al. (2013) suggest that this be considered only for patients without intracranial signs and who respond rapidly to antibiotic therapy[11].

Mastoid surgical intervention is generally advised and will vary according to the underlying pathology. In AOM simple mastoid drainage is indicated but definitive surgery will be required for cholesteatoma. Surgical management of a brain abscess or subdural empyema will take precedence over mastoid surgery, however if it is considered necessary to act emergently on the mastoid and the patient's condition permits, this could be performed under the same anaesthetic.

Following mastoid exploration the sinus is addressed, this may be simply exposed or its contents evaluated. Wong et al. (2015) found the most common procedure performed was mastoidectomy and decompression of the bony covering of the sinus[1]. The sinus contents can be evaluated by a needle passed into the sinus to assess for the presence of pus, before incision of the sinus wall is contemplated[25,26]. Any pus should be drained by formally opening the sinus but free blood or "dry" thrombus typically would not require sinus opening. Rates of recanalization are probably not influenced by surgical technique[20-22]. Studies have suggested a length-of-stay benefit associated with surgical drainage as opposed to a conservative approach[23,24].

There is controversy regarding IJV ligation, which is now rarely indicated and reserved for cases with extension of thrombus[6,25], refractory septicaemia or septic pulmonary emboli[1,11].

Brain abscess

Intraparenchymal abscesses form a higher proportion of the complication burden in developing countries, and carry a potentially high mortality, whilst in developed countries incidence is decreasing with time[27,28], and mortality is low[2]. A report of 122 consecutive cases of brain abscess in a Taiwanese hospital stated that "otitis" was the third-most common underlying cause of intraparenchymal brain abscess[27]. Various studies and reports note that such lesions are more common in males, in those of low socioeconomic status, and more common ipsilateral to the otitic lesion[29-32].

These lesions typically present with nonspecific symptoms and can be surprisingly silent for a long time resulting in a delay in diagnosis[33]. The most common symptom is severe headache (insidious or sudden in onset), which is usually ipsilateral to the abscess[34]. Neck stiffness occurs in only 15% of patients, and vomiting generally only as a result of raised ICP. Fever occurs in only 45 to 53% of cases and is therefore not a reliable sign. Focal neurology is documented in 50% of cases and is often delayed whilst seizures occur in 25%[34,35]. Deteriorating mental state indicates worsening cerebral oedema and is a poor prognostic sign.

A brain abscess is a space-occupying lesion and in the context of focal headache, focal neurology (eg unilateral cranial nerve deficits, hemiparesis) or papilloedema, LP is contraindicated. Imaging is recommended and care must be taken in the interpretation of images, since many patients with an abscess will have a second intracranial complication. An abscess appears as an area of low density or low signal, surrounded by a ring of enhancing tissue, and is seen more clearly on MRI than CT, although CT may be easier and quicker to obtain.

Otogenic abscesses are typically either cerebellar or temporal lobe. A cerebellar abscess may additionally present with horizontal nystagmus, tremor or ataxia, and a temporal lobe abscess with seizures, speech and visual disturbance. Symptoms and signs of raised ICP are typically more constant and definite in the case of a cerebellar abscess, owing to the restricted space in the posterior fossa and proximity to the brainstem. It can be the result of extension from posterior fossa dura, and in theory is then in continuity with an infected mastoid and middle ear cleft. It is possible to perform needle drainage of a cerebellar abscess through the posterior fossa dura via the opened mastoid cavity. A distant brain abscess may have arisen secondary to petrositis, but is more likely to be a result of retrograde thrombophlebitis. It is likely to develop over a longer timescale than the local posterior fossa abscess, and should be managed by a neurosurgeon. If indicated, mastoidectomy should be performed contemporaneously, through a separate surgical field. UK guidelines recommend 4-6 weeks of antimicrobial therapy if an abscess has been drained or 6-8 if not[36]. Again empirical treatment with metronidazole with ceftriaxone or cefotaxime is recommended before simplifying treatment based on culture results.

Otitic hydrocephalus

This is a condition in which symptoms and signs of acute hydrocephalus followed some form of otitis[37]. There is a spectrum of opinion on the nature of this entity; ranging from a distinct form of benign intracranial hypertension related to acute otitis media but unrelated to a space-occupying lesion, flow obstruction or to sigmoid thrombophlebitis, to the increasingly accepted pathophysiological consequences of sigmoid sinus thrombosis related to any cause[3,38]. In this former definition, the exact cause of hydrocephalus is unknown, other than being related in some way to acute otitis media.

The predominant symptom is a diffuse severe headache, and imaging of cerebral ventricles will suggest the diagnosis. CSF collected at LP is normal. In the simplest disease course, collateral venous outflow opens over approximately 3 to 7 days, and the headache improves as ICP begins to fall. Signs of worsening disease include visual disturbance, reduction in mental ability and reduction in conscious level. Such developments constitute an emergency, and high doses of corticosteroid and diuretics should be administered and consideration for CSF diversion.

References

1. Wong B, Hickman S, Richards M, Jassar P, Wilson T. Management of paediatric otogenic cerebral venous sinus thrombosis: a systematic review. Clin Otolaryngol. 2015;40:704-14.
2. Scott-Brown's Otorhinolaryngology, Head & Neck Surgery. 7th ed. London: Hodder Arnold; 2008.
3. Gower D, McGuirt W. Intracranial complications of acute and chronic infectious ear disease: a problem still with us. Laryngoscope. 1983;93:1028-33.
4. Ryan M, Antonelli P. Pneumococcal antibiotics resistance and rates of meningitis in children. Laryngoscope. 2000;110:961-4.
5. Otorhinolaryngology Head & NEck Surgery. Berlin: Springer; 2010.
6. Ballenger's Otorhinolaryngology Head and Neck Surgery. 16th ed. Hamilton: BC Decker; 2003.
7. Liu C, Bayer A, Cosgrove S, Daum R, Fridkin S, Gorwitz R, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011;52:e18.
8. Pfausler B, Spiss H, Beer R, Kampl A, Engelhardt K, Schober M, et al. Treatment of staphylococcal ventriculitis associated with external cerebrospinal fluid drains: a prospective randomized trial of intravenous compared with intraventricular vancomycin therapy. Journal of neurosurgery. 2003;98(5):1040-4.
9. Tunkel A, Hartman B, Kaplan S, Kaufman B, Roos K, Scheld W, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39:1267.
10. Logan Turner's Diseases of the Nose, Throat and Ear - Head and Neck Surgery. 11th ed. Boca Raton: CRC Press; 2016.
11. Au J, Adam S, Michaelides E. Contemporary management of pediatric lateral sinus thombosis: A twenty year review. American Journal of Otolaryngology Head and Neck Medicine and Surgery. 2013;34:145-50.
12. Southwick FS, Richardson EP, Jr., Swartz MN. Septic thrombosis of the dural venous sinuses. Medicine. 1986;65(2):82-106.
13. Shah UK, Jubelirer TF, Fish JD, Elden LM. A caution regarding the use of low-molecular weight heparin in pediatric otogenic lateral sinus thrombosis. International journal of pediatric otorhinolaryngology. 2007;71(2):347-51.
14. Bradley DT, Hashisaki GT, Mason JC. Otogenic sigmoid sinus thrombosis: what is the role of anticoagulation? Laryngoscope. 2002;112(10):1726-9.
15. Novoa E, Podvinec M, Angst R, Gürtler N. Paediatric otogenic lateral sinus thrombosis: Therapeutic management, outcome and thrombophylic evaluation. Int J Pediatric Otorhinolaryngol. 2013;77:996-1001.
16. Chalmers E, Ganesen V, Liesner R, Maroo S, Nokes T, Saunders D, et al. Guideline on the investigation, management and prevention of venous thrombosis in children. British journal of haematology. 2011;154(2):196-207.
17. DeWeber G, Andrew M, Adams C, Bjornson B, Booth F, Buckley DJ, et al. Cerebral sinovenous thrombosis in children. N Engl J Med. 2001;345(6):417-23.
18. Stam J, De Bruijn SF, DeVeber G. Anticoagulation for cerebral sinus thrombosis. The Cochrane database of systematic reviews. 2002(4):Cd002005.
19. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke; a journal of cerebral circulation. 2004;35(3):664-70.
20. Zanoletti E, Cazzador D, Faccioli C, Sari M, Bovo R. Intracranial venous sinus thrombosis as a complication of otitis media in children: Critical review of diagnosis and management. Int J Pediatric Otorhinolaryngol. 2015;79:2398-403.
21. Agarwal A, Lowry P, Isaacson G. Natural history of sigmoid sinus thrombosis. The Annals of otology, rhinology, and laryngology. 2003;112(2):191-4.
22. Ropposch T, Nemetz U, Braun EM, Lackner A, Walch C. Low molecular weight heparin therapy in pediatric otogenic sigmoid sinus thrombosis: a safe treatment option? Int J Pediatric Otorhinolaryngol. 2012;76(7):1023-6.
23. Syms MJ, Tsai PD, Holtel MR. Management of lateral sinus thrombosis. Laryngoscope. 1999;109(10):1616-20.
24. Kaplan DM, Kraus M, Puterman M, Niv A, Leiberman A, Fliss DM. Otogenic lateral sinus thrombosis in children. International journal of pediatric otorhinolaryngology. 1999;49(3):177-83.
25. Middle Ear Surgery. Berlin: Springer; 2006.
26. Ear Surgery. Berlin: Springer; 2008.
27. Yen PT, Chan ST, Huang TS. Brain abscess: with special reference to otolaryngologic sources of infection. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 1995;113(1):15-22.
28. Kangsanarak J, Fooanant S, Ruckphaopunt K, Navacharoen N, Teotrakul S. Extracranial and intracranial complications of suppurative otitis media. Report of 102 cases. The Journal of laryngology and otology. 1993;107(11):999-1004.
29. Singh B, Maharaj TJ. Radical mastoidectomy: its place in otitic intracranial complications. The Journal of laryngology and otology. 1993;107(12):1113-8.
30. Osma U, Cureoglu S, Hosoglu S. The complications of chronic otitis media: report of 93 cases. The Journal of laryngology and otology. 2000;114(2):97-100.
31. Kurien M, Job A, Mathew J, Chandy M. Otogenic intracranial abscess: concurrent craniotomy and mastoidectomy--changing trends in a developing country. Archives of otolaryngology--head & neck surgery. 1998;124(12):1353-6.
32. Murthy PS, Sukumar R, Hazarika P, Rao AD, Mukulchand, Raja A. Otogenic brain abscess in childhood. International journal of pediatric otorhinolaryngology. 1991;22(1):9-17.
33. Chalstrey S, Pfleiderer AG, Moffat DA. Persisting incidence and mortality of sinogenic cerebral abscess: a continuing reflection of late clinical diagnosis. Journal of the Royal Society of Medicine. 1991;84(4):193-5.
34. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. Neurology. 2014;82(9):806-13.
35. Seydoux C, Francioli P. Bacterial brain abscesses: factors influencing mortality and sequelae. Clin Infect Dis. 1992;15(3):394-401.
36. The rational use of antibiotics in the treatment of brain abscess. British journal of neurosurgery. 2000;14(6):525-30.
37. Symonds C. Otitic hydrocephalus. Brain. 1931;54:55.
38. Kuczkowski J, Dubaniewicz-Wybieralska M, Przewozny T, Narozny W, Mikaszewski B. Otitic hydrocephalus associated with lateral sinus thrombosis and acute mastoiditis in children. International journal of pediatric otorhinolaryngology. 2006;70(10):1817-23.

The large vestibular aqueduct syndrome

Cheka R. Spencer
ENT dept., Birmingham Children's Hospital, Steelhouse Lane, Birmingham

Correspondence:
Cheka. R. Spencer, MSC., MRCS, DOHNS, AFHEA
ENT dept., Birmingham Children's Hospital, Steelhouse Lane, Birmingham
Email: drchekaspencer@doctors.org.uk

Abstract

The large vestibular aqueduct syndrome is the most common radiological and morphogenetic abnormality of the inner ear among children accounting for 13-15% of sensorineural hearing loss. The hearing loss appears in early childhood and may be stable, fluctuating or progressive. Vestibular symptoms are infrequent but it may delay a child's onset of ambulation. The size criterion for diagnosis of a large vestibular aqueduct has been the subject of much debate. It is associated with a host of syndromes including Pendred's syndrome. It has at times been misdiagnosed for otosclerosis due to its propensity to create an air bone gap. Theories to account for the air bone gap as well as hearing loss in general have been widely hypothesised in the literature.

This review provides an up to date overview of the syndrome including its controversial aspects.

J ENT Masterclass 2016; 9 (1): 9 - 12.

Key words

Large Vestibular Aqueduct Syndrome, Endolymphatic Sac, Hearing Loss

Introduction

The large vestibular aqueduct syndrome (LVAS) or enlarged vestibular aqueduct syndrome (EVAS) is the most common structural cause of sensorineural hearing loss (SNHL) in childhood, it often occurs with other inner ear anomalies or systemic syndromes.[1] Both auditory and vestibular dysfunction have been attributed to large vestibular aqueducts (LVA)[2]. Enlargement of the vestibular aqueducts (VA) was first mentioned by Carlo Mondini in 1791 during temporal bone dissection[3] when he associated it with a hypoplastic cochlea ie Mondini's dysplasia. It was in 1978 that the radiological observation of this malformation was identified by Valvassori and Clemis in 50 cases in a retrospective review of 3700 consecutive patients.[4] They found that most of these cases had congenital hearing loss with many also suffering from vestibular dysfunction. LVA diameters in their cohort ranged from 1.5 mm to 8 mm.[5] A VA has subsequently been considered enlarged if it has an anteroposterior diameter greater than 1.5 mm (measured halfway between the common crus and the operculum).[6-9] The hearing loss appears in early childhood and may be stable, fluctuating or progressive. It may also occur suddenly after a minor head trauma, barotrauma and upper respiratory tract infections. The demonstrated hearing loss may be sensorineural or mixed.[10] Factors that influence progression of symptom severity are still controversial.[2,11]

Anatomy

The inner ear is composed of a bony and membranous labyrinth. The membranous labyrinth in mammals is composed of several specialised structures. The cochlea responds to acoustic energy. The vestibule is made up of the saccule and utricle which are otolithic organs responsive to linear acceleration. The semi-circular canals conversely respond to angular acceleration. The endolymphatic duct is a component of this membranous labyrinth and is in itself contained within a bony canal called the VA. The VA is a bony canal in the otic capsule of the temporal bone. It originates in the anteromedial aspect of the vestibule and courses posteriorly and superiorly parallel to the common crus. The endolymphatic duct having begun in the vestibule merges with the endolymphatic sac located on the posterior aspect of the temporal bone adjacent to the posterior fossa dura mater.

Physiology

Endolymph is a critical component of inner ear function. It is a potassium rich fluid in which the inner ear sensory cells are located. The endolymphatic sac is widely considered to have an essential role in endolymphatic homeostasis. It is responsible for the regulation of the volume and pressure of endolymph, the immune response of the inner ear as well as the elimination of endolymphatic waste products by phagocytosis.[12] Alteration of this function leads to inner ear dysfunction namely hearing

loss, tinnitus and vertigo as seen in Meniere's disease and LVAS.[1]

Pathogenesis

In normal development, by the age of four years old, the growth of the posterior fossa pulls the endolymphatic duct from a short broad column into an elongated inverted 'J' shape.[13] The outcome is a vestibular aqueduct diameter of 0.4 – 1.00 mm (mean of 0.62) in adults. In LVAS there is aberrant development in the seventh week of gestation which results in an enlarged endolymphatic sac, duct and vestibular aqueduct. Genetic mutations and teratogenic insults have been implicated.[14] LVAS is speculated to be a result of developmental arrest of the endolymphatic duct due to decreased stretch of the temporal bone during growth of the posterior fossa. The endolymphatic sac in LVAS is described histologically as being thin walled and devoid of the rugal folds and perisaccular vascular tissue which play a vital role in its function.[5,6] The enlarged hypofunctioning sac leads to increased hydrostatic pressure which in turn leads to enlargement of the vestibular aqueduct. This is supported by histopathological findings of bony erosion leading to some authors referring to the syndrome as EVAS.[2,11]

Epidemiology

LVAS is the most common radiological and morphogenetic abnormality of the inner ear among children accounting for 13-15% of sensorineural hearing loss. In patients with unknown causes of sensorineural hearing loss, the prevalence of LVAS ranges between 0.64% to 13%.[8] The malformation is overwhelmingly bilateral and has a female to male preponderance.[7]

Diagnosis

Computer-assisted tomography (CT) scanning of the temporal bones is the best tool to assess the bony VA (Figure 1). Magnetic resonance imaging (MRI) is most suited for visualising the endolymphatic duct and sac (Figure 2). The size criterion for diagnosis of LVAS, as suggested by Valvassori and Clemis[4], is a VA or endolymphatic duct measuring >1.5mm at the midpoint between the common crus and the external aperture. Whilst this has been the standard, it is the subject of much debate: some have defined LVAS in cases where the midpoint is greater than 2mm,[14] others when greater than 4mm.[15] More recently the criterion has been revised down to 0.9 mm at the midpoint and 1.9 mm at the operculum. This has resulted in classifying previously unexplained sensorineural hearing loss as LVAS.[16]

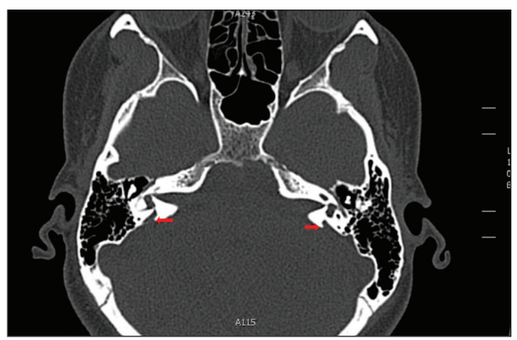


Figure 1: *CT scan of the temporal bones depicting bilateral vestibular aqueducts (see red arrows) in a 43 years old with congenital deafness. The midpoint diameters are 3.4 on the right and 2.1 mm on the left*

Association with other syndromes

The SLC26A4 (PDS) gene encodes Pendrin, a protein involved in the transport of chloride, iodine, and bicarbonate anions across cell membrane. Mutations in the PDS gene are associated with both syndromic LVAS ie Pendred's syndrome,[17] and nonsyndromic LVAS. Pendred syndrome has an autosomal recessive inheritance and is characterised by thyroid goitres and hearing loss. LVAS has also been associated with distal renal tubular acidosis, X-linked congenital mixed deafness, Waardenburg syndrome, otofaciocervical syndrome, branchio-oto-renal syndrome(BOR), and Noonan's syndrome. Differences in hearing loss fluctuation and other clinical features have been reported across the different associated syndromes: patients with BOR and LVA are described as suffering from neither fluctuating hearing loss nor vertigo in contrast to those with Pendred syndrome and LVAS.[11]

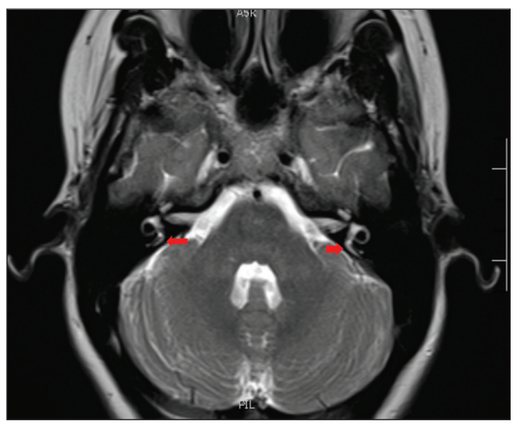


Figure 2: *T2 weighted MRI scan of the internal acoustic meati of the same 43 year old with congenital deafness. Her large endolymphatic ducts and sac are depicted (see red arrows)*

Clinical Features

The symptoms are reported to manifest before the age of 10 years in 90% of patients. The most prevalent symptom at onset is hearing loss. Dizziness, vertigo and imbalance are only present in a minority of patients.[11]

Head trauma is most commonly reported as the precipitating event for hearing loss in up to 26% of patients.[2,5,7,8,11] This is thought to be due to increased cerebrospinal fluid (CSF) pressure. This is corroborated by barotrauma and the Valsalva manoeuvre also precipitating hearing loss in up to 17% of patients.[11] Other factors include upper respiratory tract infections, high fevers, acoustic trauma and physical exercise. Vestibular symptoms are usually disequilibrium or episodic attacks of vertigo. Younger children may present with poor coordination or an inability to walk.

Relation to hearing loss

Hearing loss severity has been found to have a linear correlation of 6 dB HL per unit of vestibular aqueduct diameter (95% CI 2-10; p = 0.003).[1] All three types of hearing loss have been reported in LVAS (sensorineural, mixed and conductive). The majority are either mixed or sensorineural. There is often an air bone gap (ABG) in the lower frequencies (see Figure 3). The ABG at times has been misdiagnosed as otosclerosis.[18,19] Many theoretical models have been proposed to account for the ABG.[9] Some studies have shown a gradual hearing loss of around 4 dB per year whilst others have reported the majority as stable. The hearing loss quite often fluctuates and is most often severe to profound with a recent large nationwide study finding a mean pure tone average (PTA) of 83.7 dB HL.[11]

Mechanisms of hearing loss

These have been widely theorised in the literature.[1-6,9,10]

1. The hyperosmolar reflux theory postulates that the large endolymphatic sac contains hyperosmolar fluid which refluxes through the LVA. It enters the inner ear thereby causing damage.
2. The electrolyte imbalance theory proposes that the endolymphatic sac is dysfunctional in its homeostatic role. This results in electrolyte derangement which damages the ion pump system of the stria vascularis.
3. The back pressure wave theory was initially suggested by Valvassori. It suggests that the conductive component is due to a back pressure of perilymphatic and endolymphatic fluid which results in decreased stapes mobility and an ABG particularly in the low frequencies (Figure 3). This is supported by the increased incidence of perilymphatic gushers. This is also said to explain head trauma and barotrauma as precipitating factors.
4. The third window lesion theory hypothesises that the change in the dimensions of the bony labyrinth affects impedance and compliance of the auditory system. This results in a third window loss of acoustic energy away from the cochlea through the VA- this leads to reduced air conduction thresholds. The enlarged VA is thought to furthermore lower impedance at the scala vestibuli. The resulting pressure difference between scala tympani and scala vestibuli leads to improved cochlear responses to bone conduction (Figure 3). This explains the supranormal bone conduction thresholds seen in some patients.

Management

Patients should be advised to minimise risk of head trauma by avoiding contact sports. Patients should be also be advised not to scuba dive, to avoid sneezing with their nose pinched as well as weightlifting, and straining as these may lead to barotrauma due to increased CSF pressure.[2,20]

Hearing aids are usually beneficial in patients whose hearing loss is established. Cochlear implants are also commonly used in LVAS. Auditory skills of infants with LVAS have been demonstrated to develop rapidly after cochlear implantation similarly to those with normal inner ears.[3,5]

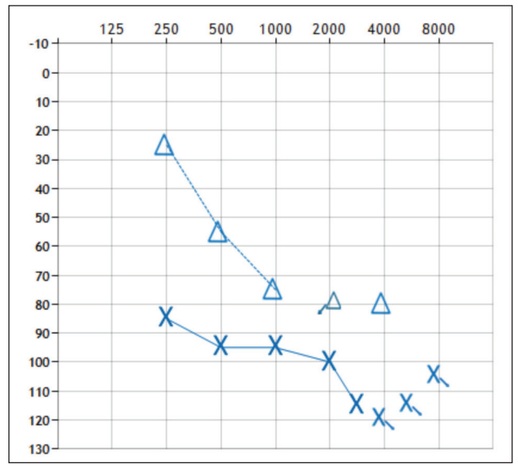


Figure 3: *Audiogram of the same 43 year old patient with congenital hearing loss prior to cochlear implantation. Her BKB score was 3%. The low frequency ABG is well demonstrated*

Corticosteroid therapy has been reported in small case series and case-control studies to produce hearing improvement in patients with LVAS.[2] This is thought to be due to a reduction in pressure.[1] Hyperbaric oxygen therapy has been administered in patients with LVAS and sudden hearing loss after head trauma.[5] It is thought to lower CSF pressure and reflux of hyperosmolar endolymph into the cochlea, as well as increase oxygen tension in the inner ear fluid. It has been shown to improve hearing thresholds in small case series. However, the natural history may have been that of fluctuating hearing loss. Endolymphatic sac surgery has been attempted to improve or stabilise hearing in LVAS. This is controversial and most studies have found it to have a deleterious effect to hearing.[2]

Conclusions

LVAS is the most common morphological cause of sensorineural hearing loss in childhood, usually presenting before the age of 10 years old. It is associated with many syndromes, in particular Pendred's syndrome due to a mutation in the SLC26A4 gene. Hearing loss severity has a linear correlation with VA diameters, it may also be mixed with a large ABG. There are many valid theories that explain hearing loss in LVAS.

References

1. Spencer CR. The relationship between vestibular aqueduct diameter and sensorineural hearing loss is linear: a review and meta-analysis of large case series. The Journal of Laryngology & Otology. 2012;126(11):1086-1090.
2. Gopen Q, Zhou G, Whittemore K, Kenna M. Enlarged vestibular aqueduct: Review of controversial aspects. The Laryngoscope. 2011;121:1971-1978.
3. Chen X, Liu B, Liu S, Mo L, Liu H, Dong R et al. The development of auditory skills in infants with isolated Large Vestibular Aqueduct Syndrome after cochlear implantation. International Journal of Pediatric Otorhinolaryngology. 2011;75(7):943-947.
4. Valvassori GE, Clemis JD. The large vestibular aqueduct syndrome. The Laryngoscope. 1978;88:723-728.
5. Shilton H, Hodgson M, Burgess G. Hyperbaric oxygen therapy for sudden sensorineural hearing loss in large vestibular aqueduct syndrome. The Journal of Laryngology & Otology. 2013;128(S1):S50-S54.
6. Spiegel J, Lalwani A. Large vestibular aqueduct syndrome and endolymphatic hydrops: two presentations of a common primary inner-ear dysfunction? The Journal of Laryngology & Otology. 2008;123(08):919-921.
7. Asma A, Anouk H, Luc V, Brokx J, Cila U, Van De Heyning P. Therapeutic approach in managing patients with large vestibular aqueduct syndrome (LVAS). International Journal of Pediatric Otorhinolaryngology. 2010;74(5):474-481.
8. Campbell A, Adunka O, Zhou B, Qaqish B, Buchman C. Large vestibular aqueduct syndrome. The Laryngoscope. 2011;121(2):352-357.
9. Merchant S, Nakajima H, Halpin C, Nadol J, Lee D, Innis W et al. Clinical Investigation and Mechanism of Air-Bone Gaps in Large Vestibular Aqueduct Syndrome. Annals of Otology, Rhinology & Laryngology. 2007;116(7):532-541.
10. Sone M, Yoshida T, Morimoto K, Teranishi M, Nakashima T, Naganawa S. Endolymphatic hydrops in superior canal dehiscence and large vestibular aqueduct syndromes. The Laryngoscope. 2016;126(6):1446-1450.
11. Noguchi Y, Fukuda S, Fukushima K, Gyo K, Hara A, Nakashima T et al. A nationwide study on enlargement of the vestibular aqueduct in Japan. Auris Nasus Larynx. 2016; http://dx.doi.org/10.106/j.anl.2016.04.012.
12. Couloigner V, Teixeira M, Sterkers O, Rask-Andersen H, Ferrary E. The endolymphatic sac: its roles in the inner ear. Med Sci (Paris). 2004;20(3):304-10.
13. Kodama A, Sando I. Postnatal development of the vestibular aqueduct and endolymphatic sac. Annals of Otology Rhinology and Laryngology. 1989;91(96)3-12
14. Jackler RK, De La Cruz A. The larger vestibular aqueduct syndrome. The Laryngoscope. 1989;99:1238-1243
15. Okumura T, Takahashi H, Honjo I, Takagi A, Mitamura K. Sensorineural hearing loss in patients with large vestibular aqueducts. The Laryngoscope. 1995;105:289-294.
16. El-Badry M, Osman N, Mohamed H, Rafaat F. Evaluation of the radiological criteria to diagnose large vestibular aqueduct syndrome. International Journal of Pediatric Otorhinolaryngology. 2016;81:84-91.
17. Okamoto Y, Mutai H, Nakano A, Arimoto Y, Sugiuchi T, Masuda S et al. Subgroups of enlarged vestibular aqueduct in relation to SLC26A4 mutations and hearing loss. The Laryngoscope. 2014;124(4):E134-E140.
18. Wieczorek S, Anderson M, Harris D, Mikulec A. Enlarged vestibular aqueduct syndrome mimicking otosclerosis in adults. American Journal of Otolaryngology. 2013;34(6):619-625.
19. Távora-Vieira DMiller S. Misdiagnosis of otosclerosis in a patient with enlarged vestibular aqueduct syndrome: a case report. J Med Case Rep. 2012;6(1):178.
20. Noordman B, van Beeck Calkoen E, Witte B, Goverts T, Hensen E, Merkus P. Prognostic Factors for Sudden Drops in Hearing Level After Minor Head Injury in Patients With an Enlarged Vestibular Aqueduct. Otology & Neurotology. 2015;36(1):4-11

Management of sudden sensorineural hearing loss

Stephen J Broomfield
ENT Consultant, University Hospitals Bristol NSH Foundation Trust

Correspondence:
ENT Department, St Michael's Hospital, Southwell Street, Bristol BS2 8EG
Email: steve_broomfield@hotmail.com

This paper was presented by the author at the British Society of Otology Annual Meeting, Bristol, February 2016

Conflicts of Interest/ Financial associations

None declared

J ENT Masterclass 2016; 9 (1): 13 - 18.

Introduction

Sudden loss of inner ear hearing is a devastating occurrence and patients must therefore be managed promptly and thoroughly; most specialists consider sudden sensorineural hearing loss (SSNHL) to be an otological emergency. Careful investigation may identify an underlying cause, though most cases are idiopathic. Our understanding of SSNHL is poor and this is reflected in the literature where there is a paucity of high quality studies and conflicting opinion on the aetiology, definition, and optimal treatment of the condition. Clinicians must therefore have a good understanding of the best available evidence and offer patients treatment on an individualised basis.

Definition, Incidence and Presentation

The most universally applied definition of SSNHL is a loss of at least 30dBHL in three contiguous frequencies on the audiogram, occurring within three days (72 hours)[1]. Hence this includes cases of sudden immediate hearing loss as well as those that progress rapidly. There is no consensus on how to define recovery from SSNHL. Previous papers have suggested systems for grading recovery[2,3]. Unfortunately these are not well utilised in the literature, making meta-analysis of studies in this field impossible[4].

Most cases of SSNHL are unilateral, the incidence of which is thought to be 5 to 20 per 100,000 per year[5]. The true incidence may be higher, as mild cases or those that recover quickly are often unreported. The commonest age group affected is adults in their forties and fifties, with an equal gender distribution. Bilateral cases usually occur sequentially and account for less than 2% of all SSNHL[6].

In addition to hearing loss, one quarter to one half of patients will have vestibular symptoms. Tinnitus and aural fullness are also common. In non-idiopathic cases there may be other symptoms to suggest the underlying diagnosis.

Cases of conductive hearing loss (not discussed further here) may present with a rapid onset and must be ruled out by careful history taking and examination.

Aetiology and Pathophysiology

The pathophysiology of SSNHL is unknown. Various theories have been proposed, including viral, vascular, autoimmune and cellular response mechanisms[7,8]. There may be multiple pathophysiological mechanisms that each culminate in the same end condition.

Between 70 and 90% of cases of unilateral SSNHL are idiopathic. One review found the commonest aetiologies to be idiopathic (71%), infection (12.8%), otologic disease (4.7%), trauma (4.2%), vascular/ haematological (2.8%), neoplastic (2.3%) and 'other' (2.2%)9. A more complete list of previously recognised aetiologies for SSNHL is shown in Table 1 (adapted from Chau et al[9]).

Bilateral SSNHL, though rare, is more commonly due to a serious underlying systemic pathology, many of which are associated with significant morbidity and mortality. Bilateral SSNHL tends to present with more severe hearing loss and has a worse prognosis[6].

Investigation of SSNHL

In the presence of an appropriate history, the diagnosis of SSNHL is confirmed with the pure tone audiogram. In the majority of cases there is no need to perform additional audiological or vestibular tests. Given the wide range of possible aetiologies for SSNHL (Table 1), it is impractical to perform additional investigations for each of them.

Table 1. List of potential causes of SSNHL (adapted from Chau et al 2010).	
Idiopathic	
Infectious	Adenovirus, Epstein-Barr, hepatitis C, herpes simplex, measles, mumps, rubella, varicella, streptococcus, pertussis, meningitis, syphilis, toxoplasma, Lyme disease, Lassa fever, mycoplasma, HIV
Otologic	Meniere's disease, secondary hydrops, otosclerosis, autoimmune inner ear disease (AIED), post-op (otologic surgery), ototoxicity, inner ear abnormality
Traumatic	Head injury, perilymphatic fistula, barotrauma, acoustic trauma, traumatic irrigation
Autoimmune	AIED, Behcet's, Cogan's, systemic lupus, anti-phospholipid, temporal arteritis, granulomatosis/ vasculitis
Vascular	Cardiovascular event, subdural/ pontine haemorrhage, transient ischaemic attack, sickle cell disease, haemodialysis, coagulopathy
Tumour	Acoustic neuroma, meningioma, cerebellar angioma, multiple myeloma, metastasis
Neurologic	Multiple sclerosis, migraine
Other	Post-op (non-otologic surgery), pregnancy, rabies vaccination, CO poisoning, functional/ malingering

Hence the extent of investigation required will be dictated by the history and the availability of tests locally[10,11]. A magnetic resonance imaging (MRI) scan (or computerised tomography (CT) scan if MRI is contraindicated) is recommended in all cases, as 10 to 20% of vestibular schwannomas will experience SSNHL at some stage, often as the presenting feature[12].

An MRI scan will also detect many cases in which there is a vascular compromise, neurological condition (e.g. demyelination) or inner ear abnormality. Although basic blood tests (including full blood count, erythrocyte sedimentation rate, urea and electrolytes) have a low yield, they are often recommended as they are readily available, inexpensive and may point towards the need for more detailed investigation. Raised cholesterol has been demonstrated in 35 to 40% of cases of SSNHL, and elevated serum glucose in 18 to 37% of cases; initiation of treatment may prevent future cardio-vascular morbidity[13].

Abnormal thyroid function (hypothyroidism) may be detected in as many as 15% of cases of SSNHL and has also been suggested as a routine test[14]. There is little evidence to support a routine infectious or auto-immune screen, though many clinicians routinely perform a screen for syphilis as the possibility of treatable latent infection may not be evident from the standard history[15].

Bilateral SSNHL is a special case, as the potential for an underlying life-threatening pathology warrants additional investigations including an urgent MRI scan, autoimmune screen and tests for infection (including HIV test)[6].

A full discussion of the management of recognised conditions causing SSNHL, as well as bilateral SSNHL, is outside the scope of this article and the sections that follow apply to the management of idiopathic cases.

Natural History and Prognostic Factors

Before treatment can be discussed, the natural history of idiopathic SSNHL must be considered. It is recognised that many cases of SSNHL recover without treatment, with 32 to 65% (average of 46.7%) showing recovery within 2 weeks[16]. A meta-analysis of SSNHL studies showed a 14.3dB recovery on the pure tone audiogram following treatment with placebo compared to 15.8dB after active medical therapy[17]. A less severe hearing loss at presentation and low frequency hearing loss are thought to be positive prognostic factors. Age over 60 or under 15 years, co-existing vertigo at presentation, and more severe hearing loss are negative prognostic factors. In addition, there is some evidence that early treatment may improve the prognosis, with spontaneous recovery rare after two months[18,19].

These factors must all be considered when determining how to treat an individual patient, as in some cases the most acceptable form of treatment may be supportive measures rather than medical therapy.

Treatment of Idiopathic SSNHL

Supportive Measures

It is crucial to remember that SSNHL is a devastating experience for the patient, and a high level of support, counselling and reassurance from the treating clinician is required[20]. In the author's experience, long-term support for patients with incomplete recovery is often lacking; adequate access to hearing rehabilitation including provision of hearing aids and treatment for single-sided deafness is important, and in selected cases tinnitus therapy, vestibular rehabilitation or formal psychological support may be required.

Medical Therapies

A variety of medical and alternative therapies have been suggested for SSNHL (Table 2). Steroids have been the mainstay of treatment for SSNHL for some years, and are recommended as first-line treatment by the majority of ENT consultants in the UK[21,22]. Despite this fact, there remains a paucity of evidence for their efficacy and there is no firm consensus on which is the best steroid agent nor on the optimal dose, timing (including the role of salvage therapy) or route of administration.

Oral steroid therapy

Some of the earliest published trials examining SSNHL suggested that oral steroid therapy may have an advantage over placebo treatment[23]. More recently, other studies, systematic review, meta-analysis and a Cochrane review on this subject have shown contradictory evidence and an uncertain benefit from oral steroids[24-28]. Whilst there is significant variation, prednisolone seems to be the most widely used agent, commonly a short (e.g. 5 days) course at 1mg/Kg daily. Potential side effects must be considered and clearly caution is required in patients who are very elderly or who have relative contra-indications for steroid treatment. Although SSNHL is considered an emergency, there is some evidence that oral steroid treatment at 1 week may be as effective as that given within 24 hours[29]. However, there is additional evidence that there may be a worse outcome after 10 days, and little benefit from treatment after 4 to 6 weeks[18,19]. Common sense therefore dictates prompt treatment whenever possible.

Intra-tympanic steroid therapy

Based on theoretical and animal studies that have shown an increased concentration of steroid in the perilymph of the inner ear when compared to oral or intravenous treatment, interest in the use of intra-tympanic (IT) steroids in SSNHL has grown in recent years. In the majority of studies dexamethasone or methylprednisolone is injected through the tympanic membrane into the

Figure 1. Technique for intra-tympanic steroid injection

1) A bleb of EMLA cream is applied to the tympanic membrane (figure 1a). An inferior site is preferred for easy access for injection (and for permeatal repair in case of perforation). Targeting of the round window niche is not required when filling the entire middle ear with fluid.
2) The cream is aspirated after 5 minutes using microsuction with fine tip.
3) A 27G spinal needle (bent so slightly angled) is used to puncture the eardrum (figure 1b)
4) Steroid solution (dexamethasone in highest available dose) at room temperature is infiltrated slowly under direct vision. Normal volume instilled is approximately 0.5mls.
5) Patient is asked to remain with head turned to side for 30 minutes, and avoid talking/ swallowing as much as possible.

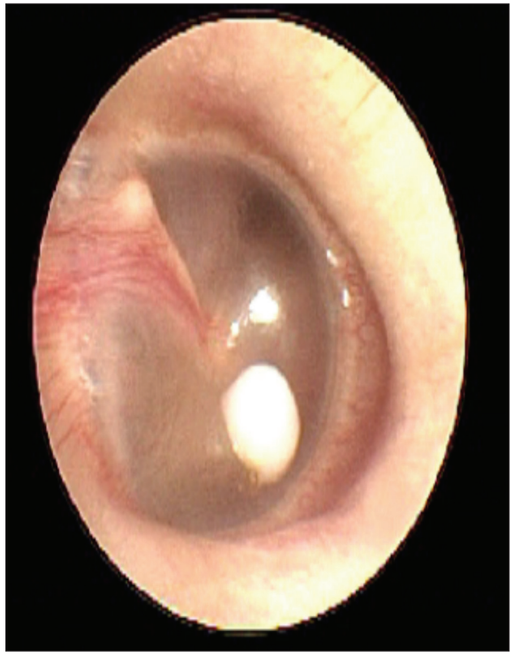


Figure 1a:

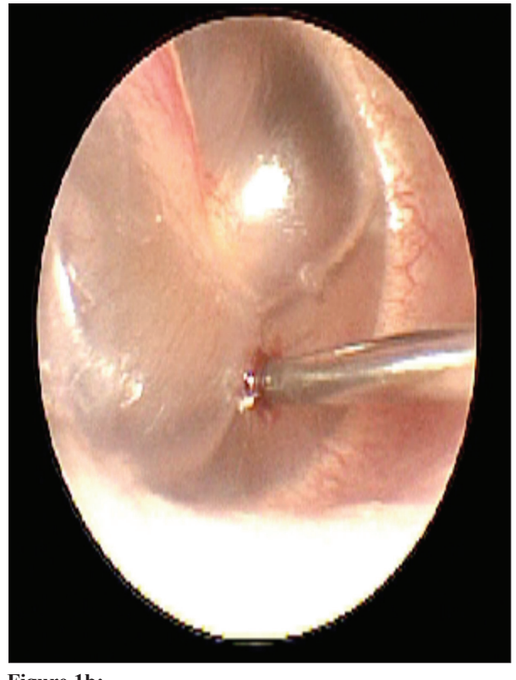


Figure 1b:

middle ear space, though some advocate use of a round window wick or steroid drops instilled through a grommet. The technique favoured by the author is described in Figure 1.

Randomised controlled trials and systematic review of the literature have shown that IT steroids are no more effective than high dose oral steroids when used as primary treatment[30-32]. There is limited evidence that combination therapy with oral and IT steroids together is more effective than oral treatment alone[31,33]. For this reason, most clinicians take a practical approach and use oral steroids alone as the preferred initial therapy unless contra-indicated, and this is reflected in published guidelines for SSNHL management[19,34]. When considering IT steroids as a salvage treatment following failed systemic steroid treatment, the balance of evidence from systematic reviews and meta-analysis seems to be towards showing some additional benefit[32,35,36]. The meta-analysis by Ng et al. pooled the results from 5 RCTs and showed an improvement in hearing outcomes in patients undergoing IT steroid injection (dexamethasone or methylprednisolone) following failed systemic steroid treatment (defined as persistent SNHL worse than 30dB or worse than 10 to 20dB than the contra-lateral ear)[36]. In these studies, treatment consisted of repeated injections (e.g. 4 times over 15 days) commenced within 4 weeks of onset of the SSNHL. No serious adverse events were reported. Whilst promising, some caution is required in interpreting these results given the small number and heterogeneity of the studies and the small absolute improvement in hearing (approximately 10dB average) which may have limited practical significance for a patient with normal hearing in the contra-lateral ear.

Other medical therapies

Aside from steroids, a wide range of medical therapies has been suggested as primary or combination treatment for SSNHL (Table 2). In particular, following on from viral and ischaemic theories for the pathogenesis of SSNHL, anti-viral treatment, vasodilators/ vasoactive substances and hyperbaric oxygen have been suggested as treatments but Cochrane reviews of their efficacy have demonstrated little or no evidence to support their routine use[37-39].

Table 2. List of therapies described in the literature as treatments for SSNHL

Steroids
Anti-virals
Hyperbaric Oxygen
Carbogen/vasoactive substances
Vasodilators
Plasma expanders
Rheopheresis
Anticoagulants
Anti-oxidants
Diuretics
Contrast dye (Hypaque)
Vitamin/ mineral supplements
Acupuncture

Future Therapies

Currently, there is much interest in the use of insulin-like growth factor in the inner ear and this may provide a promising treatment for SSNHL. It is clear that as our understanding of inner ear biology improves, new treatments (e.g. stem cell and gene therapies) will emerge to treat sensory hearing loss including SSNHL.

Conclusion

Sudden sensorineural hearing loss is a rare but potentially devastating condition. Our understanding of the pathophysiology of SSNHL remains poor, with only a minority of cases having an identifiable aetiology. The evidence for medical treatment in SSNHL is weak. Nonetheless, there is some consensus that the potential benefit of oral steroids as primary treatment outweighs the risks in most cases. Intra-tympanic steroid therapy is emerging as a potential salvage treatment and as primary treatment when oral steroids are contra-indicated. Clinicians treating SSNHL must take an individualised approach to managing each patient and be prepared to discuss the options before deciding on a treatment plan, which should include adequate counselling, support and rehabilitation.

References

1. National Institute of Deafness and Communication Disorders. Sudden deafness. 2000. http://www.nidcd.nih.gov/health/hearing/sudden.htm. Accessed Sept 22nd 2016.
2. Furuhashi A, Matsuda K, Asahi K, Nakashima T. Sudden deafness: long term follow-up and recurrence. Clin Otol 2002;27:458-63.
3. Siegel LG. The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngol Clin N Am 1975;8:467-73.
4. Plontke SK, Bauer M, Meisner C. Comparison of pure-tone audiometry analysis in sudden hearing loss studies: lack of agreement for different outcome measures. Otol Neurotol 2007;28:753–63.
5. Byl FM. Sudden hearing loss: eight years' experience and suggested prognostic table. Laryngoscope 1984;94:647-661.
6. Sara SA, Teh BM, Friedland P. Bilateral SSNHL: A Review. JLO 2014;1 28(Suppl S1):S8-S15.
7. Merchant SN, Adams JC, Nadol JB: Pathology and pathophysiology of idiopathic SSNHL. Otol Neurotol 2005; 26: 151–160
8. Merchant SN, Durand ML, Adams JC. Sudden Deafness: Is It Viral? ORL 2008;70:52-62
9. Chau J, Lin JR, Atashband S, et al. Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. Laryngoscope 2010;120: 1011–21.
10. Heman-Ackah SE, Jabbour N, Huang TC. Asymmetric SSNHL: Is all this testing necessary? Otolaryngol NHS 2010;39:486-490.
11. Chau JK, Cho JJW, Fritz DK. Evidence-Based Practice – Management of adult sensorineural hearing loss. Otolaryngol Clinc N Am 2012;45:941-958.
12. Sauvaget E, Kici S, Kania R, Herman P, Tran Ba Huy P. Sudden sensorineural hearing loss as a revealing symptom of vestibular schwannoma. Acta Otolaryngol 2005;125(6):592-595.
13. Aimoni C, Bianchini C, Borin M et al. Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: a case-control study. Audiol Neurotol 2010;15(2):111-5.
14. Narozny W, Kuczkowski J, Mikaszewski B. Thyroid dysfunction – underestimated but important prognostic factor in sudden sensorineural hearing loss. Otolaryngology HNS 2006;135:995-996.
15. Yimtae K, Srirompotong S, Lertsukprasert K. Otosyphilis: a review of 85 cases. Otolaryngol HNS 2007;136(1):67-71.
16. Kuhn M, Heman-Ackah SE, Shaikh JA, Roehm PC. Sudden sensorineural hearing loss: A review of diagnosis, treatment and prognosis. Trends in Amplification 2011;15(3):91-105.
17. Labus J, Breil J, Stutzer H, Michel O. Meta-analysis for the effect of medical therapy vs placebo on recovery of idiopathic sudden hearing loss. Laryngoscope 2010;120:1863-1871.
18. Edizer DT et al. Recovery of Idiopathic Sudden Sensorineural Hearing Loss. J Int Adv Otol 2015;11(2):122-6
19. Stachler RJ, Chandrasekhar SS, Archer SM, Rosenfeld RM, Schwartz SR, Barrs DM et al. Clinical Practice Guideline: Sudden Hearing Loss. Otolaryngology HNS 2012;146:S1-S35.
20. Dallan I, Fortunato S, Casani AP, Bernardini E, Sellari-Franceschini S, Berrettini S, Nacci A. Long-term follow up of sudden sensorineural hearing loss patients treated with intratympanic steroids: audiological and quality of life evaluation. JLO 2014;128:669-673.
21. Loughran S. Management of sudden sensorineural hearing loss: a consultant survey. J Laryngol Otol 2000;114:837-839.
22. Jarvis SJ, Giangrande V, John G, Thornton ARD. Management of acute idiopathic sensorineural hearing loss: a survey of UK ENT Consultants. Acta Otorhinolaryngol Ital 2011;31(2):85-89.
23. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. Arch Otolaryngol 1980; 106(12):772–6.
24. Cinamon U, Bendet E, Kronenberg J. Steroids, carbogen, or placebo for sudden hearing loss: a prospective double-blind study. Eur Arch Otorhinolaryngol 2001;258(9):477–80.
25. Nosrati-Zarenoe, Ramesh, Hultcrantz, E. Corticosteroid treatment of idiiopathic sudden sensorineural hearing loss: randomized triple-blind placebo-controlled trial. Otol Neurotol 2012,;33:523-531
26. Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss: I. A systematic review. Arch Otolaryngol Head Neck Surg 2007;133(6):573–81.
27. Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss: II. A metaanalysis. Arch Otolaryngol Head Neck Surg 2007;133(6):582–6.
28. Wei BPC, Stathopoulos D, O'Leary S. Steroids for idiopathic sudden sensorineural hearing loss. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD003998. DOI: 10.1002/14651858.CD003998.pub3.
29. Huy PT, Sauvaget E. Idiopathic sudden sensorineural hearing loss is not an otologic emergency. Otol Neurotol 2005;26:896–902.
30. Rauch SD, Halpin CF, Antonelli PJ, et al. Oral vs intratympanic corticosteroid therapy for idiopathic sudden sensorineural hearing loss: a randomized trial. JAMA 2011;305(20):2071–9
31. Vlastarakos PV, Papacharalampous G, Maragoudakis P, et al. Are intratympanically administered steroids effective in patients with sudden deafness? Implications for current clinical practice. Eur Arch Otorhinolaryngol 2012;269(2):363–80.
32. Spear SA, Schwartz SR. Intratympanic steroids for sudden sensorineural hearing loss: a systematic review. Otolaryngol Head Neck Surg 2011;145(4):534–43.
33. Battaglia A, Lualhati A, Lin H, Burchette R, Cueva R. A prospective, multi-centre study of the treatment of idiopathic sudden sensorineural hearing with combination therapy versus high dose prednisone alone: a 139 patient follow-up. Otol Neurotol 2014;35(6):1091-1098.
34. Lawrence R, Thevasagayam R. Controversies in the management of sudden sensorineural hearing loss: an evidence-based review. Clin Otolaryngol 2015;40:176-182.
35. Li H, Feng G, Wang H, Feng Y. Intratympanic steroid therapy as salvage treatment for sudden sensorineural hearing loss after failure of conventional therapy: A meta-analysis of randomised controlled trials. Clinical Therapeutics 2015;37(1):178-187
36. Ng JH, Ho RCM, Cheong CSJ, Ng A, Yuen HW, Ngo RYS. Intratympanic steroids as a salvage treatment for sudden sensorineural hearing loss? A meta-analysis. Eur Arch Otorhinolaryngol 2015;272:2777-2782
37. Awad Z, Huins C, Pothier DD. Antivirals for idiopathic sudden sensorineural hearing loss. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD006987. DOI: 10.1002/14651858.CD006987.pub2
38. Agarwal L, Pothier DD. Vasodilators and vasoactive substances for idiopathic sudden sensorineural hearing loss. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD003422. DOI: 10.1002/14651858.CD003422.pub4
39. Bennett MH, Kertesz T, Perleth M, Yeung P, Lehm JP. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD004739. DOI: 10.1002/14651858.CD004739.pub4

Patulous eustachian tube

Sam MacKeith[1] and **Ian Bottrill**[2]
[1]ENT SPR, Department of Otolaryngology, John Radcliffe Hospital, Oxford
[2]Consultant ENT Surgeon, Department of Otolaryngology, John Radcliffe Hospital, Oxford

Correspondence:
Sam MacKeith, FRCS (ORL HNS)
Dept of Otolaryngology, John Radcliffe Hospital
Headley Way, Oxford OX3 9DU
Email: samuelmackeith@doctors.org.uk

J ENT Masterclass 2016; 9 (1): 19 - 23.

Key words
Patulous Eustachian tube, augmentation, injection

Introduction

TThe Patulous Eustachian Tube (PET) can be defined as an abnormal patency of the Eustachian Tube (ET)[1]. A normally functioning ET is closed in its resting state and only opens briefly during maneuvers such as swallowing and yawning. The ET opening is understood to be achieved by a coordinated contraction of the peritubal muscles; tensor veli palatini and levator veli palatini[2]. In PET, the ET can remain patent for hours, allowing for a direct communication of sound and air pressure between the nasopharynx and middle ear.

Aetiology

The increased incidence of PET following weight loss (such as in malignancy) supports the theory that loss of volume in Ostman's (peritubal) fat pad may be implicated in the aetiology of this condition. In addition, loss of volume to the mucosa or submucosa in this valve region has been suggested as the explanation for its occurrence following radiotherapy. Hormonally induced changes to nasal mucosa are also thought to explain the increased incidence of PET in pregnancy (which resolves after delivery), and the onset with hormonal treatment of prostate cancer and the OCP. However, paradoxically high levels of oestrogen are also believed to cause mucosal oedema as seen in rhinitis of pregnancy, in addition, topical oestrogen drops have been used as a treatment for PET. The mechanisms here remain to be clarified. Other risk factors identified include neuromuscular disorders and scarring from previous surgery such as adenoidectomy[1].

Presentation

Typically patients present with autophony to voice and respiration (also termed breath synchronous tinnitus), due to reflux of sound via the column of air between the nasopharynx and middle ear. Patients can also complain of aural fullness, which may be misleading in suggesting a dilatory dysfunction of the ET. Although other otological symptoms have been reported, PET does not classically cause hearing loss or vertigo. The key alternative differential diagnosis to exclude is superior semicircular canal dehiscence (SSCD) that has some overlap in presentation. Table 1 shows the key presenting features of both for comparison with the most important differentiating features in red. Ultimately if there is any doubt in the diagnosis a CT temporal bones should be sought to assess for SSCD.

Table 1

Presenting Symptoms	PET	SSCD
Autophony to voice	++	++
Aural fullness	+	+
Autophony to respiration	++	-
TM excursions with respiration	++	-
Conductive hearing loss	-	+
Vertigo	-	+

It is not uncommon for patients to present to more than one ENT doctor prior to receiving the correct diagnosis. In the senior authors series of patients treated for PET, all 12 had been seen by at least one ENT doctor without their PET being diagnosed and the mean duration of symptoms prior to treatment was 6.7 years. This delay may be due to a reduced awareness of PET and subtle clinical signs without abnormalities on routine otoscopy, pure tone audiometry and standard tympanometry.

Examination of the ear is best performed with magnification (microscope/endoscope) to detect breath synchronous medial and lateral excursions of the tympanic membrane (TM). These may be more obvious in an atrophic segment

of the TM. Some authors have suggested occlusion of the contralateral nostril and forced breathing with the aim of exaggerating this sign. Nasendoscopy may show a scalloped concavity to the appearance of the antero-lateral wall of the ET orifice[3].

Frequently patients describe certain exacerbating and relieving factors. Common exacerbating factors are weight loss, dehydration, alcohol/caffeine intake, prolonged talking and exercise. Relieving factors include lying supine and nasal irrigation such as in the shower or when swimming. It is thought that the cessation of symptoms on lying supine is due to venous engorgement, indeed temporary compression of the internal jugular vein can lead to prompt resolution of symptoms. This should be borne in mind when performing otomicroscopy, ensuring it is done in the upright position. Conversely, if the symptoms are not present in clinic, asking the patient to exercise may bring on symptoms, allowing confirmation on examination.

It is the senior authors opinion that one should be wary of offering surgical treatment for symptoms of PET in cases where respiratory TM excursions have not been seen.

Investigations

Tuning fork tests and a pure tone audiometry are typically normal. The most useful objective test is continuous (long time base) tympanometry. This can indirectly record the movement of the TM and demonstrates a respiratory synchronous compliance pattern which appears as a 'saw-tooth' type trace, reflecting changes in compliance in time with inspiration and expiration[4]. See Figure 1 for example. Sonotubometry can also detect a patent ET but is not usually available in routine clinical practice. A CT scan may be indicated to exclude SSCD but also to identify a dehiscence of the carotid canal if ET augmentation surgery is planned.

Figure 1: *shows a long time based tympanometry over a 20 second period with the typical 'saw-tooth trace' as seen in PET. Courtesy of Gemma Crundwell, Specialist Audiologist, Addenbrooke's Hospital, Cambridge*

Management

The management of PET should be tailored to each individual patient depending on the severity of symptoms. We know that PET does not progress to cause hearing loss or any other otological complication and can therefore be safely left untreated. For many patients, an explanation and reassurance is sufficient and they can be discharged with their PET being merely an annoyance. However we know from more recent published studies using patient reported outcome measures (PROMs) that for some patients PET symptoms have a significant impact on their quality of life[5,6].

All patients may receive initial management with conservative measures aimed at addressing potential exacerbating factors including, encouraging hydration, reducing diuretics (caffeine and alcohol), stopping topical nasal steroids/decongestants and regaining lost weight.

For those with persisting problematic symptoms, there are no RCTs demonstrating optimal management of PET, however, a wide range of treatments have been reported. These can broadly be divided into 4 different treatment strategies.

1 Topical nasal medications

The simplest of these is instillation of saline into the nasopharynx presumably creating a meniscus of fluid over the ET orifice although this is clearly very temporary. Other agents aim to induce a chemical rhinitis causing increased mucous production or mucosal swelling (such as potassium iodine drops with boric acid powder insufflation)[7]. Some of these irritant solutions are available commercially as over the counter preparations. In addition to these, topical oestrogen drops (Premarin) have been used to induce mucosal hypertrophy.

Although worthwhile trialing as a non-invasive first line option, benefit is often limited and temporary meaning their use may be limited to patients with less severe PET.

2 Altering tympanic membrane mechanics

Mass loading of the tympanic membrane with layers of paper or even Blue Tac has been shown to reduce symptoms of PET[8,9]. This has led to surgical manipulation of the tympanic membrane to stiffen any potentially flaccid segments of the TM with modest benefit[10]. The rationale for this is that in PET there is loss of the middle ear air cushion dampening effect with a resulting increased compliance of the TM to sound/pressure waves transmitted via the PET. Whilst stiffening the TM may allow for some improvement in symptoms, it does not appear to address the underlying pathophysiology of the condition and has the potential risk to damage middle ear structures and hearing.

Interestingly 3 of the patients in our series had previously undergone grommet insertion as an attempted treatment with no improvement and in 2 the symptoms were worse.

3 Augmentation of the ET via the middle ear

Given that patients with PET often present to otologists, it is not surprising the middle ear has been used as the route to augment the ET. This has been performed via myringotomy and tympanotomy to insert a shim/silicone plug with good results[11,12]. Again there, is clearly a risk to middle ear structures and hearing. One of the patients in our series had previously undergone attempted augmentation of the ET via this route resulting in TM injury and a conductive hearing loss.

4 Augmentation of the ET via the nasopharynx

This approach is probably the most established strategy and its use dates back to Zollner who injected paraffin into the peritubular region. Since then a wide range of procedures have been used with success, all aiming to augment the ET to convert it from being patulous to competent. These include; cautery to the ET[13], ligation of the ET[5], tuboplasty[14], shim insertion[7] and injection augmentation with soft tissue bulking agents including Teflon[13], fat[15], cartilage[1,16], hydroxyapatite[17,18], and other soft tissue bulking agents[19].

We believe that this is the preferred strategy for patients with troublesome symptoms refractory to conservative measures.

Surgical technique – Eustachian tube augmentation with injection of soft tissue bulking agent

Over the last 6 years the senior author has performed this procedure with the following technique using Vox® (a silicone elastomer implant material previously termed Bioplastique®).

Following topical nasal preparation with Moffett's solution, the patient is placed supine with the mouth held open with a Boyle-Davis gag and a catheter passed through the nose and out through the mouth to retract the soft palate on the contralateral side to the ET being treated.

A 30 degree 4mm Hopkins rod is used through the ipsilateral nasal passage to view the Eustachian tube orifice as the angle instruments are introduced into the post nasal space via the mouth. Initially the eustachian tube orifice is opened using the Kujawski 800 angled instruments (Karl Storz). See figure 2. This permits an improved view of the lateral wall of the Eustachian tube, facilitating injection into the more superolateral narrower segment of the eustachian tube rather than simply the eustachian tube cushion. Sufficient Vox® is injected until the typically concave lateral wall is filled thereby becoming convex and occluding the eustachian tube (usually 1-2ml per side).

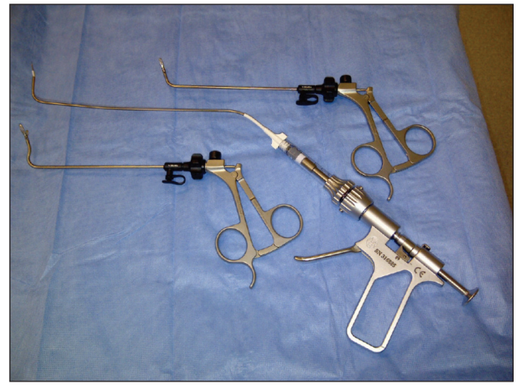


Figure 2: *the Kujawski 800 angled instruments*

All patients are followed up with PTA and tympanometry to assess for the development of glue ear and those with only temporary improvement are offered a repeat procedure.

Outcome measures

It is well recognized that patients can be observed to have breath synchronous tympanic membrane excursions without symptoms of PET, analogous to the incidental finding of dehiscence of the superior semicircular canal without symptomatic correlation. With this in mind, objective outcome measures may be less useful, leaving us more reliant on patient reported outcome measures (PROMs) to compare efficacy of different treatments. In recent years Poe has developed a PROM symptom scoring scale to determine benefit from treatment that has been adopted by other authors.

Treatment benefit PROM adapted from Poe[1,17]

1 = Complete relief (no symptoms at all)

2 = Significant improvement, satisfied (no longer experience under normal circumstances, only on exercising/prolonged talking)

3 = significant improvement, dissatisfied (desired further medical/surgical treatment

4 = unchanged

5 = worse

In addition, Rotenberg et al have devised a scoring system that measures impact on quality of life before and after treatment[6,20]:

1 = Absence of autophony

2 = occasional autophony but not enough to affect activities of daily living

3 = consistent autophony throughout activities of daily living

4 = problematic autophony affecting ability to perform activities of daily living

5 = distracting symptoms leaving patient unable to cope on a daily basis

We used these measure to determine effectiveness of treatment in our series of patients. After a mean follow up of 18months, 73% (8/11) were satisfied gaining either complete or significant improvement in symptoms. One patient had an improvement but was dissatisfied and two patients derived no persisting benefit from the procedure.

Regarding the quality of life outcome scores (as devised by Rotenberg et al), when comparing pre-operative with post-operative, the 8 satisfied patients reported an improvement where as the remaining 3 patients had no change to their score see Fig 3. This improvement was statistically significant when tested with the Wilcoxon Signed-Rank Test $p<0.01$ ($W=0$).

Table 2 lists and compares some of the more recently published series of surgical treatment strategies for PET showing success rates and outcome measures used[1,5,6,8,10,12,14-17,19,20].

Series author with publication year and journal	Treatment intervention	Number of patients with follow up	Efficacy outcome measure	Outcome/ Success rate
Polymethylsiloxane Elastomer (Vox®) Injection Augmentation ET- Bottrill, unpublished data		**11**	**Poe PROM and Rotenberg QOL impact score**	**73% (Score 1 or 2)1**
Rotenberg et al 2014 Laryngoscope	Transnasal shim into ET (wax filled catheter) secured with suture	7	Poe PROM and Rotenberg QOL impact score	100% complete resolution of symptoms (score 1/5)
Vaezeafshar et al 2013 Laryngoscope	Hydroxyapatite injection	14	PROM adapted from Poe	50% satisfied with complete or partial resolution (score 1 or 2)
Boedts 2014 JLO	Paper patching of TM	33	Retrospective review of case notes	50% of patients noted to have 'responded'
Brace et al 2014 Otol Neurotol	Tympanic membrane manipulation with laser myringoplasty (LM) or cartilage tympanoplasty (CT)	20	PET symptom specific PROM score	73% overall 11 ears in CT group improved but symptoms worse in 7/15 of LM group
Schröder et al 2014 Otol Neurotol	ET injection augmentation with Vox-Implant	15 with follow up	Improvement and patient satisfaction	10/15 satisfied (67%)
Rotenberg et al 2012 Laryngoscope	Endoscopic transnasal ligation of ET	11	PROM adapted from Poe	87.5% but late failures not included in subseuent report by same author.
Yañez et al 2011 Otolaryngol.-HNS	Curvature Inversion Technique Tuboplasty	11	Resolution of autophony	Voice autophony resolved in 73% Breathing autophony 82%
Kong et al 2011 Am J ORL	Autologous cartilage injection to ET	2	Resolution of symptoms	100%
Poe 2007 Otol Neurotol	Endoluminal cartilage shim ET reconstruction	14	Poe PROM	Improved and satisfied (1 0r 2) 50%
Sato et al 2005 Acta oto-laryngologica	Transtympanic ET silicone plug	37	Relief from symptoms	71%
Doherty et al 2003 Otolaryngol-HNS	Autologous fat injection to ET	2	Resolution of symptoms	100%

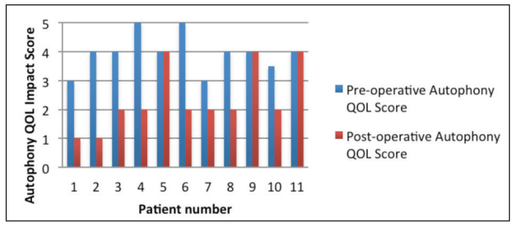


Figure 3: *Pre and Post Operative Autophony QOL Impact Scores*

Conclusion

Patulous Eustachian tube causes symptoms of autophony to voice and respiration, sometimes with aural fullness and is due to an abnormally patent Eustachian tube. Diagnosis is often delayed and whilst the majority can be managed with conservative measures and reassurance, a minority have more severe symptoms which lead them to seek further treatment.

There is a lack of evidence to support any one treatment strategy over another however consensus in the use of outcome measures will allow for more direct comparison of techniques in the future.

References

1. Poe D. Diagnosis and Management of the Patulous Eustachina Tube. Otol. Neurotol. 2007;28(5):668-677.
2. Poe D. Measurements of Eustachian tube dilation by video endoscopy. Otol. Neurotol. 2011;32(5):794-798.
3. Poe D. Pathophysiology and Surgical Treatment of Eustachian Tube Dysfunction.; PhD Thesis, University of Tampere, Finland, 2011.
4. McGrath AP, Michaelides EM. Use of middle ear immittance testing in the evaluation of patulous eustachian tube. J. Am. Acad. Audiol. 2011;22(4):201-7.
5. Rotenberg BW, Busato GM, Agrawal SK. Endoscopic ligation of the patulous eustachian tube as treatment for autophony. Laryngoscope 2013;123:239-243.
6. Rotenberg B, Davidson B. Endoscopic transnasal shim technique for treatment of patulous eustachian tube. Laryngoscope 2014;124(11):2466-9.
7. Adil E, Poe D. What is the full range of medical and surgical treatments available for patients with Eustachian tube dysfunction? Curr. Opin. Otolaryngol. Head Neck Surg. 2014;22(1):8-15.
8. Boedts M. Paper patching of the tympanic membrane as a symptomatic treatment for patulous eustachian tube syndrome. J. Laryngol. Otol. 2014;128(3):228-35.
9. Bartlett C, Pennings R, Ho A. et al. Simple mass loading of the tympanic membrane to alleviate symptoms of patulous eustachian tube. J. Otolaryngol. Head Neck Surg. 2010;39(3):259-68.
10. Brace MD, Horwich P, Kirkpatrick D, Bance M. Tympanic membrane manipulation to treat symptoms of patulous eustachian tube. Otol. Neurotol. 2014;35(7):1201-6.
11. Dyer RK, McElveen JT. The Patulous Eustachian Tube: Management Options. Otolaryngology--head and neck surgery. 1991;105, 832-835.
12. Sato T, Kawase T, Yano H. et al. Trans-tympanic silicone plug insertion for chronic patulous Eustachian tube. Acta Otolaryngol. 2005;125:1158-1163.
13. O'Connor AF, Shea JJ. Autophony and the Patulous Eustachian Tube. The Laryngoscope 1981; 91, 1427-1435.
14. Yañez C, Pirrón J, Mora N. Curvature Inversion Technique: a Novel Tuboplastic Tehnique for Patulous Eustachina Tube-A Preliminary Report. Otolaryngol. Neck Surg. 2011;145(3):446-51
15. Doherty J, Slattery W. Autologous fat grafting for the refractory patulous Eustachian tube. Otolaryngol. Neck Surg. 2003; 128(1): 88-91.
16. Kong S-K, Lee I-W, Goh E-K, Park S-H. Autologous cartilage injection for the patulous eustachian tube. Am. J. Otolaryngol. 2011;32(4):346-8.
17. Vaezeafshar R, Turner JH, Li G, Hwang PH. Endoscopic hydroxyapatite augmentation for patulous Eustachian tube. Laryngoscope 2014;124(1):62-6.
18. Oh S-J, Kang D-W, Goh E-K, Kong S-K. Calcium hydroxylapatite injection for the patulous Eustachian tube. Am. J. Otolaryngol. 2014;35(3):443-4.
19. Schröder S, Lehmann M, Sudhoff HH, Ebmeyer J. Treatment of the Patulous Eustachian Tube With Soft-Tissue Bulking Agent Injections. Otol. Neurotol. 2014:1-5.
20. Rotenberg B, Busato G, Agrawal S. Endoscopic Ligation of the Patulous Estachian Tube as Treatment for Autophony. Laryngoscope 2013; 123(1):239-43.

Principles of facial reanimation

Ahmed Allam[1] and Glen J. Watson[1]
[1]The Department of Otology and Neurotology, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, South Yorkshire, UK

Correspondence:
Mr. Ahmed Allam, FRCS, EBORL-HNS, M.D
Otology/Skull base fellow ENT department, Royal Hallamshire hospital, Sheffield Teaching NHS Foundation Trust, Glossop Rd, Sheffield S10 2JF
Email: ahmed.allam@sth.nhs.uk

Abstract:
Long-term facial nerve paralysis can be devastating for the patient. It not only has associated morbidity due to its cosmetic and functional consequence but there is also a significant psychosocial impact. Although many surgical options are available, the choice of treatment should take into consideration age and medical condition of the patient as well as both the duration and the type of paralysis.

In this paper, we discuss the general principles of facial nerve reanimation as well as static and dynamic procedures available to the patient.

J ENT Masterclass 2016; 9 (1): 24 - 28.

Key words:
Facial reanimation, Reconstruction, facial paralysis.

Introduction:

A functioning facial nerve is not only important to providing conscious and subconscious control of the facial musculature but also provides ocular protection, nasal airflow, oral continence and clear articulation[1]. Loss of facial function is not only devastating from a functional perspective but also has a significant psychosocial impact[2].

Whenever an insult occurs to the facial nerve with loss of function, the patient needs a focused history and examination and an underlying cause sought (table 1). For nerves that remain intact, the treatment is usually medical with strict eye care and ongoing support of the patient whilst awaiting recovery.

However, for those cases in which the nerve is damaged, the surgeon should attempt to repair the nerve as soon as possible in order to restore continuity and maintain neural signals to the facial musculature. If this is not possible then other methods need to be employed in an attempt restore symmetry, tone and function as facial asymmetry play a valuable role in the patient quality of life[3].

Facial reanimation is a complex process, which ideally needs a multidisciplinary approach including input from neurotologists, facial plastic surgeons, ophthalmologists as well as physiotherapists.

Throughout the pathway, the patient needs a complete understanding of the different methods of treatment available in order to obtain realistic expectations of outcomes[4].

At best the patient the patient can expect a House-Brackmann grade three after any form of reanimation surgery[5].

General considerations:

Patient selection

Prior to undertaking any static or dynamic facial reanimation procedures, a number of points need to be taken into consideration. Foremost the duration of nerve injury with resulting viability of distal facial musculature as well as the age of the patient and general medical condition will determine which technique will be employed. This is best to be discussed in a multidisciplinary setting with the patient and a family member present and may take numerous visits to come to a final agreement[6].

For those patients that are elderly, unfit ,unwilling to go through lengthy procedures, patients with temporary weakness awaiting recovery or failed microvascular procedures then static procedures may be in their best interest. For the remaining patients dynamic procedures should be considered[7]. Often in the later group, both techniques are employed to provide a tone, smile, and eye closure.

Table 1: List of cause of facial palsy

Causes	Example
Congenital	Mobius Syndrome, Goldenhar Syndrome Hemifacial microsomia Melkersson-Rosenthal Syndrome Birth related
Inflammatory	Malignant otitis externa Ramsy Hunt syndrome Acute and chronic otitis media, Deep neck space infection.
Traumatic	Temporal bone fracture, Parotid injury
Iatrogenic	Skull base surgery, Mastoidectomy, and Parotidectomy
Metabolic	Diabetes Mellitus Hyperthyroidism Hypertension Vitamin A Deficiency Pregnancy
Neurologic	Opercular Syndrome. Millard-Gubler Syndrome Guillain Barre
Hematologic	Leukamia
Toxic	Diptheria Tetanus Arsenic Intoxication Alcoholism
Neoplastic	**Cerebellopontine Angle Tumors:** Acoustic Neuromas, Meningioma, Facial nerve shwanoma **Parotid Tumor:** Pleomorphic Adenoma, Squamous cell carcinoma, Adenoid Cystic Carcinoma, Adenocarcinoma, Mucoepidermoid Carcinoma **Skull Base tumor:** Glomus tumor, Temporal bone squamous cell carcinoma.
Idiopathic	Bells Palsy

Static procedure:

Static procedures do not reproduce dynamic movement of the face however, they are used to provide corneal protection, improve nasal airflow, prevent drooling and provide facial symmetry

Dynamic procedures

Dynamic procedures are utilized to improve facial symmetry and tone as well as providing learned and spontaneous facial movement. Choosing a dynamic technique (table 3) for facial reanimation depends on the duration of palsy and facial muscle condition[8].

Table 2: Examples of static procedures

Anatomical area	Procedures examples
Eye Brow	Brow lifts
Eyelid	Tarsorrhaphy, Canthopexy, Gold weight.
Nasal valves	Nasal valve surgery i.e. Alar batton graft, suspension sutures
Oral commissure and lip	Static facial sling, Lip resection

Table 3: Dynamic facial reanimation procedures

< 12 month duration	> 12-month duration
Primary nerve repair	Muscle transfers
Cable grafting	Free neurovascular muscle flaps
Cross-facial nerve grafting	
Nerve transfers (jump grafts)	

Static Procedures

1.Tarsorrhaphy

Tarsorrhaphy (lateral or medial) narrows the palpebral fissure by approximating parts of the eyelids. It helps eyelid closure preventing dryness of the eye and exposure keratitis. It can be temporary or permanent[9].

2. Gold weights

Eye closure may be aided by insertion of a gold weight into the upper eyelid. Lid magnets, palpebral springs and platinum chains have also been described. These procedures are easy techniques for relief of exposure keratitis (Fig 1). The gold weight is inserted through an incision in the upper eyelid and sutured to the tarsal plate. Long-term extrusion can occur[10].

3. Brow lift

Paralysis of frontalis muscle causes ptotic/drop eye brows. Brow lift improves the aesthetic and function as it removes obstruction of upper visual field. Brow lift can be done endoscopic or open with minimal scars[11,12]

4. Nasal valve Surgery

Facial paralysis leads to weakness of the external nasal valve[13]. Multiple surgeries have been described, the most common are Batten grafts where a cartilage graft is inserted into a small pocket to support nasal cartilage[14]. Suspension sutures are also used[15].

5. Static facial sling

Static sling is an excellent option in case of comorbidities that prevent active muscle transfer to maintain facial symmetry at rest. Tensor fascia lata (TFL) is most commonly used with acceptable results[16]. Synthetic materials as Gore-Tex/polytetrafluoroethylene and Alloderm have been described[5]. The static slings are inserted between the corner of the mouth, ala of the nose or cheek and anchored onto the deep temporalis fascia.

Dynamic Procedures

1. Facial nerve anastomosis and cable grafting

This is direct end-to-end repair of the facial nerve or the use of a cable graft to allow for a tension-free anastomosis. In a recent literature review, Barrs et al[17] concluded that early repair before 2 months had the best results. However, grafting can occur anytime between 3 weeks up to a year after the injury. Thereafter there is general motor end-plate degeneration and facial muscle fibrosis. After about a month, the proximal viable nerve starts to regenerate at about 1mm a day. Depending where the insult to the nerve occurred will determine the rate of recovery which can be up to 24 months[18,19].

The principles for repair include: finding the proximal and distal ends of the nerve under magnification, mobilizing them in order to facilitate a tension free repair (not > 2 cm risk of devascularization), freshening the edges, orientating the ends and using 8/0 suture material to suture the epineurium. In the case of intratemporal injuries placing the two ends of the nerve together, surrounding it in fascia with or without applying tissue glue will suffice[20-22]. For all those defects that result in a significant distance between the proximal and distal nerve end then a cable graft using the great auricular nerve (GAN) or sural nerve (SN) can be used with minimal morbidity to the patient (GAN paraesthesia angle mandible and lower 2/3 of ear; SN paraesthesia outer aspect of foot)[23].

2. Cross-facial nerve grafting (CFNG)

This technique enhances neural activity form a functioning contralateral facial nerve to power the distal end of an injured nerve or to innervate a free muscle transfer. When used in combination with a free muscle transfer this will lead to spontaneous and symmetrical facial movement[24]. It is usually employed when the proximal end of the facial nerve is unavailable, the distal end is viable and there is functioning facial musculature (< 1year post injury).

This can be performed as a single or two-staged technique. In the single-stage technique, the sural nerve is harvested (for length) and anatomised in an end-to-end fashion with the buccal nerve on the functioning side. A tunnel is created between the face and the other end is anatomised onto the distal end of the facial nerve or a selected branch (usually buccal branch to allow for a spontaneous smile)

In a two-stage procedure, the distal end of the sural graft is placed in a pocket above the canine tooth. Nine to twelve months are allowed to pass until a positiveTinel's sign is elicited when tapping over the distal end of the graft indicating the presence of healthy neural fibers. The site is opened, the neuroma excised and an anastomosis is performed with the distal facial nerve trunk or a selected branch[1,25].

3. Nerve transfers

Nerve transfer is a reasonable choice in cases where there is irreversible proximal facial nerve injury with intact distal nerve and viable musculature detected on EMG. Ideally, the repair should be within 12 to 18 month to avoid muscle fibrosis[26]. There are two situations where the transfer is indicated: First is in skull base surgery were the proximal stump is lost but the distal stump is intact and ananastomosis or interposition is not achievable. The second is where the nerve is anatomically intact, but with no evidence of function after 12 months. Advantages of this techniques include a lower degree of technical difficulty, shorter time to movement (4 to 6 months), one suture line and reasonable motion with practice[27]. This, however, does not allow for spontaneous movement as with CFNG.

This technique is contraindicated if the facial palsy is associated with other lower cranial nerve neuropathies or skull base pathology.

The most commonly used crossover technique is the hypoglossal-facial anastomosis due to proximity to the facial nerve, multiple nerve fibres, and accepted morbidity in the form of hemiglossal weakness. In the past, the hypoglossal–facial anastomosis was done by completely transecting the hypoglossal nerve and anastomosing it end to end with the distal facial nerve[28]. However split hypoglossal transfer using 30% of the diameter of the hypoglossal nerve with an end to side anastomosis with the distal facial nerve can also be performed to prevent hemi-glossal weakness. Similarly, a hypoglossal jump graft can be performed (Figure 1). This is achieved by opening the hypoglossal nerve 30% and performing an end-to-side anastomosis with a mobilized distal facial nerve or a gable graft between the hypoglossal and distal facial[8].

Recently the masseter branch from the trigeminal nerve has been used to anastomose to the distal facial nerve with

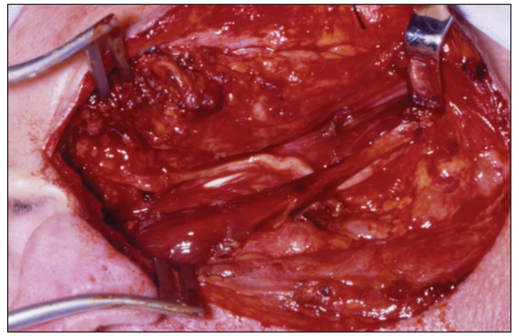


Figure 1: *Hypoglossal-facial jump nerve anastomosis. This is the right side demonstrating a greater auricular nerve jump graft with an end-to-side anastomosis onto the hypoglossal nerve (partly obscured by the reattached digastric muscle) and an end-to-end anastomosis onto the facial nerve*

good results. Anastomosis of hypoglossal and masseter branches can be used to keep viable motor end plate functioning whilst waiting for axons to migrate through cross facial nerve grafts[29-31].

4. Muscle transposition (dynamic slings)

Regional muscle transfer has been described in the situation where the crossover techniques are not applicable such as congenital facial nerve absence as in Mobius Syndrome, cranial nerve sacrificed in skull base surgery or loss of motor end plates in long-standing facial palsy (> 2 years). For quick results or a low life expectancy. The most reliable are the temporalis muscle[32] followed by the masseter muscle[33]. By insertion of the muscle fibers around the oral commissar, there is static support of the lower face and a trigeminal nerve induced smile. This should be discussed with the patient as the smile will need retraining, as it is associated with the clenching of teeth.

Also, it is important before planning surgery to be sure that the neurovascular supply to the muscle flap is intact as it may be affected by neurotological surgery or congenital disorders[8]. Muscle transposition can also be used whilst waiting for natural facial nerve recovery following skull base surgery and cross facial nerve grafting.

5. Free muscle transfers

Free muscle transfer has been described as a reliable technique for active restoration of the facial symmetry and smile. According to the facial nerve status, it can be done in one stage or two stages. Numerous free muscle pedicles have been described but the gracilis muscle is the most commonly used[34,35]. It is thin, compliant with minimum donor site morbidity. There is also an added advantage that two teams can work preparing the graft and donor site. The indications are similar to muscle transposition grafts. The vascular pedicle is anastomosed to the facial artery and vein whilst the nerve is either anastomosed to the healthy proximal end of the facial nerve, hypoglossal or masseter branch in a one stage procedure or it is attached to a cross facial nerve graft during in a second stage procedure once the axons have migrated across the graft. The latter will allow for dynamic facial movement whilst the use of the masseter and hypoglossal nerve will rely on retraining and eventual cerebral plasticity[36,37].

Conclusion

Both the cosmetic and functional loss following facial nerve weakness can have a significant effect on the quality of life of the patient. However through careful planning in a multidisciplinary setting, numerous surgical techniques can be explored in order to provide the patient with an achievable outcome.

References

1. Oghalai JS, Driscoll CL. Facial Nerve Surgery. Atlas of Neurotologic and Lateral Skull Base Surgery: Springer; 2016. p. 263-79.
2. Finsterer J. Management of peripheral facial nerve palsy. European Archives of Oto-Rhino-Laryngology. 2008;265(7):743-52.
3. Dey JK, Ishii M, Boahene K, Byrne PJ, Ishii LE. Changing perception: Facial reanimation surgery improves attractiveness and decreases negative facial perception. The Laryngoscope. 2014;124(1):84-90.
4. Hadlock TA, Urban LS. Toward a universal, automated facial measurement tool in facial reanimation. Archives of facial plastic surgery. 2012;14(4):277-82.
5. Chan JY, Byrne PJ. Management of facial paralysis in the 21st century. Facial Plastic Surgery. 2011;27(04):346-57.
6. Tate JR, Tollefson TT. Advances in facial reanimation. Current opinion in otolaryngology & head and neck surgery. 2006;14(4):242-8.
7. Harris BN, Tollefson TT. Facial reanimation: evolving from static procedures to free tissue transfer in head and neck surgery. Current opinion in otolaryngology & head and neck surgery. 2015;23(5):399-406.
8. Volk GF, Pantel M, Guntinas-Lichius O. Modern concepts in facial nerve reconstruction. Head & Face Medicine. 2010;6:25-.
9. Tan ST, Staiano JJ, Itinteang T, McIntyre BC, MacKinnon CA, Glasson DW. Gold weight implantation and lateral tarsorrhaphy for upper eyelid paralysis. Journal of Cranio-Maxillofacial Surgery. 2013;41(3):e49-e53.
10. Rofagha S, Seiff SR. Long-term results for the use of gold eyelid load weights in the management of facial paralysis. Plastic and reconstructive surgery. 2010;125(1):142-9.
11. Rozen SM, Harrison BL, Isaacson B, Kutz Jr JW, Roland PS, Blau PA, et al. Intracranial Facial Nerve Grafting in the Setting of Skull Base Tumors: Global and Regional Facial Function Analysis and Possible Implications for Facial Reanimation Surgery. Plastic and reconstructive surgery. 2016;137(1):267-78.
12. Leckenby J, Ghali S, Butler D, Grobbelaar A. Reanimation of the brow and eye in facial paralysis: Review of the literature and personal algorithmic approach. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2015;68(5):603-14.
13. Ramakrishnan Y, Alam S, Kotecha A, Gillett D, D'Souza A. Reanimation following facial palsy: present and future directions. The Journal of Laryngology & Otology. 2010;124(11):1146-52.
14. Cervelli V, Spallone D, Bottini JD, Silvi E, Gentile P, Curcio B, et al. Alar batten cartilage graft: treatment of internal and external nasal valve collapse. Aesthetic plastic surgery. 2009;33(4):625-34.
15. Nuara MJ, Mobley SR. Nasal valve suspension revisited. The Laryngoscope. 2007;117(12):2100-6.

16. Leckenby JI, Harrison DH, Grobbelaar AO. Static support in the facial palsy patient: a case series of 51 patients using tensor fascia lata slings as the sole treatment for correcting the position of the mouth. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2014;67(3):350-7.
17. Barrs DM. Facial nerve trauma: optimal timing for repair. The Laryngoscope. 1991;101(8):835-48.
18. Aviv JE, Urken ML. Management of the paralyzed face with microneurovascular free muscle transfer. Archives of Otolaryngology–Head & Neck Surgery. 1992;118(9):909-12.
19. Ghali S, MacQuillan A, Grobbelaar AO. Reanimation of the middle and lower face in facial paralysis: review of the literature and personal approach. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2011;64(4):423-31.
20. Bento RF, Miniti A. Comparison between Fibrin Tissue Adhesive, Epineural Suture and Natural Union in Intratemporal Facial Nerve of Cats: Part I. Acta Oto-Laryngologica. 1989;108(sup465):1-18.
21. Júnior EDP, Valmaseda-Castellón E, Gay-Escoda C. Facial nerve repair with epineural suture and anastomosis using fibrin adhesive: an experimental study in the rabbit. Journal of oral and maxillofacial surgery. 2004;62(12):1524-9.
22. Ramos DS, Bonnard D, Franco-Vidal V, Liguoro D, Darrouzet V. Stitchless fibrin glue-aided facial nerve grafting after cerebellopontine angle schwannoma removal: technique and results in 15 cases. Otology & Neurotology. 2015;36(3):498-502.
23. Guntinas-Lichius O, Streppel M, Stennert E. Postoperative functional evaluation of different reanimation techniques for facial nerve repair. The American journal of surgery. 2006;191(1):61-7.
24. Gur E, Stahl S, Barnea Y, Leshem D, Zaretski A, Amir A, et al. Comprehensive approach in surgical reconstruction of facial nerve paralysis: a 10-year perspective. Journal of reconstructive microsurgery. 2010;26(3):171.
25. Reddy S, Redett R. Facial paralysis in children. Facial Plastic Surgery. 2015;31(02):117-22.
26. Koh KS, Kim J-k, Kim CJ, Kwun BD, Kim S-y. Hypoglossal-facial crossover in facial-nerve palsy: pure end-to-side anastomosis technique. British journal of plastic surgery. 2002;55(1):25-31.
27. Fattah A, Borschel GH, Manktelow RT, Bezuhly M, Zuker RM. Facial palsy and reconstruction. Plastic and reconstructive surgery. 2012;129(2):340e-52e.
28. Catli T, Bayazit Y, Gokdogan O, Goksu N. Facial reanimation with end-to-end hypoglossofacial anastomosis: 20 years' experience. The Journal of Laryngology & Otology. 2010;124(01):23-5.
29. Faria JCM, Scopel GP, Ferreira MC. Facial reanimation with masseteric nerve: babysitter or permanent procedure? Preliminary results. Annals of plastic surgery. 2010;64(1):31-4.
30. Klebuc MJ. Facial reanimation using the masseter-to-facial nerve transfer. Plastic and reconstructive surgery. 2011;127(5):1909-15.
31. Biglioli F, Frigerio A, Colombo V, Colletti G, Rabbiosi D, Mortini P, et al. Masseteric–facial nerve anastomosis for early facial reanimation. Journal of Cranio-Maxillofacial Surgery. 2012;40(2):149-55.
32. Har-Shai Y, Gil T, Metanes I, Labbé D. Intraoperative muscle electrical stimulation for accurate positioning of the temporalis muscle tendon during dynamic, one-stage lengthening temporalis myoplasty for facial and lip reanimation. Plastic and reconstructive surgery. 2010;126(1):118-25.
33. Schaverien M, Moran G, Stewart K, Addison P. Activation of the masseter muscle during normal smile production and the implications for dynamic reanimation surgery for facial paralysis. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2011;64(12):1585-8.
34. Bhama PK, Weinberg JS, Lindsay RW, Hohman MH, Cheney ML, Hadlock TA. Objective outcomes analysis following microvascular gracilis transfer for facial reanimation: a review of 10 years' experience. JAMA facial plastic surgery. 2014;16(2):85-92.
35. Frey M, Michaelidou M, Tzou C-HJ, Pona I, Mittlböck M, Gerber H, et al. Three-dimensional video analysis of the paralyzed face reanimated by cross-face nerve grafting and free gracilis muscle transplantation: quantification of the functional outcome. Plastic and reconstructive surgery. 2008;122(6):1709-22.
36. Meltzer NE, Alam DS. Facial paralysis rehabilitation: state of the art. Current opinion in otolaryngology & head and neck surgery. 2010;18(4):232-7.
37. Zuker RM, Goldberg CS, Manktelow RT. Facial animation in children with Mobius syndrome after segmental gracilis muscle transplant. Plastic and reconstructive surgery. 2000;106(1):1-8; discussion 9.

A multidisciplinary approach to the management of paediatric drooling

C Paul and **A Addison**
Department of ENT, Oxford University Hospitals, John Radcliffe

Correspondondence:
Ms Ciba Paul, FRCS(ORL-HNS)
Department of ENT, Oxford University Hospitals, John Radcliffe
Headley Way, Oxford OX3 9DU
Email: Ciba.paul@ouh.nhs.uk

Abstract
This article explores the concept of the multidisciplinary team (MDT) approach in the management of children with drooling. We discuss the management strategies such as behavioural, oral motor therapy, pharmacotherapy, Botulinum toxin, surgical treatment and the effective use of the MDT in this complex group of patients.

J ENT Masterclass 2016; 9(1): 29 - 33.

Key words
multidisciplinary team, paediatric drooling, pharmacotherapy, surgical management

Introduction
Drooling is generally defined as the involuntary loss of saliva from the mouth. As the daily production of saliva ranges between 1-1.5 L, drooling can lead to severe functional, social and clinical consequences for the children, their family and care providers. The physical and psychological complications of drooling include, but are not limited to skin maceration, aspiration and recurrent chest infections, halitosis, dehydration and social stigmatisation[1]. In the unstimulated state, it is estimated that approximately 70% of the total saliva produced is from the submandibular gland, with the parotid and sublingual glands producing 25% and 5% respectively[2]. Conversely, in the stimulated state, saliva flow increases fivefold (7ml/ min[3]), with the parotid gland providing the majority of saliva. Drooling can be due to excessive production of saliva or poor control of saliva which may be due to poor head control, open mouth posture, disorganised tongue mobility, abnormal swallow, macroglossia, dental malocclusion, nasal obstruction and decreased tactile sensation. In children with neurologic disorders, especially cerebral palsy, drooling appears to be mainly due to inefficient tongue and/or bulbar control, rather than increased saliva secretion. In children with normal neurology, drooling beyond four years of age is considered abnormal. In this group of children, it is worth considering nasopharyngeal or oropharyngeal obstruction and oromotor dyspraxia. Drooling in children is a complex problem and therefore requires a multidisciplinary team approach for effective management.

Multidisciplinary Team Approach
Paediatric drooling is a complex clinical problem which presents various challenges for both patients and healthcare providers alike and a multidisciplinary approach is often necessary. The team usually includes otolaryngologists, paediatricians, radiologists, speech and language and occupational therapists, paediatric dentists, nurses, teachers and social workers. Evaluation of these patients is undertaken in a multidisciplinary setting using various caregiver reported subjective qualitative scales such as the Teachers, Modified Teachers scoring and drooling severity and frequency scales[3]. Currently, there is no specific scoring system for posterior drooling, however frequency of oropharyngeal suctioning and recurrent chest infections can be used as a tool for assessment. It is important to distinguish between anterior and posterior drooling as this impacts treatment options[4].

Management
As with many interventions in children, the evidence for effective non-medical treatment is scarce. Although there are no randomised controlled or controlled clinical trials to support the use of the various behavioural, physical and oral motor therapies for patients with drooling, there is increasing level 3 evidence to support the use of these interventions[5,6]. Various programmes are currently being utilised in different centres and there is no particular evidence for or against any particular programme. Full assessment of the individual is often required to identify the needs of the child and the programme tailored to their specific needs. Good team work between occupational and

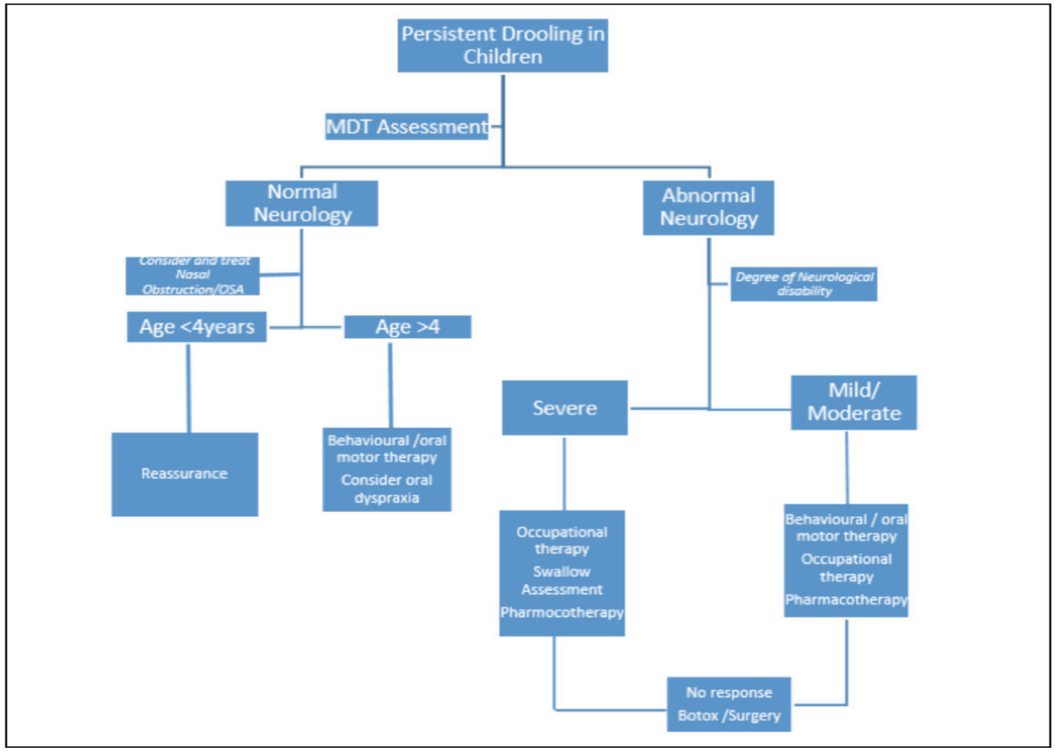


Figure 1: *Schematic of multidisciplinary team approach in the management of persistent drooling in ch `ildren*

speech and language therapists is often required to achieve the desired outcome. It is generally accepted that the initial step in drooling management is elimination of contributing factors; these are described below[7].

Postural control

Current literature supports the use of postural control to initially address saliva control; this usually leads to better head and trunk alignment resulting in improved saliva control[8]. These studies have mainly included patients with cerebral palsy and have shown that without trunk and head stability, jaw stability will not be attained and will result in inefficient tongue and lip movement and hence ineffective saliva control[9].

Behaviour and Oral Motor Therapies

These programmes are usually employed by speech and language therapists solely or as part of a feeding programme, to target the jaw, lips and tongue movements and include exercises to improve oral control and normalisation of oral sensitivity through graded stimulation[10]. These programmes can be laborious and time consuming, but have shown promise in patients with less severe neuromuscular and cognitive dysfunction. As such these protocols are recommended either in conjunction with or without medical management, for at least six months prior to the trial of other interventions[11]. Physiotherapy may markedly reduce drooling by improving jaw stability and closure, increasing mobility, strength and positioning of the tongue, improving lip closure especially during swallowing, and decreasing nasal regurgitation during swallowing.

Neuromuscular electrical stimulation devices may have a role to play in oral motor control in drooling, but their use is yet to be fully evaluated. There has been limited study in pharyngeal dysphagia, but their use has shown promise in improving symptoms in children[12].

Biofeedback is another treatment option; where a repeated auditory stimulus is presented as a behavioural management approach, in an attempt to condition the patient to swallow following presentation of the stimulus. The patient usually wears headphones, which transmit the stimulus in the form of a sound[13].

Other adjunct therapies such as the use of acupuncture have also not been fully studied; a single study from Hong Kong looking at the use of tongue acupuncture in ten drooling patients with neurological disability, found significant improvements in their mean drooling scores following thirty treatment sessions[14].

Prosthetics and Oral Care

A number of prosthesis have been developed by dentists and speech and language therapists to help with jaw stability and lip seal. These devices include the chin cup developed by orthodontists to decrease jaw protrusion[15]. There are children who genuinely produce too much saliva and the causes of this may include habitual finger chewing and dental decay, hence appropriate oral care and dental evaluation may be necessary in some cases. Functional appliances using the principles of Castillo-Morales; consisting of an acrylic palatal plate with vestibular and lingual stimulators which induce sucking and subsequent tongue retraction, have been used successfully to manage drooling[16,17].

Pharmacotherapy

The most frequently studied drugs in the treatment of drooling have been those that inhibit the secretion of saliva, typically anticholinergics. A systematic review described the benefits of anticholinergics in drooling[18].

A review undertaken by the National Institute for Health and Care Excellence (NICE) in 2013, showed moderate evidence for oral glycopyronium bromide in reducing hypersalivation in children with neurological conditions when compared with placebo, however there is no evidence of its long term efficacy or safety in treating hypersalivation. Although oral glycopyronium bromide is unlicensed in the UK, NICE supports its use where there are good clinical indications for its use[19]. Studies have shown 70-90% response rates, but with a high rate of antimuscarinic side effects in approximately 30-35% of patients, hence their guardians may prefer to discontinue the medication due to dry mouth, excessive sweating, urinary retention, irritability and behavioural changes[20].

Hyoscine provides good results in the treatment of paediatric drooling, with the advantage of a single transdermal application and is believed to render adequate serum concentrations, lasting three days. This offers a good treatment option, especially in children with neurological impairment. Side effects include skin reactions, dry mouth, constipation, blurring of vision, behavioural abnormalities and mild sedation[21,22].

Trihexiphenidyl has been used in the treatment of patients with cerebral palsy, as it offers the additional benefit of treating dystonia as well as drooling. Studies have shown significant improvement with some sources quoting improvements of up to 90% in patients with cerebral palsy. However acute/chronic colonic obstruction in patients using this therapy has been reported[23].

Botulinum Toxin

A Cochrane review by Walshe et al (2012) found six randomised controlled trials using either Botulinum toxin (BTx-A) or oral medications to decrease drooling[24]. All studies demonstrated effectiveness up to one month's duration for both treatments[24]. Another systematic review by Rodwell et al (2012) found sixteen articles on the use of BTx-A for paediatric drooling and also concluded that BTx-A was an effective but temporary therapy[25]. Of importance there have been mixed results, with some studies showing no improvement in over 30% of patients using BTx-A[25].

The dose of BTx-A administered for injection varies widely, due to variations in practise at different centres. The recommended dose in children is 30-40units of BTx-A, which is injected into the parotid and submandibular glands, and is usually enough to control symptoms[25]. Although several studies have suggested that ultrasound guidance is not required; it is generally recommended that injections are given under ultrasound guidance to ensure injection into the salivary gland and avoid injury to nerves, muscles and vessels. The main complications of BTx-A treatment are dysphagia (due to diffusion into adjacent bulbar musculature), weak mastication, infection, facial nerve injury and dental caries[25].

Surgical Management

Surgery is the treatment of choice in patients with severe drooling unresponsive to medical management. Surgery is generally deferred until 5-6 years of age. However it may be considered earlier in cases of severe posterior drooling with recurrent chest infections and intensive care unit admissions. There are several surgical procedures described in the treatment of drooling. These include, those aimed at reducing the amount of saliva (tympanic neurectomy, submandibular and parotid duct ligation, submandibular gland excision and sublingual gland excision) and those that redirect the flow of saliva (submandibular and parotid duct transposition), or a combination of these procedures. High overall subjective success rates for surgical options (81.6%) have been

reported in paediatric patients with sialorrhoea in meta-analysis; despite this there was insufficient evidence to support any particular procedure[26].

Bilateral submandibular duct relocation/rerouting was first described in 1969 and provided the mainstay of surgical treatment for non-aspirating children with drooling. A meta-analysis of surgical treatments performed for drooling revealed submandibular duct rerouting to be the most popular procedure; accounting for 31% of procedures with success rates ranging from 84-96%[26]. Reported complications include post-operative pain, ranula formation (8–12%), lingual nerve injury, dental caries (3%) and aspiration pneumonia (3%)[27,28,29,30]. Simultaneous excision of the sublingual glands has been performed, thereby greatly reducing the risk of ranula formation[30,31].

Bilateral submandibular gland excision and parotid duct ligation have been used as treatment options for paediatric drooling since 1964[32]. The procedure first described by Theodore F Wilkie, comprising of excision of both submandibular glands and rerouting of both parotid ducts had high success rates (87.5%), however it carried the potential risk of xerostomia with dental caries[32]. Over the years parotid duct transposition has been replaced with parotid duct ligation. The subjective success rates of bilateral submandibular gland excision and parotid duct ligation reported in the literature are 86-87%, with fewer lower respiratory tract infections[33,34]. The most frequent complication reported has been swelling of the parotid gland (25.8%), which resolves after 48 hours[34]. Postoperative sequelae include; parotid duct fistulas (9.6%), retention cysts in the buccal area adjacent to the duct ligation site (6.4%), dry mouth (3.8-7.5%) and dental caries (2.1%)[33,34,35].

Bilateral submandibular duct ligation with or without parotid duct ligation is a further surgical treatment option described for drooling. Studies recording the results of salivary gland duct ligation show varying success rates ranging from 32-81%3[6,37]. Known complications are chronic sialadenitis, ranula formation and recurrence of symptoms[36,37].

To date there is no specific procedure that is regarded as the gold standard for drooling. Compounding this issue is the difficulty in evaluating the surgical efficacy of these procedures and defining success. Our specialised tertiary multidisciplinary drooling clinic centre has noted recurrence of symptoms and ranula formation with salivary duct ligation; therefore this is not the preferred surgical modality for drooling in our centre.

In a child with no neurological impairment and no neuromuscular pathology and adenotonsillar hypertrophy, adenotonsillectomy may improve drooling.

In our experience bilateral submandibular gland excision and single parotid duct ligation is the preferred surgical treatment option, with optimal outcomes, in paediatric drooling unresponsive to medical management in children with neurological and neuromuscular conditions.

Radiotherapy

The use of radiotherapy as a treatment modality in drooling has only been described in adult patients with Amyotrophic Lateral Sclerosis and Parkinson's disease. Oncologists are understandably cautious of administering radiotherapy for drooling in children due to the long-term risk of malignancy[38,39].

Conclusion

A multidisciplinary multiprofessional team based approach together with guardian involvement is essential, in order to fully evaluate and institute the best management approach, with the best outcomes, in children with drooling. Various treatment strategies are described. In our experience when drooling is refractory to conservative measures and pharmacotherapy in children with neurological and neuromuscular conditions, bilateral submandibular gland excision and single parotid duct ligation is the preferred surgical option.

References

1. Leung AK, Kao, C.P. Drooling in children. Paediatr Child Health. 1999; 4(6):406
2. Jongerius PH, Van Tiel P, Van Limbeek J et al. A systematic review for evidence of efficacy of anticholinergic drugs to treat drooling. Arch Disease Child. 2003; 88(10):911-914
3. Montgomery J, McCusker S, Lang K et al. Managing children with sialorrhoea (drooling): Experience from the first 301 children in our saliva control clinic. Int J Pediatr Otorhinolaryngol. 2016; 85:33-39
4. Gerber ME, Gaugler MD, Myer CM, Cotton RT. Chronic aspiration in children: when are bilateral submandibular gland excision and parotid duct ligation indicated? Arch Otolaryngol Head Neck Surg. 1996; 122(12):1368-1371
5. Reddihough D, Johnson H, Ferguson E. The role of a saliva control clinic in the management of drooling. Journal Paediatr Child Health. 1992; 28(5):395-397
6. Reid SM, McCutcheon J, Reddihough DS, Johnson H. Prevalence and predictors of drooling in 7-to 14-year-old children with cerebral palsy: a population study. Dev Med Child Neurol. 2012; 54(11):1032-1036
7. Crysdale WS, Raveh E, McCann C et al. Management of drooling in individuals with neurodisability: a surgical experience. Dev Med Child Neurol. 2001; 43(6):379-383
8. Fairhurst CBR, Cockerill H. Management of drooling in children. Arch Disease Child Educ Pract Ed. 2011; 96(1):25-30
9. Lal D, Hotaling AJ. Drooling. Curr Opin Otolaryngol Head Neck Surg. 2006; 14(6):381-386
10. Arvedson JC, Brodsky L. Pediatric swallowing and feeding: Assessment and management. Singular Publishing Group Inc 2002. Pages 495-527.
11. Koheil R, Sochaniwskyj AE, Bablich K et al. Biofeedback techniques and behaviour modification in the conservative remediation of drooling by children with cerebral palsy. Dev Med Child Neurol. 1987; 29(1):19-26
12. Blasco PA, Allaire JH. Drooling in the developmental disabled: management practices and recommendations. Dev Med Child Neurol. 1992; 34(10):849-862
13. Domaracki LS, Sisson LA. Decreasing drooling with oral motor stimulation in children with multiple disabilities. Am J Occup Ther. 1990; 44(8):680-684
14. Wong V, Sun JG, Wong W. Traditional Chinese medicine (tongue acupuncture) in children with drooling problems. Pediatr Neurol. 2001; 25(1):47-54
15. Gangil A, Patwari AK, Aneja S et al. Feeding problems in children with cerebral palsy. Indian Paediatr. 2001; 38(8): 839-846
16. Limbrock GJ, Castillo-Morales R, Hoyer H et al. The Castillo-Morales approach to orofacial pathology in Down syndrome. Int J Orofacial Myology. 1993; 19: 30-37
17. Hoyer H, Limbrock GJ. Orofacial regulation therapy in children with Down syndrome, using the methods and appliances of Castillo-Morales. ASDC J Dent Child. 1989; 57(6):442-444
18. Jongerius PH, Van Tiel P, Van Limbeek J et al. A systematic review for evidence of efficacy of anticholinergic drugs to treat drooling. Arch Dis Child. 2003; 88(10):911-914
19. Parr JR, Weldon E, Pennington, L et al. The drooling reduction intervention trial (DRI): a single blind trial comparing the efficacy of glycopyrronium and hyoscine on drooling in children with neurodisability. Trials 2014; 15(1):60
20. Kay S, Harchik AE, Luiselli JK. Elimination of drooling by an adolescent student with autism attending public high school. Journal of Positive Behavioral Interventions 2006; 8(1):24-28
21. Adams RC, Dodge NN, Ekmark EM et al. A double-blind crossover study of two medications vs. placebo measuring functional drooling rates by a semi-quantitative method. Dev Med Child Neurol. 1996; 38:39–40
22. Blasco PA. Management of drooling: 10 years after the Consortium on Drooling 1990. Dev Med Child Neurol 2002; 44(11):778-781
23. Begbie F, Walker G, Kubba H, Sabharwal A. Acute colonic pseudo-obstruction in a child taking trihexyphenidyl for drooling: Prescribers beware. Int J Pediatr Otorhinolaryngol. 2015; 79(6):932-934
24. Walshe M, Smith M, Pennington L. Interventions for drooling in children with cerebral palsy. Cochrane Database Syst Rev 2012. Available at http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008624.pub3/full (accessed 1 June 2016).
25. Rodwell K, Edwards P, Ware RS, Boyd R. Salivary gland botulinum toxin injections for drooling in children with cerebral palsy and neurodevelopmental disability: a systematic review. Dev Med Child Neurol. 2012; 54(11):977-987
26. Reed J, Mans CK, Brietzke SE. Surgical management of drooling: a meta-analysis. Arch Otolaryngol Head Neck Surg. 2009; 135(9): 924-931
27. Crysdale WS, White A. Submandibular duct relocation for drooling: a 10-year experience with 194 patients. Otolaryngol Head Neck Surg. 1989; 101(1):87-92
28. De M, Adair R, Golchin K, Cinnamond MJ. Outcomes of submandibular duct relocation: a 15-year experience. J Laryngol Otol. 2003; 117(10):821-823
29. Mankarious LA, Bottrill ID, Huchzermeyer PM, Bailey CM. Long-term follow-up of submandibular duct rerouting for the treatment of sialorrhea in the pediatric population. Otolaryngol Head Neck Surg. 1999; 120(3):303-307
30. Glynn F. Does the addition of sublingual gland excision to submandibular duct relocation give better overall results in drooling control? Clin Otolaryngol. 2007; 32(2):103-107
31. Crysdale WS, McCann C, Roske L et al. Saliva control issues in the neurologically challenged: a 30 year experience in team management. Int J Pediatr Otorhinolaryngol. 2006; 70(3):519-527
32. Wilkie TF. The surgical treatment of drooling. A follow-up report of five years' experience. Plastic Reconstr Surg.1970; 45(6):549-554
33. Manrique D, do Brasil ODOC, Ramos, H. Drooling: analysis and evaluation of 31 children who underwent bilateral submandibular gland excision and parotid duct ligation. Braz J Otorhinolaryngol. 2007; 73(1):40-44
34. Stern Y, Feinmesser R, Collins M et al. Bilateral submandibular gland excision with parotid duct ligation for treatment of sialorrhea in children: long-term results. Arch Otolaryngol Head Neck Surg. 2002; 128(7):801-803
35. Delsing CPA, Cillessen E, Scheffer A et al. Bilateral submandibular gland excision for drooling: Our experience in twenty-six children and adolescents. Clin Otolaryngol. 2015; 40(3):285-290
36. Wiatrak BJ. Salivary gland duct ligation for the management of chronic sialorrhea in children. Operative Techniques in Otolaryngology-Head and Neck Surgery 2002; 13(1):68-70
37. Martin TJ, Conley SF. Long-term efficacy of intra-oral surgery for sialorrhea. Otolaryngol Head Neck Surg. 2007; 137(1):54-58.
38. Stalpers LJ, Moser EC. Results of radiotherapy for drooling in amyotrophic lateral sclerosis. Neurology 2002; 58(8):1308
39. Hawkey NM, Zaorsky NG, Galloway TJ. The role of radiation therapy in the management of sialorrhea: A systematic review. Laryngoscope. 2016; 126(1):80-85

Extra-uterine intrapartum treatment (EXIT) and upper airway obstruction of the newborn

Colin R Butler, **Elizabeth F Maughan** and **Richard Hewitt***,
*Department of Otolaryngology, Great Ormond Street Hospital for Children NHS Foundation Trust

Correspondence:
Richard Hewitt, FRCS ORL-HNS
Department of Otolaryngology, Great Ormond Street Hospital for Children NHS Foundation Trust, Great Ormond Street, London WC1N 3JH
Email: richard.hewitt@gosh.nhs.uk

Abstract
Improvements in the antenatal diagnosis of congenital malformations have led to increased detection of foetal airway obstructing lesions, and paediatric ear, nose and throat (ENT) surgeons are increasingly involved in these cases. Traditionally, difficulty in obtaining a patent airway at delivery was a major factor in the dismal prognosis of these pregnancies. The EXIT procedure, which involves controlled partial delivery of the foetus whilst maintaining placental circulation, allows various airway manoeuvres to be performed to secure the airway in a controlled fashion. This article outlines the typical range of pathology seen, the logistics in providing support for anticipated deliveries and the multidisciplinary management of complex airway cases.

J ENT Masterclass 2016; 9(1): 34 - 40.

Key words
paediatric airway; EXIT; foetal; CHAOS

Introduction
The ex utero intrapartum treatment (EXIT) procedure is a multidisciplinary management plan that can be deployed following the prenatal diagnosis of foetal, and impending neonatal, airway obstruction. It allows for time at delivery for airway securement and other resuscitative measures whilst remaining on placental oxygen support, thereby converting an emergency neonatal airway situation into an elective controlled one[1-3]. A successful EXIT outcome is heavily dependent on prenatal investigation techniques and a sufficiently high index of suspicion to detect potentially compromised infants. In addition to a surgical team with foetal medicine, ENT and anaesthetic neonatal airway expertise, highly specialist obstetric anaesthetic and surgical skill sets are required to ensure maternal safety and placental sufficiency throughout the procedure.

Indications for EXIT
Foetuses with airway obstruction may have one of a number of underlying defects affecting the head and neck. Obstructive lesions can be intrinsic, i.e. the so-called CHAOS infant (Congenital High Upper Airway Obstruction Syndrome)[4], but are more commonly caused by extrinsic compression by pharyngeal[5,6], cervical[3,7,8] or thoracic mass lesions[3,9]. In principle and in practice, the EXIT procedure can be considered in any prenatally diagnosed situation where difficulty or compromise in neonatal cardiopulmonary resuscitation is anticipated, such as reversal of tracheal occlusion in congenital diaphragmatic hernia[10], pulmonary pathologies such as congenital cystic adenomatoid malformations or unilateral pulmonary agenesis, pre-separation of conjoined twins and as a bridge to extracorporeal membrane oxygenation (ECMO)[3, 9, 11].

Extrinsic lesions
Patient series at large tertiary treatment centres have demonstrated that the location of an extrinsic lesion is a more relevant factor in the development of airway distortion and compromise more than the absolute size of the mass[9]. Lesions are likely to be isolated anomalies (Table 1), so securement of the airway at birth is key in allowing postnatal surgical treatment and good long-term outcomes[2,7,12,13].

Cervical Lymphangioma
Benign lymphatic cystic malformations commonly affect the neck (as cystic hygromas), likely following failure of the jugular lymph sacs to connect with lymph channels[14]. Their overall UK incidence may be as high as 1 in 1000 pregnancies[15], making them the second most common type of neonatal soft tissue lesion after haemangiomas[16]. Given their highly variable morphology, there is a wide spectrum of clinical severity. Posterior triangle lymphangiomas that are diagnosed early in the first or early-second trimester are more likely to be associated with underlying chromosomal defects and a poor pregnancy outcome[17]. Anterior lesions, especially those diagnosed later in gestation, are not usually associated with other abnormalities and may even regress in utero[18]. If the foetus is of a normal karyotype, without hydrops, and no septae are visible within the mass, then a good prognosis is expected and the main risk is that of perinatal airway compromise[19].

Table 1: Extrinsic Causes of Foetal Airway Obstruction. Adapted from Liechty & Crombleholme, 1999[1]

Extrinsic Causes of Foetal Airway Compromise	
Cervical lymphangioma (cystic hygroma)	Lipoma
Cervical teratoma	Hamartoma
Congenital goitre	Neuroblastoma
Haemangioma	Parotid masses
Branchial cleft cyst	Nuchal oedema
Thyroglossal duct cyst	Choristoma
Congenital thyroid tumour	Neural tube defects (e.g cervical myelomeningocele)
Laryngocele	Twin sac of blighted ovum

Head and neck teratoma
Teratomas are ectopic tissue neoplasms, far removed from their normal anatomical site, which contain elements from all three germ layers (the most common types are neural, cartilage and thyroid tissue). The head and neck is the fourth most common site for congenital teratoma. Tumours may be extensive, sometimes spanning from oral floor and mandible into the anterior mediastinum inferiorly or trapezius posteriorly, and can present with polyhydramnios from impaired foetal swallowing and oesophageal compression[20] (Figure 1). Even in the presence of lymph node metastases, total tumour removal is achieved in the great majority of cases with excellent long-term follow-up results[21].

Intrinsic lesions
Most cases of CHAOS are due to laryngeal atresia, but can also be caused by obstructing laryngeal webs or cysts, subglottic stenosis or tracheal stenosis (Figure 1). Embryologically, the larynx and upper airway becomes occluded at around 10 weeks gestation with an epithelial lamina that recanalises by week 12[22]. In CHAOS foetuses, it is likely that failure of this membrane to recanalise properly leads to a near-total stenosis or complete atresia, which prevents the escape of accumulating lung fluid from the tracheobronchial tree[4,23]. The use of the EXIT procedure to deliver these children is usually required to secure a tracheostomy at birth[2].

The sequence by which CHAOS worsens prognosis is by backpressure of accumulating lung fluid. This congestion of the foetal lungs causes compression of the heart within the mediastinum, impairing cardiac filling and leading to secondary heart failure and ascites[24,25]. If the obstruction to lung fluid drainage is left for the duration of gestation, the lungs remain poorly developed and inefficient in gas exchange at birth. In the case of tracheal atresia, cardiopulmonary sequelae may spontaneously resolve over the course of the pregnancy if coexistent tracheo-oesophageal fistulae are present, which allow for lung

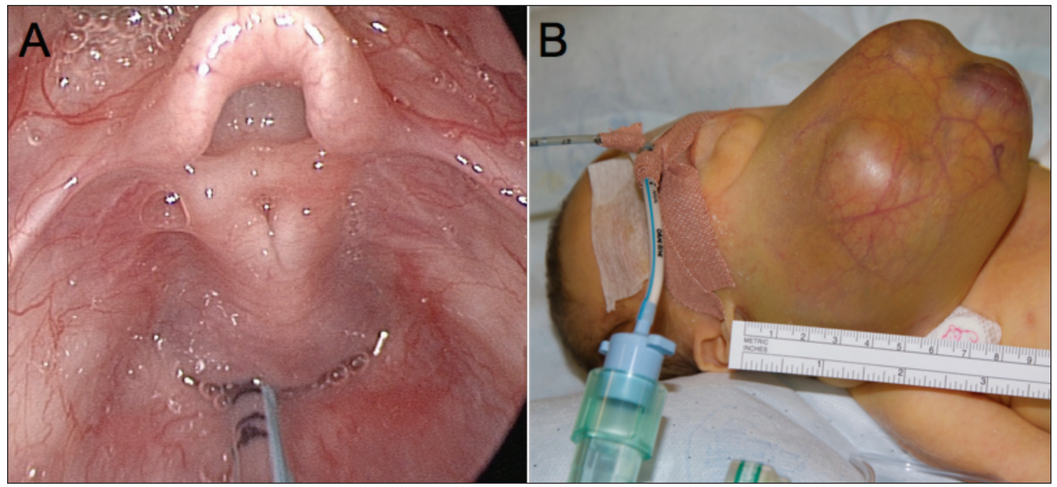


Figure 1: (A) *Microlaryngoscopy demonstrating a laryngeal web with the endotracheal tube (ETT) intubated through a tracheo-oesophageal fistula.* **(B)** *Typical appearance of a neonate with a large cervical teratoma.*

Table 2: Congenital malformations associated with CHAOS Syndrome	
Systemic anomalies associated with CHAOS Syndrome	
Gastrointestinal	Oesophageal atresia, tracheo-oesophageal fistula, imperforate anus
Genitourinary/ Reproductive	Renal agenesis, ambiguous genitalia, uterine anomalies
Neurological	Hydrocephalus
Eyes	Anophthalmia, cryptophthalmos
Musculoskeletal	Vertebral anomalies, absent radius, syndactyly

fluid to decompress into the oesophagus[26]. The EXIT procedure is of considerable use in these cases to allow time for distal airway cannulation via the oesophagus. Some foetuses have smaller posterior connections between the developing trachea and pharynx, potentially explaining reports in the literature of foetuses born with laryngeal atresia without CHAOS[27].

Most intrinsic airway anomalies leading to CHAOS are sporadic isolated lesions, but may be associated with a number of other congenital malformations (Table 2) or may be the presenting feature of genetic syndromes such as Fraser Syndrome[24,28] or Fragile X Syndrome[29]. This is a major factor in why spontaneous miscarriage or stillbirth occurs in a significant proportion of reported cases[1].

In cases of isolated anomalies or otherwise mild syndromic manifestations, excellent long-term survival has been reported in several CHAOS cases following EXIT[9,30].

Prenatal assessment and diagnosis

A suspected diagnosis of upper airway obstruction is typically made during standard prenatal ultrasonography (US) screening. Swallowing can be visualized as early as 14 weeks gestation and is suggestive of a continuous aero-digestive tract. As amniotic fluid is normally reabsorbed via the gastrointestinal tract, any lesion that compresses the oropharyngeal tract can lead to polyhydramnios due to a partial or complete failure of foetal swallowing. In some case series, 20% of pregnancies with polyhydramnios were found to have an underlying head and neck anomaly[31].

The foetal head may be held in an opisthotonic position, especially if the lesion is quite extensive. The classical CHAOS US features are of large hypoechoic lungs, distention of the trachea and bronchi, flattening or eversion of the diaphragm, restriction to cardiac filling, placentomegaly and non-immune hydrops fetalis[32-34]. In severe cases, mothers can mirror this heart failure[35].

Improved US resolution has meant these lesions can be identified by single modality imaging alone, and three-dimensional reconstructions can provide more precise anatomical information and extent of disease. Doppler is a useful adjunct to provide information on the vascularity of the lesion and clues to the degree of foetal heart strain from umbilical cord blood flow patterns.

Foetal magnetic resonance imaging (MRI) has an increasing role in defining exact sites of anticipated obstruction, for confirmation of US features and for follow-up monitoring of foetal lung volume[33,36]. Foetal MRI is also excellent for diagnostic confirmation in equivocal cases, e.g. to differentiate between herniation of posterior fossa contents and posterior cystic hygroma[37], and in identifying syndromic features, without resorting to invasive foetoscopy[38] (Figure 2). It is also highly useful for parent counseling and aids in delivery planning[39], and is an extremely useful tool for surgical planning where foetal surgery may be under consideration[40]. Other specialised tests include amniocentesis for karyotyping, and foetoscopy to directly visualise the airway.

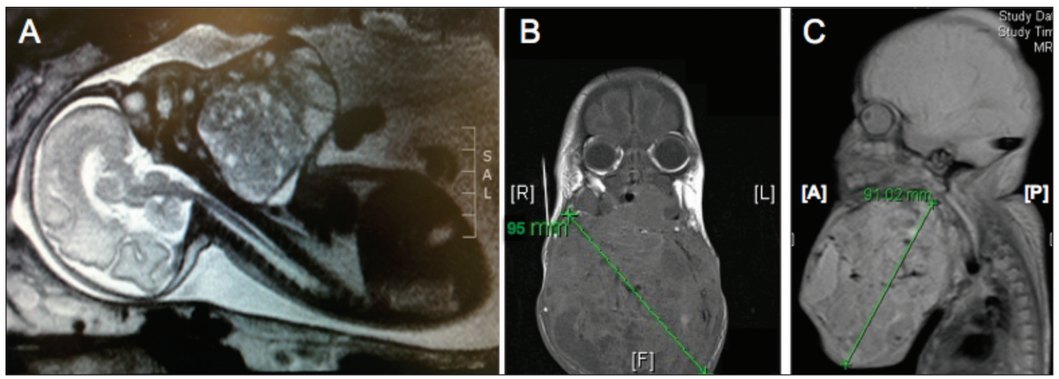


Figure 2: (A) *Foetal MRI demonstrating a cervical teratoma obstructing the airway in utero, MRI of neonate post-delivery demonstrating* **(B)** *coronal view and* **(C)** *sagittal view of the same cervical teratoma in excess of 9cm in diameter.*

Prenatal management

Prenatal management is often conservative by monitoring the pregnancy, such that foetus can be delivered when fully developed. EXIT procedures are typically considered at a gestational age of more than 38 weeks. If there is a degree of polyhydramnios, amniodrainages may be required at certain stages throughout the pregnancy. Direct management of the obstructing lesion *in utero* is very limited; however foetoscopic or laser techniques to relieve obstructive pressures are reported in the literature with increasing frequency[41]. Foetoscopic puncture or laser of the laryngeal atretic cartilage or membrane[33,42] can be performed, with placement of stents to try and lengthen the duration of the puncture patency. Successful decompression is seen as an immediate decrease in tracheal diameter on ultrasound, followed by normalisation of cardiovascular parameters over the next few hours[42]. These features should be monitored throughout the remainder of the pregnancy, however, as punctures may close over time necessitating repeat foetoscopic treatment or early delivery[33]. Foetoscopy is also useful for confirming the presence or absence of phenotypic features of other syndromic features if ultrasound findings are inconclusive (such as in cases of large maternal body habitus)[33,42].

Management

Following initial diagnosis, onward referral is recommended to a designated tertiary care centre where a multidisciplinary team (MDT) encompassing foetal, obstetric and airway ENT expertise can further assess these complex pregnancies and children. The MDT consists of the following: foetal medicine specialists, obstetricians, midwives, radiologists, paediatric surgeons, neonatologists, anaesthetists and paediatric airway otolaryngologists.

To EXIT or not to EXIT

The MDT is essential in this decision making process, as the risk to mother and foetus must both be considered along with the child's likely long-term outcome. In our unit, all cases have assessment by foetal US and MRI. Genetic analysis is performed as required. The severity of associated anomalies is carefully evaluated and, if very severe, may lead to a decision towards terminating the pregnancy. Conditions such as Fraser Syndrome require sensitive and in-depth counseling of the parents, who may decide to continue with the pregnancy given the wide spectrum of clinical severity in affected Fraser infants[42].

Maternal medical conditions (e.g. pre-eclampsia) may necessitate emergent delivery of the infant. Our unit currently does not advocate an emergency EXIT procedure in these situations, as considerable personnel and expertise are required to be available. In these situations, the baby is delivered through an emergency caesarean section and standard neonatal resuscitative measures are performed.

When considering an EXIT procedure, the team has to predict the likelihood of securing airway access. Much information can be garnered from imaging alone, such as whether the lesion is seen infiltrating the tongue base or is particularly vascular in nature. Other anticipated considerations beyond the immediate delivery of the infant may need addressing, such as immediate cardiac anomaly management and/or early gastrointestinal and genitourinary malformation management. Early surgical intervention to remove the lesion post-delivery may be necessary to ensure continued control of the airway, however cardiac issues may take equal priority and require correction in a combined procedure. A further consequence of persistent *in utero* airway obstruction is the possibility of an underdeveloped respiratory tree. The neonate may therefore need prolonged respiratory support following delivery.

Theatre Procedure

Theatre set-up requires coordinated action by multiple personnel from various disciplines. As there are 'two patients' to consider in this procedure, surgical teams are divided into those principally addressing the mother and those addressing the child. Similar to other units that deliver EXIT procedures, our team consists of an obstetric team with two surgeons with their dedicated anaethetists and own scrub team and a paediatric airway team that includes an airway anaesthetist and assistant, paediatric ENT surgeons and dedicated scrub staff. Foetal medicine specialists monitor foetal physiology during the procedure and neonatologists are present for management of the child after delivery.

The surgical approach to EXIT is similar to a standard caesarean delivery but differs in the anaesthesia, as uterine hypotonia is the priority to prevent placental separation[43]. Whilst this is essential for preserving uteroplacental circulation[12], a hypotonic uterus can be more challenging for haemostatic control and should be anticipated pre-operatively by having blood on standby for maternal transfusion. There is a low threshold to terminate the EXIT procedure if the mother is at risk from haemorrhage – the child is then delivered before securing the airway. Other considerations include the 'lie' of the placenta where an anterior position may limit the incision (and thus the position for the delivery of the foetal head). On delivery, the head is rotated in an occipitoposterior

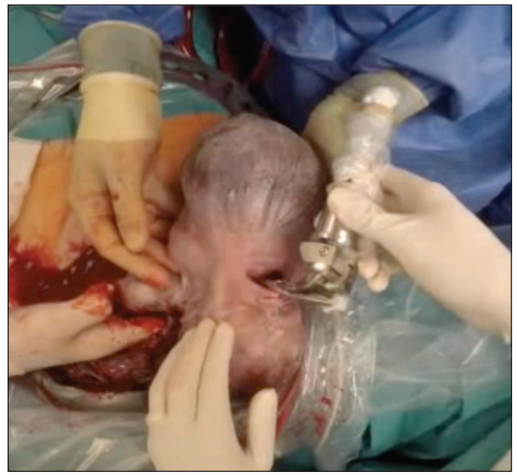


Figure 3: *EXIT procedure demonstrating foetal positioning on delivery of the head and arm of an infant with a large lymphatic malformation. The positioning allows for attempts at intubation. The size of the lesion may require retraction to aid intubation.*

position (Figure 3). The arm is also delivered with preservation of as much amnion as possible to limit amniotic fluid loss. Foetal continual monitoring equipment is attached, which includes an oxygen saturation monitor and a pH scalp probe. An echocardiogram (ECHO) machine is made available but is not routinely used unless the other sensors fail. Foetal anaesthetic medications are immediately delivered which include intramuscular injection of Vecuronium (0.1mg/kg) and Fentanyl (10mcg/kg) into the deltoid.

We use the following algorithm for securing the airway in our centre (Figure 4). Following delivery of the head, the child can be immediately evaluated by direct laryngoscopy with an anaesthetic intubating laryngoscope (Miller 0 or 00 blades). Reliable suction needs to be on standby to evacuate thick secretions. A Benjamin operating laryngoscope can be used next if the above fails, followed by flexible bronchoscopy. Large masses can be retracted away from the airway to aid intubation. Standard intubating adjuncts (stylettes and bougies) should be deployed to aid intubation. Rigid bronchoscopy is attempted prior to front of neck access. We have found a y–splitting light lead is

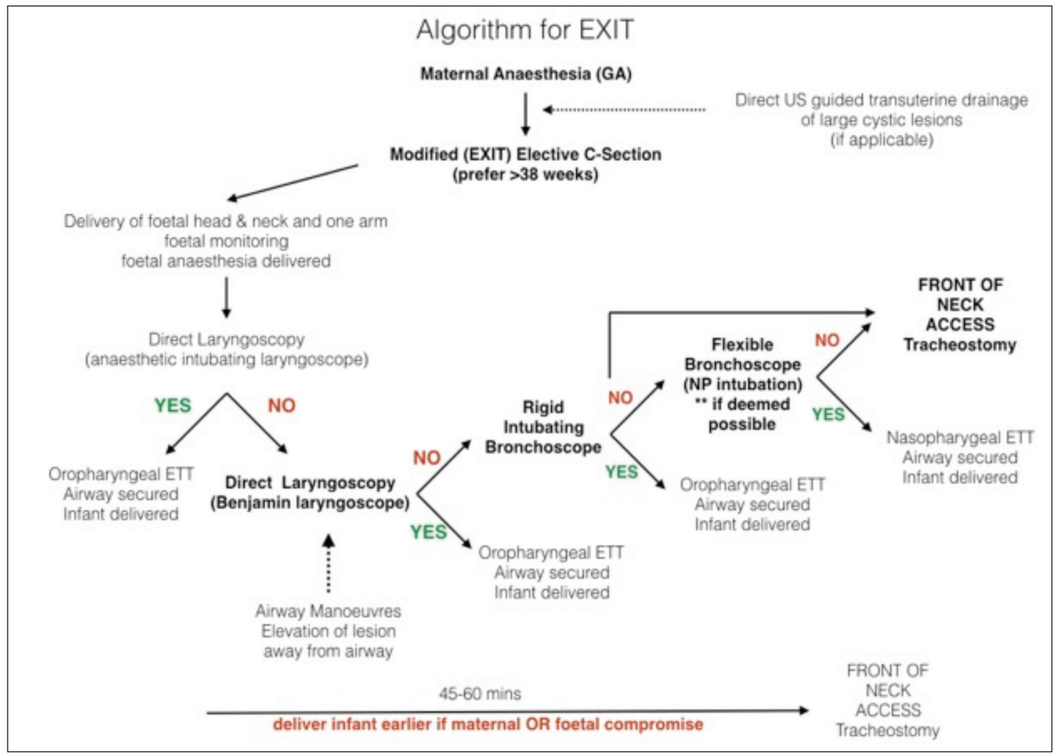


Figure 4: *Alogrithm for EXIT*

particularly helpful for swapping between scopes. Ultimately, if all of the above standard attempts fail, a tracheostomy is performed and, if lesions are infiltrating the front of the neck, a major neck tray is required.

Potential Complications

Foetal complications may occur if placental gas exchange cannot be preserved. This can occur secondary to loss of uterine relaxation, placental abruption or cord compression. Umbilical cord vessels are also at risk of vasospasm, particularly if exposed to changes in temperature. Inhalational anaesthetic agents are essential for uterine relaxation, but may lead to uterine atony. This can cause severe bleeding and could theoretically require hysterectomy to control bleeding in severe cases, though none have been reported in the literature or in our experience. Close surgical-anaesthetic communication is required to allow restoration of uterine tone as soon as the umbilical cord has been clamped. Uterine rupture may occur in subsequent pregnancies if vaginal delivery is attempted in the future, so mothers should be counseled during the EXIT decision-making process about the high likelihood of caesarean sections being required for all subsequent pregnancies. Lower uterine incisions may lower this risk but the feasibility of this is dependent on placental position[2].

The Role of Foetal Surgery

Open foetal surgical techniques are becoming increasingly reported in several US centres for the management of time-sensitive life-threatening thoracic foetal conditions[44,45]. The maternal risks surrounding open foetal airway surgery must be weighed in ethical terms against the likelihood of obtaining a more favourable foetal outcome than those obtained by delivery via EXIT and subsequent postnatal surgery (with or without foetoscopic interventions)[46,47]. The severe sequelae of CHAOS that could be avoided with early intervention, such as cardiac failure and impaired gas exchange development, may render foetal surgery ethically favourable but must be balanced against increased maternal risks and the likely presence of other foetal abnormalities, many of which are difficult to diagnose prior to birth even with the deployment of foetal MRI and foetoscopy[29]. Open surgery would be of particular use in long-segment stenoses which are not amenable to foetoscopic treatment[29].

Conclusion

Foetal upper airway obstruction has been transformed with the use of the EXIT procedure, as congenital malformations that were previously fatal to the foetus at delivery can now be managed with a semi-elective procedure that allows time for securing the airway. Essential to this is a multidisciplinary team that can provide expertise from diverse disciplines to deliver specialised and individualised care to both mother and child. Paediatric ENT surgeons should have an awareness of the pathologies and management strategies, even if not directly involved with the EXIT procedure itself, to aid the long-term local management of these children.

References

1. Liechty KW, Crombleholme TM, editors. Management of fetal airway obstruction. Seminars in perinatology; 1999: Elsevier.
2. Liechty KW, editor Ex-utero intrapartum therapy. Seminars in Fetal and Neonatal Medicine; 2010: Elsevier.
3. Bouchard S, Johnson MP, Flake AW et al. The EXIT procedure: experience and outcome in 31 cases. Journal of pediatric surgery. 2002;37(3):418-26.
4. Hedrick MH, Ferro MM, Filly RA et al. Congenital high airway obstruction syndrome (CHAOS): a potential for perinatal intervention. Journal of pediatric surgery. 1994;29(2):271-4.
5. Glynn F, Sheahan P, Hughes J, Russell J. Successful ex utero intrapartum treatment (EXIT) procedure for congenital high airway obstruction syndrome (CHAOS) owing to a large oropharyngeal teratoma. Irish medical journal. 2006;99(8):242-3.
6. Umekawa T, Sugiyama T, Yokochi A et al. A case of agnathia otocephaly complex assessed prenatally for ex utero intrapartum treatment (EXIT) by three dimensional ultrasonography. Prenatal diagnosis. 2007;27(7):679-81.
7. Liechty KW, Crombleholme TM, Flake AW et al. Intrapartum airway management for giant fetal neck masses: the EXIT (ex utero intrapartum treatment) procedure. American journal of obstetrics and gynecology. 1997;177(4):870-4.
8. Tapper D, Lack EE. Teratomas in infancy and childhood. A 54-year experience at the Children's Hospital Medical Center. Annals of surgery. 1983;198(3):398.
9. Hedrick HL, editor Ex utero intrapartum therapy. Seminars in pediatric surgery; 2003: Elsevier.
10. Mychaliska GB, Bealer JF, Graf JL et al. Operating on placental support: the ex utero intrapartum treatment procedure. Journal of pediatric surgery. 1997;32(2):227-31.
11. Kunisaki SM, Barnewolt CE, Estroff JA et al. Ex utero intrapartum treatment with extracorporeal membrane oxygenation for severe congenital diaphragmatic hernia. Journal of pediatric surgery. 2007;42(1):98-106.
12. Catalano PJ, Urken ML, Alvarez M et al. New approach to the management of airway obstruction in high risk neonates. Archives of Otolaryngology–Head & Neck Surgery. 1992;118(3):306-9.
13. Sheikh F, Akinkuotu A, Olutoye OO et al. Prenatally diagnosed neck masses: long-term outcomes and quality of life. Journal of pediatric surgery. 2015;50(7):1210-3.
14. Chervenak FA, Isaacson G, Blakemore KJ et al. Fetal cystic hygroma: cause and natural history. New England Journal of Medicine. 1983;309(14):822-5.
15. Fisher R, Partington A, Dykes E. Cystic hygroma: Comparison between prenatal and postnatal diagnosis. Journal of pediatric surgery. 1996;31(4):473-6.
16. Isaacs H. Tumors of the fetus and newborn: Saunders; 1997.
17. Scholl J, Chasen ST. First trimester cystic hygroma: does early detection matter? Prenatal diagnosis. 2016;36(5):432-6.
18. Langer JC, Fitzgerald PG, Desa D et al. Cervical cystic hygroma in the fetus: clinical spectrum and outcome. Journal of pediatric surgery. 1990;25(1):58-62.
19. Nadel A, Bromley B, Benacerraf BR. Nuchal thickening or cystic hygromas in first-and early second-trimester fetuses: prognosis and outcome. Obstetrics & Gynecology. 1993;82(1):43-8.
20. Rosenfeld CR, Coln CD, Duenhoelter JH. Fetal cervical teratoma as a cause of polyhydramnios. Pediatrics. 1979;64(2):176-9.
21. Martino F, Avila LF, Encinas JL et al. Teratomas of the neck and mediastinum in children. Pediatric surgery international. 2006;22(8):627-34.

22. Adamiec E, Dzieciolowska-Baran E, Czerwinski F et al. Prenatal development of the human trachea. FOLIA MORPHOLOGICA-WARSZAWA-ENGLISH EDITION-. 2002;61(2):123-5.
23. Vidaeff A, Szmuk P, Mastrobattista J et al. More or less CHAOS: case report and literature review suggesting the existence of a distinct subtype of congenital high airway obstruction syndrome. Ultrasound in obstetrics & gynecology. 2007;30(1):114-7.
24. Balcı S, Altınok G, Ozaltin F et al. Laryngeal atresia presenting as fetal ascites, oligohydramnios and lung appearance mimicking cystic adenomatoid malformation in a 25-week-old fetus with Fraser syndrome. Prenatal diagnosis. 1999;19(9):856-8.
25. Morrison P, Macphail S, Williams D et al. Laryngeal atresia or stenosis presenting as second-trimester fetal ascites—diagnosis and pathology in three independent cases. Prenatal diagnosis. 1998;18(9):963-7.
26. Floyd J, Campbell Jr DC, Dominy DE. Agenesis of the Trachea 1, 2. American Review of Respiratory Disease. 1962;86(4):557-60.
27. Smith I, Bain A. XXX Congenital Atresia of the Larynx A Report of Nine Cases. Annals of Otology, Rhinology & Laryngology. 1965;74(2):338-49.
28. Schauer G, Dunn L, Godmilow L et al. Prenatal diagnosis of Fraser syndrome at 18.5 weeks gestation, with autopsy findings at 19 weeks. American journal of medical genetics. 1990;37(4):583-91.
29. Saadai P, Jelin EB, Nijagal A et al. Long-term outcomes after fetal therapy for congenital high airway obstructive syndrome. Journal of pediatric surgery. 2012;47(6):1095-100.
30. Crombleholme TM, Sylvester K, Flake AW, Adzick NS. Salvage of a fetus with congenital high airway obstruction syndrome by ex utero intrapartum treatment (EXIT) procedure. Fetal diagnosis and therapy. 2000;15(5):280-2.
31. Stocks RM, Egerman RS, Woodson GE et al. Airway management of neonates with antenatally detected head and neck anomalies. Arch Otolaryngol Head Neck Surg. 1997;123(6):641-5.
32. Witters I, Fryns JP, De Catte L, Moerman P. Prenatal diagnosis and pulmonary pathology in congenital high airway obstruction sequence. Prenatal diagnosis. 2009;29(11):1081-4.
33. Kohl T, Van de Vondel P, Stressig R et al. Percutaneous fetoscopic laser decompression of congenital high airway obstruction syndrome (CHAOS) from laryngeal atresia via a single trocar–current technical constraints and potential solutions for future interventions. Fetal diagnosis and therapy. 2009;25(1):67-71.
34. Kalache KD, Franz M, Chaoui R, Bollmann R. Ultrasound measurements of the diameter of the fetal trachea, larynx and pharynx throughout gestation and applicability to prenatal diagnosis of obstructive anomalies of the upper respiratory–digestive tract. Prenatal diagnosis. 1999;19(3):211-8.
35. Ren S, Bhavsar T, Wurzel J. CHAOS in the Mirror: Ballantyne (mirror) Syndrome Related to Congenital High Upper Airway Obstruction Syndrome. Fetal and pediatric pathology. 2012;31(6):360-4.
36. Kalache KD, Chaoui R, Tennstedt C, Bollmann R. Prenatal diagnosis of laryngeal atresia in two cases of congenital high airway obstruction syndrome (CHAOS). Prenatal diagnosis. 1997;17(6):577-81.
37. Poutamo J, Vanninen R, Partanen K et al. Magnetic resonance imaging supplements ultrasonographic imaging of the posterior fossa, pharynx and neck in malformed fetuses. Ultrasound in obstetrics & gynecology. 1999;13(5):327-34.
38. Saleem SN. Fetal MRI: An approach to practice: A review. Journal of Advanced Research. 2014;5(5):507-23.
39. Kathary N, Bulas DI, Newman KD, Schonberg RL. MRI imaging of fetal neck masses with airway compromise: utility in delivery planning. Pediatric radiology. 2001;31(10):727-31.
40. Coakley FV. Role of magnetic resonance imaging in fetal surgery. Topics in Magnetic Resonance Imaging. 2001;12(1):39-51.
41. Mathis J, Raio L, Baud D. Fetal laser therapy: applications in the management of fetal pathologies. Prenatal diagnosis. 2015;35(7):623-36.
42. Kohl T, Hering R, Bauriedel G et al. Fetoscopic and ultrasound guided decompression of the fetal trachea in a human fetus with Fraser syndrome and congenital high airway obstruction syndrome (CHAOS) from laryngeal atresia. Ultrasound in obstetrics & gynecology. 2006;27(1):84-8.
43. Marwan A, Crombleholme TM, editors. The EXIT procedure: principles, pitfalls, and progress. Seminars in pediatric surgery; 2006: Elsevier.
44. Peranteau WH, Moldenhauer JS, Khalek N et al. Open fetal surgery for central bronchial atresia. Fetal diagnosis and therapy. 2014;35(2):141-7.
45. Simpson JL, Greene MF. Fetal surgery for myelomeningocele. N Engl J Med. 2011;364(11):1076-7.
46. Deprest JA, Flake AW, Gratacos E et al. The making of fetal surgery. Prenatal diagnosis. 2010;30(7):653-67.
47. Roybal JL, Liechty KW, Hedrick HL et al. Predicting the severity of congenital high airway obstruction syndrome. Journal of pediatric surgery. 2010;45(8):1633-9.

The management of paediatric facial nerve palsy

Sachin Patil[1], **Neeraj Bhangu**[2], **Kate Pryde**[3] and **Andrea Burgess**[1]

[1]Department of Otorhinolaryngology, University Hospital Southampton NHS Foundation Trust, Southampton SO16 6YD

[2]Department of Paediatrics, Queen Alexandra Hospital, Southwick Hill Road, Portsmouth, PO6 3LY

[3]Department of Paediatrics, University Hospital Southampton NHS Foundation Trust, Southampton SO16 6YD

Correspondence:

Sachin Patil, MS ENT

Department of Otorhinolaryngology, University Hospital Southampton NHS Foundation Trust, Southampton SO16 6YD

Email: sachin.patil6@me.com

Abstract

The facial nerve is a mixed nerve containing motor, sensory and autonomic fibres. Facial nerve palsies may be upper motor neurone (UMN) or lower motor neurone (LMN), unilateral or bilateral. Incidence rates vary between 6.1-25 children per 100,000 per year. There are numerous causes both congenital and acquired, which vary from idiopathic to serious underlying pathology such as tumours. In approximately 50% of cases, the cause of the facial nerve palsy remains unknown. It is essential that a thorough history and appropriate investigations are undertaken to identify potentially treatable causes and minimise morbidity. The management of facial nerve palsy in the paediatric age group may prove challenging for children, caregivers and clinicians. The prognosis of paediatric facial nerve palsy depends on the aetiology, severity, and time of presentation. In this article, we suggest a strategy for assessment, investigation and management of paediatric facial nerve palsy with a multidisciplinary team approach.

J ENT Masterclass 2016; 9(1): 41 - 49.

Key words

Facial palsy, paediatric, congenital, management

Acknowledgements

We would like to acknowledge Mrs Hasnaa Ismail-Koch, who greatly contributed to the text, editing, clinical cases, images and development of the management approach described. We would also like to recognise the valued contributions of Mr Tim Mitchell and Mr Sebastien Thomas for their expert advice on the management of paediatric facial nerve palsy.

Introduction

The facial nerve is a mixed nerve containing motor, sensory and autonomic fibres. It is the nerve of the second branchial arch, which supplies structures derived from Reichert's cartilage (table 1) and is responsible for essential functions including hearing, chewing, facial expressions, and facial movements. Approximately 58% of the facial nerve fibres in humans are motor, 18% sensory, and 24% autonomic[1].

The facial nerve arises from the facioacoustic primordium, which appears in the third week of gestation. The facial and acoustic primordium separate from each other by the end of the sixth week. By week 16 all communications of the facial nerve are established and by week 26 the formation of the fallopian canal is complete[2]. At this gestation approximately 25-55% of fallopian canals show dehiscence, the commonest location being around the oval window. At birth, the facial nerve is fully developed but lies in a more superficial position than in adults due to the underdeveloped mastoid process.

Table 1: Derivatives of the second pharyngeal arch

Pharyngeal Arch	Nerve and Artery	Muscles	Derivatives
Reichert's cartilage/ second pharyngealarch cartilage	Facial nerve	Facial expression muscles	Malleus (manubrium)
		Buccinator	Incus (long process)
	Stapedial Artery	Stapedius muscle	Stapes (except for footplate)
		Stylohyoid muscle	Facial canal
		Platysma	Styloid process
		Posterior belly of digastric	Stylohyoid ligament
			Hyoid bone (lesser cornu & upper part of body)

Epidemiology and causes

Paediatric facial nerve palsy (partial weakness) or paralysis (complete weakness) refers to weakness of the facial nerve either present from birth (congenital) or developing after birth (acquired). Reported incidence rates vary between 6.1-25 children per 100,000 per year[3,4,5].

Facial nerve palsies may be classified as upper motor neurone (UMN) or lower motor neurone (LMN), unilateral or bilateral. Facial nerve palsies may be isolated or occur as part of a syndrome, in conjunction with other cranial nerve palsies or other abnormalities, suggesting a developmental aetiology. In cases of congenital facial nerve palsy associated with congenital malformations, understanding the abnormality of the malformed organ or structures based on embryological development can indicate the foetal stage at which the insult occurred and development was arrested.

There are numerous causes of paediatric facial nerve palsy both acquired and congenital[3,4,6]. In approximately 50% of cases, the cause of the LMN facial nerve palsy remains unknown, and these patients are collectively grouped under the term 'Bells palsy' much like their adult counterparts[7]. The commonest cause of congenital facial nerve palsy accounting for 75-80% of the cases is birth trauma. Factors predisposing to birth trauma induced facial nerve palsy include prematurity, birth weight >3500 grams, forceps delivery, caesarean delivery and first child[8]. Full recovery of facial nerve function occurs in the vast majority of these patients within a few months[9]. Other congenital causes include a variety of genetic syndromes and congenital malformations (table 2).

There are many acquired causes of facial palsy and presentation depends on the underlying aetiology (table 3). Acquired facial nerve palsies, in general, have a relatively good prognosis compared to syndromic causes.

Table 2: Congenital causes of Paediatric facial palsy

Syndromic	Features
DiGeorge Syndrome	Craniofacial, visceral & cardiovascular anomalies, hypoplastic or absent thymus and parathyroid, aural anomalies, facial nerve palsy
Goldenhar syndrome	Unilateral facial asymmetry, maxillary hypoplasia, microstomia, microtia, facial nerve palsy
Moebius syndrome	Limb deformities,aplasia of brachial and thoracic muscles, unilateral or bilateral facial, and abducens nerve palsies
Melkersson-Rosenthal syndrome	Recurrent facial nerve palsy, fissured tongue, oedema oflips, eyelids and cheilitis
Neurofibromatosis type 1/ Von Recklinghausen's disease/ Neurofibromatosis type 2	Autosomal dominant disorder, multiple neurofibromas, café-au-lait spots, vestibular schwannomas, facial nerve schwannomas (leading to facial nerve palsy)
Bulbopontine paralysis with progressive sensorineural hearing loss	Autosomal recessive disorder, bulbar muscle involvement, unilateral or bilateral partial facial nerve palsy, progressive sensorineural hearing loss
Osteopetrosis	Deafness, abnormalities of the ear, facial nerve palsy
Sclerostenosis	Autosomal recessive disorder, mandibular, calvarial, clavicular, and pelvic osteosclerosis and hyperostosis, bilateral hearing loss, unilateral and bilateral facial nerve palsies
Dominant craniometaphyseal dysplasia	Metaphyseal widening of limbs, unilateral or bilateral facial nerve palsies, hearing loss, sclerotic mastoid, facial and bony skull overgrowth
Recessive craniometaphyseal dysplasia	Glabella and paranasal prominence, hypertelorism, mandibular prognathism, facial nerve palsy, progressive hearing loss,blindness
Genetic or Hereditary	
Hereditary myopathies	
3q21-22 mutation	
10q21.3-22.1 mutation	
Non- Syndromic	
Birth Trauma	Prematurity, birth weight >3500 grams,forceps delivery, caesarean delivery, first child
Sickle cell crisis	

Table 3: Acquired causes of Paediatric facial palsy

Infective		
	Bacterial	Acute Otitis Media (Pneumococcus, H. influenzae, Moraxella)
		Chronic Otitis Media
		Tuberculosis
		Lyme Disease (Borrelia burgdorferi)
		Syphilis
		Botulism (Clostridium Botulinum)
	Viral	Ramsay Hunt Syndrome (Herpes Zoster Oticus)
		Epstein-Barr Virus
		Guillain-Barre Syndrome
		Measles
		Mumps
		Rubella
		Cytomegalovirus (CMV)
		Adenovirus
		HIV
		Poliomyelitis (type 1)
	Mycoplasma	Mycoplasma pneumonia
Inflammatory		
		Temporal arteritis
		Henoch-Schönlein purpura
		Thrombotic thrombocytopenic purpura
		Kawasaki disease
Traumatic		
	Temporal bone fracture	
	Iatrogenic	Mastoid/middle ear surgery, Parotidectomy, Local anesthesia, Embolisation
	Facial injuries	Altitude paralysis (barotrauma)
		Scuba diving (barotrauma)
Neoplastic		
	Benign	Glomus jugulare/ glomus tympanicum
		Facial nerve schwannoma
		Vestibular schwannoma
		Meningioma
		Parotid tumours (benign)
	Malignant	Metastasis
		Squamous cell carcinoma of temporal bone
		Parotid tumours (malignant)
		Leukaemia
		Sarcoma
Neurologic		
		Multiple Sclerosis
		Myasthenia gravis
		Opercular syndrome (cortical lesion in facial motor area)
Metabolic		
		Diabetes Mellitus
		Pregnancy
		Hypothyroidism
		Acute Porphyria
		Vitamin A deficiency
Drug/ Toxin		
		Thalidomide
		Alcoholism
		Ethylene glycol
		Arsenic intoxication
		Carbon monoxide poisoning
		Tetanus toxin
		Diphtheria
Idiopathic/ Bells palsy		

DIAGNOSIS

History

A thorough history should include the onset and progression of the facial nerve palsy. Specific questioning regarding associated otological symptoms such as hearing loss, otorrhoea, facial numbness or hyperacusis should be undertaken. Additionally, history of recent infections, tick bites, trauma, neck lumps, salivary gland pathology, weight loss and systemic symptoms should be sought[10,11,12-15].

Clinical Examination

It is essential that clinical examination includes general systemic aspects, assessment for syndromic features, complete neurological examination and examination of the cranial nerves to ascertain whether the facial nerve palsy is upper or lower motor neurone (figure 1). The severity of the LMN facial nerve palsy should be assessed and recorded according to the House Brackmann grading system[16] (table 4). Other commonly used systems are Sunnybrook[17] and Yanagihara scales[18].

Figure 1: *Child with right LMN facial palsy.*

Systemic examination, for signs of potential underlying disease, should include checking for weight loss, bruises and organomegaly (oncological causes), tick bites and rashes (Lyme disease), and blood pressure measurement (hypertension) which has been reported to be associated with recurrent facial palsy[10,15].

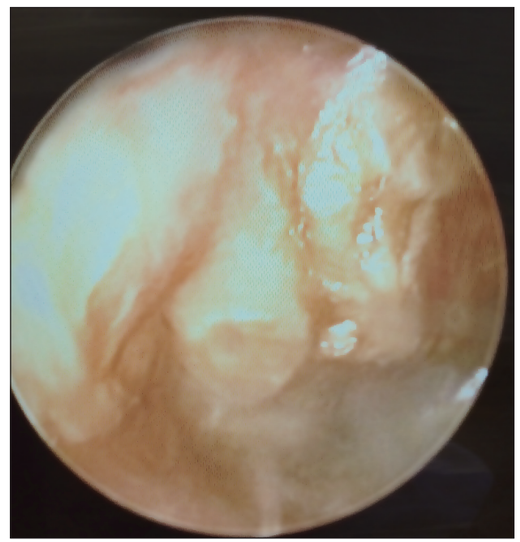


Figure 2: *Right acute otitis media.*

Table 4: House-Brackmann facial nerve grading system				
Grade	**Characteristics**			
	Gross	**Forehead**	**Eye**	**Mouth**
I	**Normal function**			
II	Slight weakness	Moderate to good function	Complete closure without effort	Slight weakness on maximal effort
III	Obvious weakness but not disfiguring Normal symmetry at rest	Slight to moderate function	Complete closure with effort	Slight weakness on maximal effort
IV	Obvious weakness Disfiguring asymmetry	No function	Incomplete closure	Asymmetry on maximal effort
V	Barely perceptible motion Asymmetry at rest	No function	Incomplete closure	Slight movement
VI	**No function**			

A detailed head and neck examination should be performed to exclude parotid tumours or lesions. Thorough examination of the ear should be performed looking for any discharge, vesicles and / or granulations of the ear canal and to rule out any middle ear pathology including acute otitis media (figure 2), cholesteatoma or glomus tumours. A triad of ipsilateral facial nerve paralysis, auricular pain, and vesicles in the external auditory canal and on the pinna is typical for Ramsay Hunt Syndrome Type II[19,20].

Full cranial nerve examination should be performed to identify a central cause of the facial nerve palsy. Further examination of the peripheral nervous system may also be required. Bilateral facial nerve palsy suggests neurological causes such as multiple sclerosis and Guillain-Barre syndrome or infective causes such as Lyme disease[21].

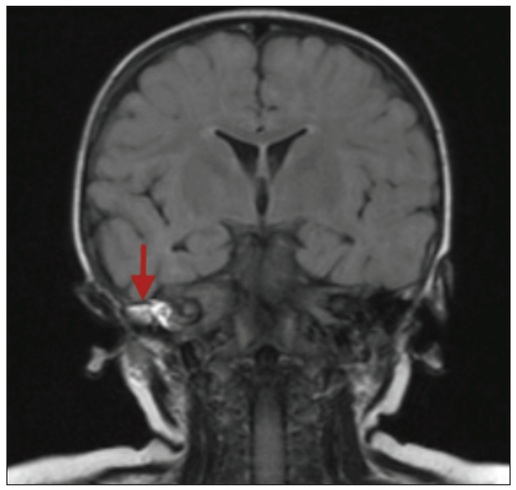


Figure 3: *MRI scan of a child who presented with a right LMN facial nerve palsy showing right petrous apex metastatic neuroblastoma (arrow).*

Investigations

The choice of investigations depends on the potential cause, associated symptoms, and mode of presentation. A full blood count and film should be undertaken to rule out rare malignant causes such as leukaemia. Lyme disease serology testing for Borrelia Burgdorferi is of great importance especially in areas with a high prevalence[22]. In the presence of otological symptoms and /or signs, a pure tone audiogram and tympanogram are required to identify the nature and severity of any associated hearing loss[11,15]. Children with normal otological findings and without any hearing loss may not need further audiological investigation.

Imaging

Radiological investigation is indicated in all patients with upper motor neurone signs as part of the initial workup[21]. These children should be referred urgently to a paediatric neurologist for further investigation. In those with lower motor neurone lesions indications for imaging include; a progressive facial nerve palsy over one month, no signs of recovery after six weeks, recurrent or bilateral facial nerve palsies and involvement of other cranial nerves[12,13,14,15].

If a child presents with an asymmetric hearing loss or positive ear signs, then imaging should be performed. Magnetic resonance imaging (MRI) (figure 3) is the investigation of choice to rule out any neurological cause or a vestibular schwannoma (acoustic neuroma). Computerised Tomography scanning (CT) (figures 4, 5 & 6) may be required when bony erosion or chronic suppurative otitis media is present.

Electrophysiological Testing

Electrophysiological testing may prove useful, but interpretation very much depends on the operator[23,24]. Electrophysiological tests employed are nerve excitability

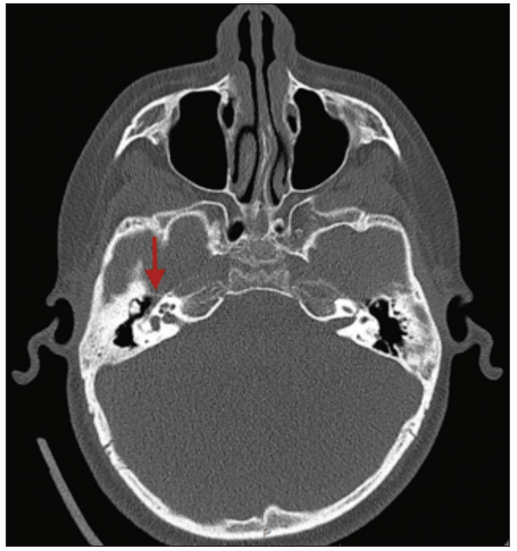


Figure 4: *CT of a patient who presented with a right LMN facial nerve palsy showing a cholesteatoma with a dehiscent facial nerve bony canal (arrow).*

testing, maximal stimulation testing, electromyography and electroneuronography. These tests are carried out at specialised centres and are useful in determining the prognosis of the facial nerve palsy.

If there is uncertainty in diagnosis urgent multidisciplinary input is suggested including otorhinolaryngology, paediatric (general, neurology, paediatric infectious diseases and immunology), ophthalmology and radiology.

Bell's palsy is a diagnosis of exclusion, once all possible causes have been ruled out. The prevalence of Bell's palsy in children varies between 9-50%[25].

Management

The management of paediatric facial nerve palsy depends on the aetiology. A complete facial nerve palsy at presentation correlates with a poor outcome when compared to patients presenting with a partial palsy. Treatment is directed towards the management of identifiable causes.

In the paediatric age group, treatment strategies should employ a multidisciplinary team approach, including specialists from otorhinolaryngology, paediatrics, neurology, ophthalmology, radiology, oromaxillofacial surgery, facial plastic subspecialist surgery, speech and language therapy and physiotherapy. Management comprises general, medical, and surgical treatment.

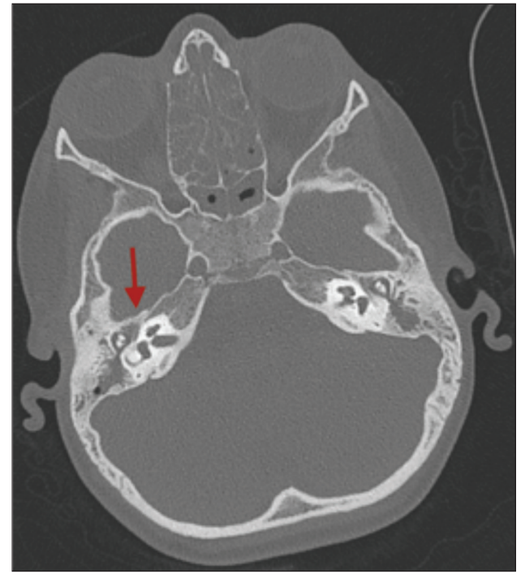


Figure 5: *CT scan of a child who presented with a right acute otitis media with right LMN facial nerve palsy with an intact bony canal showing a right middle ear effusion (arrow).*

In our experience a practical flow chart providing a framework for the management of paediatric facial nerve palsy, produced by the multidisciplinary team at Southampton Children's Hospital has proved very useful (figure 7, reproduced with kind permission from www.PIER.uhs.nhs.uk).

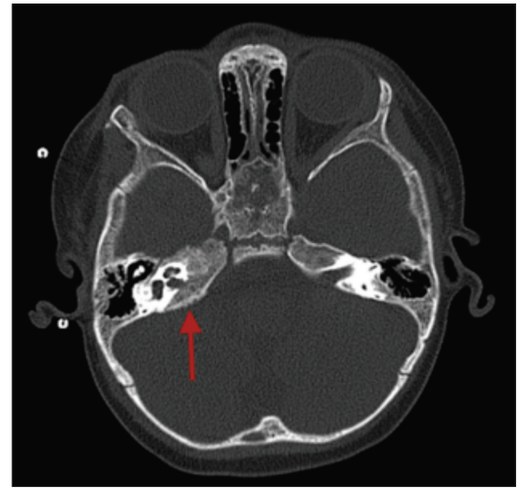


Figure 6: *CT scan of of a child who presented with a right LMN facial nerve palsy showing right petrous apex metastatic neuroblastoma (arrow).*

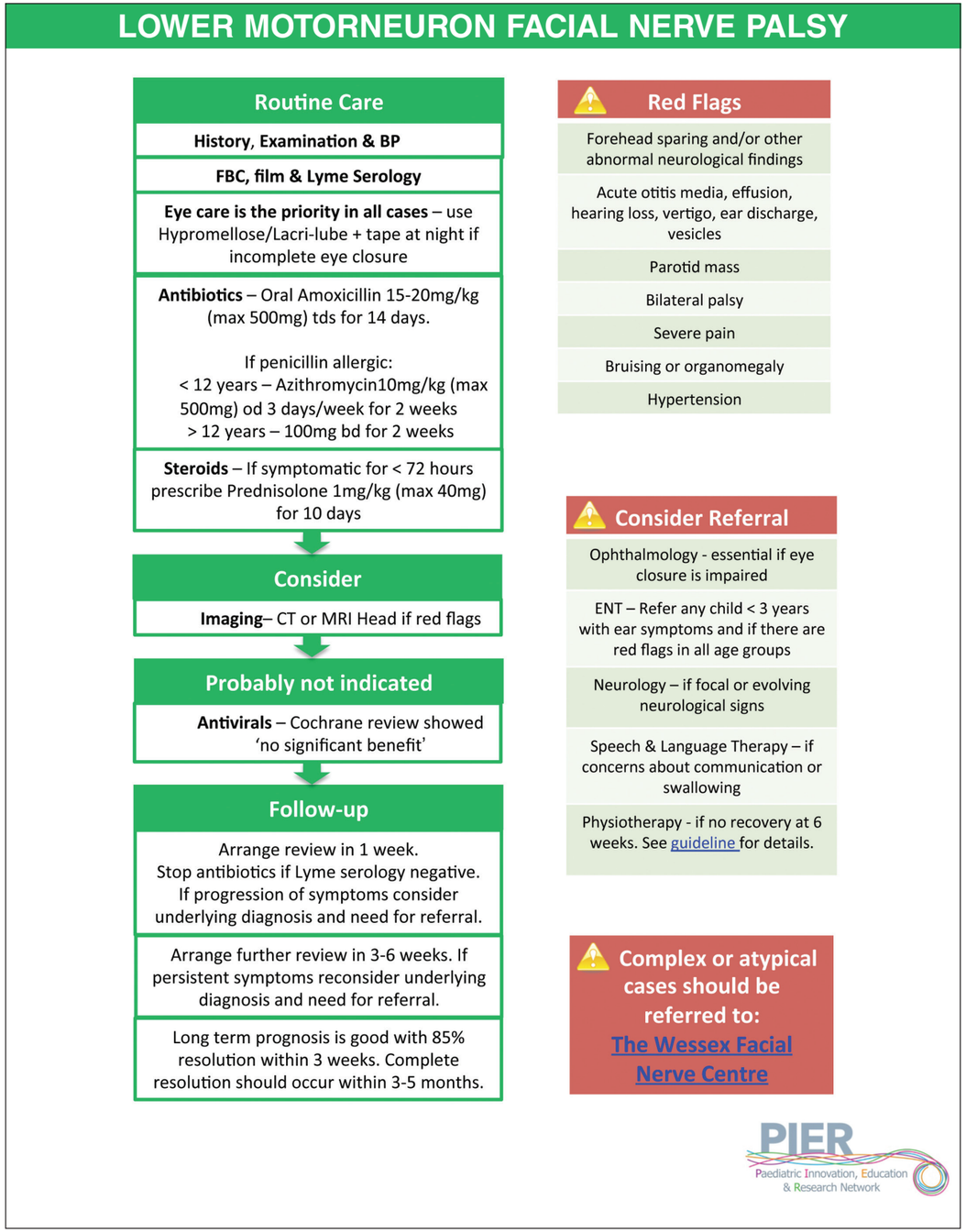


Figure 7: *Flow chart for the management of paediatric facial nerve palsy (reproduced with kind permission from www.PIER.uhs.nhs.uk).*

Eye care

If there is incomplete eye closure patients should be referred to ophthalmology and given eye protection advice. This includes taping the eye at night (figure 8), eye patch and artificial tears or lacri-lube ointment at night to prevent corneal ulceration.

Medical management

The majority of idiopathic cases of facial nerve palsy (Bell's Palsy) recover spontaneously. There is a lack of high quality evidence for the management of facial nerve palsy in children, most being inferred from adult studies. There is no clear evidence that children treated with steroids do better but as this has been found in adults, steroids are given (e.g. prednisolone 1-2mg/kg, maximum 40mg) for ten days duration[14,21,26,27].

In certain regions of the UK, for example the New Forest, Lyme disease is particularly prevalent. This caused 50% of LMN paediatric facial nerve palsy cases in our local 5-year review. Our local policy guideline recommends antibiotic treatment for all children whilst awaiting Lyme serology. The choice and dosage of the antibiotic depends on age. Amoxicillin three times daily for 14 days (15-20mg/kg) is recommended for children under eight years of age. Doxycycline 1-2mg/kg twice daily for 14 days is recommended for children equal to or older than eight years of age.

Children with a definite diagnosis of Ramsay Hunt Syndrome should be treated with acyclovir (>two years old) or valacyclovir (>12 years old) to improve the chance of spontaneous recovery[28].

Surgical management

Surgical management of paediatric facial nerve palsy (LMN) depends the cause. In acute infective cases such as acute otitis media, myringotomy, +/-grommet insertion, +/- cortical mastoidectomy should be considered[29,30]. Chronic suppurative otitis media with active squamous disease (cholesteatoma) requires urgent mastoid exploration and facial nerve decompression by a senior otologist. Vestibular schwannomas (acoustic neuromas) or any cerebellopontine angle tumours should be referred to the skull base MDT for further management.

There are no explicit algorithms for the optimal surgical management of acute facial nerve palsy in the literature. Gantz et al (1999) recommended performing facial nerve decompression in patients with > 90% loss on electrical activity on electroneuronography (ENoG) testing[31]. However, the participants in this study were adults. In acute paediatric facial nerve palsy, almost 100% of children recover spontaneously within a year, therefore

Figure 8: *Eye care; eye tape and lacri-lube tube.*

surgical decompression of the facial nerve is not generally recommended, although there are no controlled trials to validate this[32,33].

In traumatic cases however, primary repair of the nerve has resulted in the best outcomes both aesthetically as well as functionally. In the paediatric age group due to the developing neural systems, early surgical intervention leads to better regeneration when compared to adults[34,35]. Performing direct end-to-end anastomosis in a tensionless repair or using a cable graft from the greater auricular nerve or sural nerve when tensionless repair is not achievable is advocated[3]. Reanimation procedures are considered for chronic irreversible causes of facial nerve palsy. The choice of reanimation procedure depends on the degree of damage and period of weakness for chronic irreversible causes. These procedures may be dynamic (when facial nerve palsy duration <18 months) or static (when facial nerve palsy duration >18 months).

Free muscle flaps or local rotational flaps are used for dynamic reanimation procedures. Ipsilateral/contralateral facial nerve, masseteric branch of the trigeminal nerve or sural nerves are used for innervation of the free muscle flaps[36,37]. Dynamic reanimation procedures are aimed mainly at regaining the tone of the ocular and oral muscles, which greatly impacts on the functional and cosmetic results in children.

Static procedures are used where dynamic procedures have failed or cannot be used. Lateral tarsorrhaphy and a gold/ platinum weight for the upper eyelid and medial canthopexy for the lower eyelid are mainly used in

adults[38,39]. These are generally avoided unless other options have failed, as there is limited evidence of when to implement static procedures[40].

Rehabilitation

Children with facial nerve palsy may also suffer nutritional deficiencies due to reduced sucking efforts and loss of oromotor tone due to the involvement of the facial muscles[9,11,21,41,42]. Active rehabilitation may be required in cases of severe synkinesis and hemifacial spasms. Botox can be administered, but the effect is temporary and frequent injections are necessary. Botox may result in facial hypersensitivity and side effects including dysphagia. Biofeedback exercises have been suggested but no clear evidence of their effectiveness exists in the literature[43,44,45,46].

Prognosis

The prognosis of paediatric facial nerve palsy depends on the time of presentation, cause, severity and progression. Isolated unilateral acute onset facial nerve palsy with an identifiable cause has a better prognosis than that associated with other cranial nerve palsies. The success of treatment depends on patient selection and on a multidisciplinary approach.

Conclusion

Paediatric facial nerve palsy is distressing for children and their carers. A thorough history and examination guides further investigation and treatment. It is essential to differentiate LMN (often idiopathic) from UMN (likely central cause) cases. A structured approach to the history, examination, investigation and management will aid clinicians in this challenging condition. A patient pathway provides a framework for optimal management in these cases. A multidisciplinary multiprofessional approach including carers is essential. The majority of acute onset LMN facial nerve palsy cases have an excellent prognosis if identified early. For long-term facial palsy, dynamic reanimation procedures can result in good functional and cosmetic outcome.

References

1. Van Buskirk, C. The seventh nerve complex. J Comp Neurol. 1945; 82: 303–333.
2. Gasser RF. The development of the facial nerve in man. Ann Otol Rhinol Laryngol. 1967; 76:37–56.
3. Barr JS, Katz KA, Hazen A. Surgical management of facial nerve paralysis in the pediatric population. J Ped Surg. 2011; 46:2168-2176.
4. Ozkale Y, Erol İ, Saygı S. Overview of pediatric peripheral facial nerve paralysis: analysis of 40 patients. J Child Neurol. 2015; 30:193-199.
5. Rowlands S, Hooper R, Hughes R. The epidemiology and treatment of Bell's palsy in the UK. Eur J Neurol. 2002; 9:63-67.
6. Sataloff RT. Embryology and Anomalies of the Facial Nerve and Their Surgical Implications. New York, NY: Raven Press; 1991.
7. Ciorba A, Corazzi V, Conz V. Facial nerve paralysis in children. World J Clinical Cases. 2015; 3:973-979.
8. Al Tawil K, Saleem N, Kadri H. Traumatic facial nerve palsy in newborns: is it always iatrogenic? Am J Perinatol. 2010; 27:711-713.
9. Pavlou E, Gkampeta A, Arampatzi M. Facial nerve palsy in childhood. Brain Dev. 2011; 33:644-650.
10. Derin S, Derin H, Sahan M. A pediatric case of Ramsay hunt syndrome. Case Reports in Otolaryngology. 2014; 2014:3 pages.
11. Finsterer J. Management of peripheral facial nerve palsy. Eur Arch Otorhinolaryngol. 2008; 265:743-752.
12. Zieli-ski R, Kobos J, Zakrzewska A. Parotid gland tumors in children - pre- and postoperative diagnostic difficulties. Pol J Pathol. 2014; 65:130-134.
13. Kang HM, Kim MG, Hong SM. Comparison of temporal bone fractures in children and adults. Acta Otolaryngol. 2013; 133:469-474.
14. Tsai HS, Chang LY, Lu CY, Lee PI. Epidemiology and treatment of Bell's palsy in children in northern Taiwan. J Microbiol Immunol Infect. 2009; 42:351-356.
15. Dushyant B. Management of facial nerve palsy in newborn period. UK: Nottingham Neonatal Service - Clinical Guidelines (No. F16), 2013. Available at https://www.nuh.nhs.uk/handlers/downloads.ashx?id=66707 (accessed on 26th June 2016).
16. House JW, Brackmann DE. Facial Nerve Grading System. Otolaryngol Head Neck Surg. 1985; 93:146-147.
17. Ross BG, Fradet G, Nedzelski JM. Development of a sensitive clinical facial grading system. Otolaryngol Head Neck Surg. 1996;114:380-386.
18. Berg T, Jonsson L, Engström M. Agreement between the Sunnybrook, House-Brackmann, and Yanagihara Facial Nerve Grading Systems in Bell's Palsy. Otol Neurotol. 2004; 25:1020-1026.
19. Sweeney CJ, Gilden DH. "Ramsay Hunt Syndrome". J. Neurology, Neurosurgery and Psychiatry, 2001; 71: 149–154.
20. Hunt JR. "On herpetic inflammations of the geniculate ganglion: a new syndrome and its complications". J Neurol Neurosurg Psych. 1907; 34: 73–96.
21. Clark GD, Nordli DR, Dashe JF. Facial nerve palsy in children. Wolters Kluwer UpToDate® 2014. Available at http://www.uptodate.com/contents/facial-nerve-palsy-in-children (accessed on 30th June 2016).
22. Esposito S, Bosis S, Sabatini C. Borrelia Burgdorferi infection and Lyme disease in children. Int J Infect Dis. 2013; 17:153-158.
23. Fisch U, Ruttner J. Pathology of intratemporal tumors involving the facial nerve. Fisch U (Ed). Facial Nerve Surgery. Zurich: Kugler/ Aesculapius Zurich; 1977: pages 448-456.
24. Ruboyianes J, Adour KK, Santos D, et al. The maximal stimulation and facial nerve conduction latency tests: Predicting the outcome of Bell's palsy. Laryngoscope. 1994; 104(suppl):1-6.
25. Cook S, Macartney K, Rose C, Hunt P. Lyme Disease and Seventh Nerve Paralysis in Children. Am J Otolaryngol. 1997; 18;320-323.
26. Wang CH, Chang YC, Shih HM. Facial palsy in children: emergency department management and outcome. Paediatr Emerg Care. 2010; 26:121-125.
27. Shih WH, Tseng FY, Yeh TH. Outcomes of facial palsy in children. Acta Otolaryngol. 2009; 129 915-920.
28. Kansu L, Yilmaz I. Herpes zoster oticus (Ramsay Hunt syndrome) in children: case report and literature review. Int J Paediatr Otorhinolaryngol. 2012; 76:772-776.
29. Wanna GB, Dharamsi LM, Moss JR, et al. Contemporary management of intracranial complications of otitis media. Otol Neurotol. 2010; 31:111-117.
30. Popovtzer A, Raveh E, Bahar G, et al. Facial palsy associated with acute otitis media. Otolaryngol Head Neck Surg. 2005; 132:327-329.
31. B.J. Gantz, J.T. Rubinstein, P. Gidley, et al. Surgical management of Bell's palsy. Laryngoscope. 1999; 109:1177–1188.
32. S.A. Marenda, J.E. Olsson The evaluation of facial paralysis. Otolaryngol Clin North Am. 1997; 30:669–682.
33. R. Micheli, C. Telesca, F. Gitti, et al. Bell's palsy: diagnostic and therapeutical trial in childhood. Minerva Paediatr. 1996; 48:245–250.
34. B. McMonagle, A. Al-Sanosi, G. Croxson, et al. Facial schwannoma: results of a large case series and review. J Laryngol Otol. 2008; 122:1139–1150.
35. J.H. Clark, P.C. Burger, D.K. Boahene, et al. Traumatic facial nerve neuroma with facial palsy presenting in infancy. Otol Neurotol. 2010; 31:813–816.
36. Lee EI, Hurvitz KA, Evans GR, et al. Cross-facial nerve graft: past and present. J Plastic Reconstr Aesthet Surg. 2008; 61:250-256.
37. Rab M, Haslik W, Frey M. Free functional muscle transplantation for facial reanimation: experimental comparison between the one- and two-stage approach. Handchir Mikrochir Plast Chir. 2010; 42: 115-123.
38. Bergeron CM, Moe KS. The evaluation and treatment of upper eyelid paralysis. Facial Plastic Surgery, 2008; 24:220-30.
39. Bergeron CM, Moe KS. The evaluation and treatment of lower eyelid paralysis. Facial Plast Surg. 2008; 24:231-241.
40. Hadlock T. Facial paralysis: research and future directions. Facial Plast Surg. 2008; 24:260-267.
41. Zandian A, Osiro S, Hudson R. The neurologist's dilemma: a comprehensive clinical review of Bell's palsy, with emphasis on current management trends. Med Sci Monit. 2014; 20:83-90.
42. Banks CA, Hadlock TA. Pediatric facial nerve rehabilitation. Facial Plast Surg Clin North Am. 2014; 22:487-502.
43. Terzis JK, Karypidis D. Therapeutic strategies in post-facial paralysis synkinesis in pediatric patients. J Plastic Reconstr Aesthet Surg. 2012; 65:1009-1018.
44. Pourmomeny AA, Asadi S. Management of synkinesis and asymmetry in facial nerve palsy: a review article. Iran J Otorhinolaryngol. 2014; 26:251-256.
45. McCaul JA, Cascarini L, Godden D. Evidence based management of Bell's palsy. Br J Oral Maxillofac Surg. 2014; 52:387-391.
46. de Almeida JR, Guyatt GH, Sud S. Management of Bell palsy: clinical practice guideline. CMAJ. 2014; 186:917-922.

Paediatric sleep physiology and sleep disordered breathing

Gahleitner F[1], **Hill CM**[2] and **Evans HJ**[3]
[1]Department of Paediatric Respiratory Medicine, University Hospitals of Southampton, UK
[2]Division of Clinical Neurosciences, School of Medicine, University of Southampton, UK

Correspondence:
Dr Florian Gahleitner, MRCPH DM.
Department of Paediatric Respiratory Medicine, Southampton General Hospital,
Tremona Road, Southampton SO16 6YD
Email: florian.gahleitner@doctors.org.uk

Abstract
Good quality sleep is crucial for physical and mental health in children. Sleep disordered breathing is increasingly being recognised as having detrimental effects on neurocognitive development, academic achievements, behaviour, cardiovascular and metabolic health. A good understanding of sleep physiology, sleep architecture including sleep stages, control mechanisms of sleep, and developmental aspects and influences on sleep enables the clinician to embark on a more focussed investigative process and arrive at a more timely diagnosis. Parasomnias usually occur in the first third of the night and can occur either isolated or in the context of a snoring child with obstructive sleep apnoeas due to overall poor quality sleep. Obstructive events predominantly occur during REM sleep (when skeletal atonia occurs) and therefore more during the second half of the night. Sleep history taking is important but has its limitations and the diagnostic process therefore often relies on further tools such as polysomnography or polygraphy studies.

J ENT Masterclass 2016; 9 (1): 50 - 56.

Key words
Sleep architecture, Sleep disordered breathing, Polysomnography, Parasomnia

Sleep
Sleep is a reversible natural state of reduced awareness of, and selective responsiveness to the environment. Arousals from sleep are clearly important in situations of external danger, or, indeed, with intrinsic problems such as severe obstructive sleep apnoea (OSA) where arousals triggered by abnormal levels of oxygen or carbon dioxide are crucial to enable protective airway responses. Sleep is not one entity but rather composed of multiple brain states called sleep stages, defined by neurophysiological parameters; surface electrode brain activity (EEG), muscle tone and eye movements. Each sleep stage orchestrates changes in multiple dimensions of physiology, for example muscle tone and autonomic nervous system activation[1].

Sleep stages
The EEG of wakefulness is a low amplitude EEG with fast, irregular beta waves that change to alpha waves during eye closure. Sleep, as defined by neurophysiological parameters, is characterised by non-rapid eye movement (NREM) and rapid eye movement (REM) sleep (Table 1). Following sleep onset, sleep progresses through the three stages of NREM sleep (I, II and III) first and reaches the first period of REM sleep after around 80-100 minutes. There are usually around four or five cycles of REM sleep during an 8 hour period interspersed with cycles of NREM sleep (Figure 1). During REM sleep generalised atonia of skeletal muscles occurs. This increases pharyngeal collapsibility and therefore the likelihood of obstructive events increases[2,3]. The length of individual REM periods increases across the night and in children over one and adults the majority of REM occurs in the second half of the night. This is important in the context of parental reporting of signs and symptoms of sleep disordered breathing (SDB) in children. While parents may be vigilant during the early part of their child's sleep they are more likely to miss, and therefore underreport, more significant symptoms such as snoring or apnoeas in the latter part of the night. Secondly in the evaluation and scoring of sleep studies: children who only achieve a short night's sleep will sacrifice relatively more REM sleep. As SDB is defined according to an apnoea/hypopnea index (AHI)[4] where the denominator is total hours of sleep this will affect the severity grading of scoring.

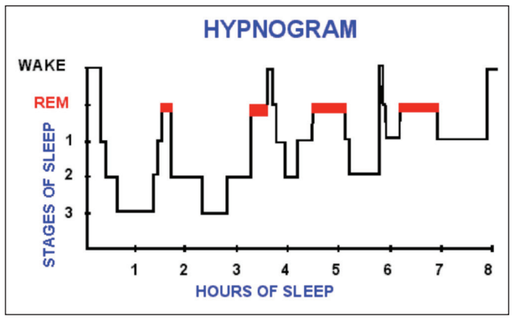


Figure 1: *Hypnogram*

Table 1: Characteristics of the NREM and REM sleep stages

	Non-REM			REM
	Stage I	**Stage II**	**Stage III**	
Percentage of total sleep	5%	45-55%	15-20%	20-25% (in infants up to 50%)
Duration per sleep cycle	generally less than 10 min	initially 10-25 min, then increasing in length with each cycle	20-40 min in first cycle, then decreasing in length and disappearing in later cycles	initially only 1-5 min; progressively occupying longer periods of the sleep cycle
Description	transitional stage between drowsy wakefulness and sleep onset	signifies the onset of sleep	known as deep / slow wave sleep that occupies much of first half of night; occurs in 2-3 cycles	occurs in repeated cycles during second half of sleep period
EEG	low voltage, mixed frequency, theta waves (4-7 Hz), Vertex waves common; scored when <50% of an epoch contains alpha waves	sleep spindles (12-14 Hz for 0.5-1.5 s) and K-complexes (high amplitude, biphasic wave of ≥ 0.5 s)	delta waves of low frequency (0.5-2 Hz), high amplitude (>75 μV); scored when present for >20% of the epoch	low voltage mixed frequency, sawtooth waves, theta waves and slow alpha waves also present
Eye movements	slow rolling eye movements	no eye movements	no eye movements	characteristic eye movements
Muscle tone	hypnic jerks and reduced muscle tone	muscle tone drops further	minimal whole body movement but muscle tone preserved	atonia of skeletal muscles
Conscious awareness	some limited conscious awareness; low arousal threshold	loss of conscious awareness; more intense stimulus required for arousal	lack of awareness; extreme resistance to arousal	vivid dreams

Stage III sleep, conversely, occupies most of the first half of night but tends to disappear from later cycles when Stage II sleep increases. NREM parasomnias during Stage III sleep (e.g. confusional arousals and night terrors) typically occur therefore in the first half of the night. The absolute sleep requirements (hours per day) and sleep architecture (duration and frequency of different sleep stages) change throughout life (Figure 2).

In the absence of EEG, Electrooculography (EOG) and Electromyography (EMG) measures of sleep stage, other correlates are used as surrogate markers to determine NREM (quiet) and REM (active) sleep. These include increased variability in respiration and heart rate during REM sleep.

Control of sleep
Two principle interacting mechanisms control our need for sleep. First of all the so called homeostatic drive (process S), which is a time dependent, linear and cumulative process. It depends on prior sleep and wakefulness and reflects the urge for sleep; it rises during times of waking, decreases during sleep and builds up with sleep deprivation. Secondly, the intrinsic circadian drive (process C) which is controlled by the "biological clock" located in the suprachiasmatic nucleus of the hypothalamus. The intrinsic circadian drive is synchronised with environmental cues, such as seasonally changing light-dark cycles, environmental sounds and meal times. Light is the most significant of these. It synchronises the intrinsic circadian clock to the 24 hour day of the surrounding environment[1]. Exposure to blue light and white light late in the day can suppress endogenous melatonin secretion and delay bedtimes. A large cross-sectional general community-based study confirmed the widespread daytime and bedtime use of electronic devices and the associated risks of short sleep duration, long sleep onset latency and overall sleep deprivation in adolescents[5]. Interestingly, and

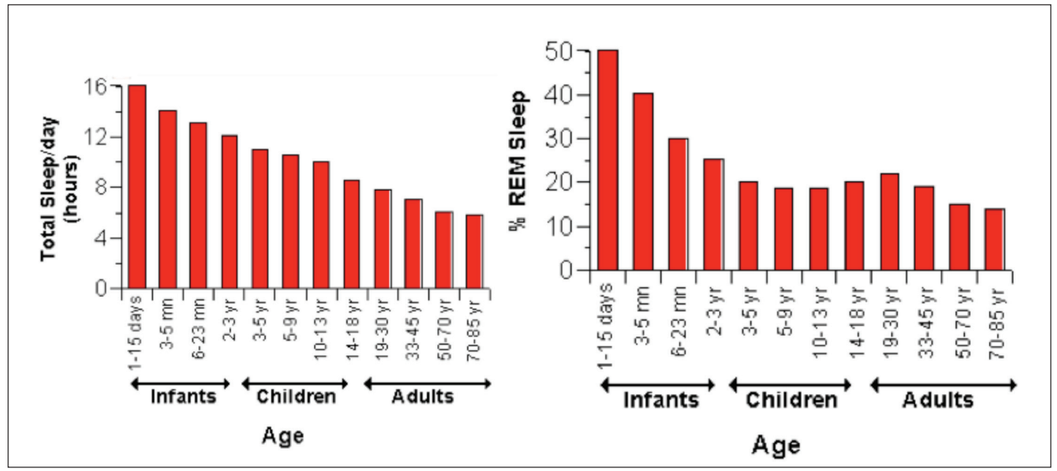


Figure 2: *Developmental differences in total sleep time per day and percentage of REM sleep. Graphs reproduced with permission from Dr Eric H Chudler, http://faculty.washington.edu/chudler/neurok.html based on data from: Roffward, H.P., Muzio, H.P., & Dement, W.C. (1966). Ontogenetic development of the human sleep-dream cycle. Science, 152, 604-619.*

at first look counterintuitively, the circadian drive for wakefulness is at its peak just before bedtime and is lowest in the early morning before waking. The rationale behind this lies in the interaction between processes C and S. As the homeostatic sleep pressure increases at the end of a day, the body requires a stronger intrinsic signal promoting wakefulness. On the other hand, as the homeostatic urge for sleep disappears gradually during night-time sleep, changes in the circadian stimulus balance out to maintain sleep.

Why (good) sleep matters

Sleep is a process during which the brain is active. It affects both mental and physical health. Good quality sleep is crucial for the normal functioning of the body and its systems down to the level of gene expression and DNA synthesis. It forms an essential part of maintaining homeostatic regulatory and repair mechanisms. Poor quality sleep, which may be due to inadequate time in bed or sleep disorders such as OSA have potentially wide-ranging negative effects on many aspects of physical and psychological well-being as well as on aspects of behaviour and academic performance.

Bryant *et al*. have reviewed studies looking at the reciprocal relationship between sleep, infections and immunity and highlighted that many components of the immune system show, like sleep, circadian rhythmicity[6]. Sleep restriction of 4 hours per night prior to influenza vaccination was associated with a 50% reduction in antibody titres 10 days post vaccination when compared to usual sleep controls in an adult study[7]. A variety of bacterial and viral infections are associated with an increase in sleep duration[8] and infants in the recuperation phase from upper respiratory tract infections often show impaired arousal from sleep[9], which also underlines the important healing and anabolic functions of sleep.

Poor quality sleep is also associated with other conditions. For example there is a linear relationship between total sleep time and obesity in children aged < 10 years. Those sleeping for less than 10 hours have a 60% increased risk for being obese or overweight. Each additional hour of sleep decreased the risk by 9%[10]. Cross-sectional studies demonstrate an increased risk of the metabolic syndrome in association with increasing severity of obstructive sleep apnoea syndrome (OSAS) in obese children[11,12]. Furthermore, OSA in children is linked to cardiovascular complications such as hypertension and blunting of the nocturnal fall in blood pressure[13,14]. Investigating children with hypertension who also have clinically benign sounding snoring for OSAS, has been recommended[15].

Jackman et al. speak of a "window of opportunity" to intervene with treatment in their study when comparing behavioural and cognitive functions of preschool children with and without SDB[16]. While two behavioural questionnaires revealed impairments in this specific domain in primary snoring and mild OSA compared to normal controls, cognitive performance did not appear affected in this age-group[16]. This is in contrast to a study of 137 older children (aged 7-12) in which a range of tests assessing intellectual ability, executive skills and academic function identified a number of neurocognitive impairments compared to controls independent of the severity of the SDB[17]. There is now incontrovertible evidence that SDB affects cognition and behaviour and that children with more severe OSA (AHI > 5/hr total sleep time) appear to experience considerable neurocognitive impairment[18]. The postulated mechanisms include sleep disruption and intermittent hypoxaemia which influence restorative processes that usually occur in sleep[19]. A large meta-analysis of 86 studies (almost 36,000 children aged 5-12) demonstrated significant positive correlation between sleep duration and cognitive performance. Sleep deprivation was associated with cognitive deficits and more behavioural problems[20].

Sleep disorders in children

Broadly defined, a sleep disorder is a condition or process that interferes with a child's previously established sleep-wake cycle. The International Classification of Sleep Disorders (3) defines the following categories[21]:

1. Insomnias: primary sleep disorders that cause either a. difficulty getting off to sleep, b. difficulty maintaining sleep, or c. non-restorative sleep
2. Hypersomnias (increased need/amount of sleep or inability to stay awake)
3. Parasomnias (e.g. night terrors, sleep walking)
4. Circadian sleep-wake rhythm disorders (disturbance of biological clock)
5. Sleep related movement disorders (e.g. restless leg syndrome and periodic limb movement disorder)
6. Sleep related breathing disorders

In the following we will focus on the two categories of sleep disorders that are common in paediatric clinical practice and appear most relevant to an ear, nose and throat (ENT) focussed readership: Sleep disordered breathing and Parasomnias. These two categories can also occur in one child at the same time as OSA can trigger parasomnias through the poor quality sleep mechanism.

Sleep disordered breathing

Increased upper airway resistance and pharyngeal collapsibility lead to snoring and increased respiratory effort, the hallmarks of obstructive SDB[22] which has a prevalence of 1-4% in the paediatric population[23]. Depending on the severity four clinical entities have been defined: Primary snoring, upper airway resistance syndrome, obstructive hypoventilation and obstructive sleep apnoea syndrome[24]. It is important to note that obstructive events and oxygen saturations below 90% rarely occur in normal children without SDB[25-27]. The Apnoea-Hypopnoea index (AHI) – the number of mixed/obstructive/central apnoeas and hypopnoeas per hour of total sleep time – is the most widely used and reported parameter to define the severity of SDB and informs the selection of the appropriate therapeutic intervention[4]. See summary of definitions and scoring criteria in table 2.

Unlike in adults the presentation of SDB in children is more varied[28], symptoms change with age, and individual symptoms by themselves are of limited value for a conclusive diagnosis. Using symptoms and physical examination alone for diagnosis can lead to over- or undertreatment in children[29]. Parental reports of frequent loud snoring, mouth breathing (leading to 'adenoid facies'), witnessed apnoeas, and restless sleep are associated with presence of obstructive SDB[24]. Attention deficit/hyperactivity symptoms[30] rather than excessive daytime sleepiness[31] appear to be more common in children with SDB. Nocturnal enuresis is linked to OSAS and improves after treatment[32]. Increased respiratory effort can lead to night sweating[33]. Tonsillar size (Brodsky score[34]) is weakly related to presence or severity of obstructive SDB; some studies however suggest no association[35,36]. A background of prematurity[37] and parental/sibling history of OSAS, adenotonsillectomy or adenotonsillar hypertrophy are important risk factors to be taken into account[38].

Some complex genetic medical conditions (e.g. Achondroplasia, Down syndrome, Prader-Willi syndrome), neuromuscular disorders (e.g. cerebral palsy, Duchenne muscular dystrophy), and syndromes with midface hypoplasia and/or mandibular hypoplasia (e.g. Apert syndrome, Pierre Robin sequence) are associated with an increased risk for obstructive SDB. Obesity is an important emerging independent risk factor for OSAS in children[39-41]. Importantly, adenotonsillectomy for OSAS in (normal and overweight) children leads to clinically significant weight gain which can place them at further risk for OSAS[42] and therefore weight reduction strategies need to be included in the long-term management of this patient group.

Risk factors for persistence of untreated OSAS are male sex, obesity, obstructive AHI>5[43,44], narrow maxilla (which can lead to crossbite and malocclusion)[45], and persistent tonsillar hypertrophy.

Objective investigations include flexible nasopharyngoscopy and lateral neck radiography. Cephalometry, computed tomography (CT) or magnetic resonance imaging (MRI) of the upper airways may be useful in selected patients. In comparison with nasopharyngoscopy cephalometry appears to underestimate

tonsillar size[46], while increased adenotonsillar size on lateral neck radiography potentially overdiagnoses OSAS in children[47]. Therefore lateral neck radiography is seldom used. While the gold standard diagnostic tool for obstructive SDB is in-laboratory polysomnography (PSG)[48] a recent guideline has suggested alternative use of (ambulatory) polygraphy and nocturnal pulse oximetry if PSG is not available[49,24]. The rules for scoring events in PSG or polygraphy are laid out in the recently updated AASM manual[4] (see also Table 2). A single diagnostic PSG study in typically developing children is sufficient as night-to-night variability is low[50].

Parasomnias

Parasomnias are "undesirable behavioural, physiological, or experiential events that accompany sleep"[51]. They can be divided into NREM and REM related parasomnias. REM parasomnias are rare in childhood and will not be discussed further here. In NREM parasomnias, behaviours are triggered by activation of functional groups of neurons called central pattern generators (CPGs)[52, 53]. Essentially they represent a state dissociation within the brain between wake and NREM sleep. They are usually brief but can last up to 30-40 minutes. Diagnostic criteria include: (ICSD III)[21].

Table 2: Definitions and scoring criteria according to AASM Manual4

Respiratory Events		Definition and findings on PSG/polygraphy
Apnoea		cessation of airflow over two or more respiratory cycles (a time in seconds is not applicable to children due to large variations in respiratory rate in different age groups)
	Obstructive apnoea	obstructive apnoea on PSG is scored where there is at least a 90% drop in airflow compared to pre-event baseline for at least 90% of the duration of the event, with continued effort in chest and abdomen
	Central apnoea	absent inspiratory effort (chest and abdominal bands flat) throughout the respiratory event; associated with arousal, an awakening or oxygen desaturation of at least 3% and or is 20 seconds or longer
Hypopnoea		there is a reduction in airflow of at least 30% for at least 90% of the duration of the event, lasting at least two missed breaths, with arousal and/or oxygen desaturation of at least 3% with ongoing respiratory effort

A. Recurrent episodes of incomplete awakening from sleep

B. Inappropriate/absent response to direction during an episode

C. Limited or no cognition during an episode and NO dream recall on waking

D. Partial/complete amnesia for the event

E. Not better explained by any other phenomena

NREM parasomnias typically occur after the first sleep cycle and comprise a family of disorders (with some overlap) including: sleep terrors, confusional arousals, sleep walking. All involve incomplete arousal from deep NREM sleep with variable levels of autonomic nervous system activation. The developing brain is particularly vulnerable to parasomnias and they typically appear in the pre-school years and may last till puberty. Occasionally they may persist to adulthood. A genetic locus (chromosome 20q12-q13.12) for sleepwalking has been found by genome-wide multipoint parametric linkage analysis[54].

Sleep terrors typically occur occasionally in 3% of children aged 3-10 years and are characterized by abrupt waking in association with intense fear, loud vocalisation, and autonomic system activation leading to agitation, flushed appearance and sweating. Children do not respond to calming efforts, they may become more agitated and disorientated when woken, and may even leave their bed and run out of the room. Children, unlike adults, with sleep terrors do not have a higher incidence of psychopathology. Factors such as sleep deprivation, fever, or certain medications can be trigger factors[21]. Sleep terrors can be dramatic and terrifying events for parents but are not usually recalled by children themselves.

Confusional arousals usually occur in toddlers, and become less common in older children. They are characterised by a child sitting up in bed, appearing distressed, crying and vocalising. Again attempts to comfort may increase agitation. Confusional arousals are not associated with higher autonomic activity. Behaviours and prognosis are usually benign.

During sleepwalking a series of complex motor behaviours are instigated that lead to walking while the child is asleep. Eyes are open, perceptual elements of the environment can be remembered, however usually amnesia exists. Sleepwalking most commonly occurs after four years and peaks around twelve years of age. A pre-disposing factor is sleep deprivation which may be environmental or behavioural but could be exacerbated by OSA.

Treatment approaches include ensuring the safety of the child and providing reassurance about the overall benign nature of NREM parasomnias. OSA as a factor that disrupts sleep should be excluded and sleep quality needs to be improved. If NREM parasomnias happen very regularly anticipatory wakening may be attempted.

Conclusion

Sleep affects mental and physical health and poor quality sleep and sleep deprivation have far reaching consequences for the affected child. Knowledge of the basics of sleep physiology and SDB in children, the important aspects and limitations of sleep history taking, and the contribution of sleep studies in the diagnostic process is important to achieve the best possible outcome for the snoring child in the ENT clinic.

References

1. Hill C. Practitioner review: effective treatment of behavioural insomnia in children. J Child Psychol Psychiatry. 2011;52(7):731-40.
2. Marcus CL, McColley SA, Carroll JL, et al. Upper airway collapsibility in children with obstructive sleep apnea syndrome. J Appl Physiol (1985). 1994;77(2):918-24.
3. Gozal D, Burnside MM. Increased upper airway collapsibility in children with obstructive sleep apnea during wakefulness. Am J Respir Crit Care Med. 2004;169(2):163-7.
4. Berry RB, Brooks R, Gamaldo CE, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications.Version 2.2. Darien, IL: American Academy of Sleep Medicine; 2015.
5. Hysing M, Pallesen S, Stormark KM, et al. Sleep and use of electronic devices in adolescence: results from a large population-based study. BMJ Open. 2015;5(1):e006748.
6. Bryant PA, Trinder J, Curtis N. Sick and tired: Does sleep have a vital role in the immune system? Nat Rev Immunol. 2004;4(6):457-67.
7. Spiegel K, Sheridan JF, Van Cauter E. Effect of sleep deprivation on response to immunization. JAMA. 2002;288(12):1471-2.
8. Smith A. Sleep, Colds and Performance. In: Broughton RJ, Ogilvie R, editors. Sleep Arousal and Performance. Boston, MA: Birkhäuser; 1992. p. 233-42.
9. Horne RS, Osborne A, Vitkovic J, et al. Arousal from sleep in infants is impaired following an infection. Early Hum Dev. 2002;66(2):89-100.
10. Chen YC, Dong GH, Lin KC, Lee YL. Gender difference of childhood overweight and obesity in predicting the risk of incident asthma: a systematic review and meta-analysis. Obes Rev. 2013;14(3):222-31.
11. Redline S, Storfer-Isser A, Rosen CL, et al. Association between metabolic syndrome and sleep-disordered breathing in adolescents. Am J Respir Crit Care Med. 2007;176(4):401-8.
12. Verhulst SL, Schrauwen N, Haentjens D, et al. Sleep-disordered breathing and the metabolic syndrome in overweight and obese children and adolescents. J Pediatr. 2007;150(6):608-12.
13. Marcus CL, Greene MG, Carroll JL. Blood pressure in children with obstructive sleep apnea. Am J Respir Crit Care Med. 1998;157(4 Pt 1):1098-103.
14. Amin RS, Carroll JL, Jeffries JL, et al. Twenty-four-hour ambulatory blood pressure in children with sleep-disordered breathing. Am J Respir Crit Care Med. 2004;169(8):950-6.
15. National High Blood Pressure Education Program Working Group. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004;114(2 Suppl 4th Report):555-76.
16. Jackman AR, Biggs SN, Walter LM, et al. Sleep-disordered breathing in preschool children is associated with behavioral, but not cognitive, impairments. Sleep Med. 2012;13(6):621-31.
17. Bourke R, Anderson V, Yang JS, et al. Cognitive and academic functions are impaired in children with all severities of sleep-disordered breathing. Sleep Med. 2011;12(5):489-96.
18. Hunter SJ, Gozal D, Smith DL, et al. Effect of Sleep-Disordered Breathing Severity on Cognitive Performance Measures in a Large Community Cohort of Young School-Aged Children. Am J Respir Crit Care Med. 2016.
19. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. J Sleep Res. 2002;11(1):1-16.
20. Astill RG, Van der Heijden KB, Van Ijzendoorn MH, Van Someren EJ. Sleep, cognition, and behavioral problems in school-age children: a century of research meta-analyzed. Psychol Bull. 2012;138(6): 1109-38.
21. AASM, editor. International Classification of Sleep Disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
22. Katz ES, D'Ambrosio CM. Pathophysiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):253-62.
23. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):242-52.
24. Kaditis AG, Alonso Alvarez ML, Boudewyns A, et al. Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. Eur Respir J. 2016;47(1):69-94.
25. Marcus CL, Omlin KJ, Basinki DJ, et al. Normal polysomnographic values for children and adolescents. Am Rev Respir Dis. 1992;146(5 Pt 1):1235-9.
26. Traeger N, Schultz B, Pollock AN, et al. Polysomnographic values in children 2-9 years old: additional data and review of the literature. Pediatr Pulmonol. 2005;40(1):22-30.
27. Verhulst SL, Schrauwen N, Haentjens D, et al. Reference values for sleep-related respiratory variables in asymptomatic European children and adolescents. Pediatr Pulmonol. 2007;42(2):159-67.
28. Guilleminault C, Lee JH, Chan A. Pediatric obstructive sleep apnea syndrome. Arch Pediatr Adolesc Med. 2005;159(8):775-85.
29. Montgomery-Downs HE, O'Brien LM, Gulliver TE, Gozal D. Polysomnographic characteristics in normal preschool and early school-aged children. Pediatrics. 2006;117(3):741-53.
30. Perfect MM, Archbold K, Goodwin JL, et al. Risk of behavioral and adaptive functioning difficulties in youth with previous and current sleep disordered breathing. Sleep. 2013;36(4):517-25B.
31. Gozal D, Wang M, Pope DW, Jr. Objective sleepiness measures in pediatric obstructive sleep apnea. Pediatrics. 2001;108(3):693-7.
32. Jeyakumar A, Rahman SI, Armbrecht ES, Mitchell R. The association between sleep-disordered breathing and enuresis in children. Laryngoscope. 2012;122(8):1873-7.
33. So HK, Li AM, Au CT, et al. Night sweats in children: prevalence and associated factors. Arch Dis Child. 2012;97(5):470-3.
34. Brodsky L. Modern assessment of tonsils and adenoids. Pediatr Clin North Am. 1989;36(6):1551-69.
35. Nolan J, Brietzke SE. Systematic review of pediatric tonsil size and polysomnogram-measured obstructive sleep apnea severity. Otolaryngol Head Neck Surg. 2011;144(6):844-50.
36. Mitchell RB, Garetz S, Moore RH, et al. The use of clinical parameters to predict obstructive sleep apnea syndrome severity in children: the Childhood Adenotonsillectomy (CHAT) study randomized clinical trial. JAMA Otolaryngol Head Neck Surg. 2015;141(2):130-6.
37. Raynes-Greenow CH, Hadfield RM, Cistulli PA, et al. Sleep apnea in early childhood associated with preterm birth but not small for gestational age: a population-based record linkage study. Sleep. 2012;35(11):1475-80.
38. Alexopoulos EI, Charitos G, Malakasioti G, et al. Parental history of adenotonsillectomy is associated with obstructive sleep apnea severity in children with snoring. J Pediatr. 2014;164(6):1352-7.
39. Kohler M, Lushington K, Couper R, et al. Obesity and risk of sleep related upper airway obstruction in Caucasian children. J Clin Sleep Med. 2008;4(2):129-36.
40. Verhulst SL, Van Gaal L, De Backer W, Desager K. The prevalence, anatomical correlates and treatment of sleep-disordered breathing in obese children and adolescents. Sleep Med Rev. 2008;12(5):339-46.
41. Redline S, Tishler PV, Schluchter M, et al. Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems. Am J Respir Crit Care Med. 1999;159(5 Pt 1):1527-32.

42. Katz ES, Moore RH, Rosen CL, et al. Growth after adenotonsillectomy for obstructive sleep apnea: an RCT. Pediatrics. 2014;134(2):282-9.
43. Li AM, Zhu Y, Au CT, et al. Natural history of primary snoring in school-aged children: a 4-year follow-up study. Chest. 2013;143(3):729-35.
44. Marcus CL, Moore RH, Rosen CL, et al. A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med. 2013;368(25):2366-76.
45. Hultcrantz E, Lofstrand Tidestrom B. The development of sleep disordered breathing from 4 to 12 years and dental arch morphology. Int J Pediatr Otorhinolaryngol. 2009;73(9):1234-41.
46. Ritzel RA, Berwig LC, da Silva AM, et al. Correlation between nasopharyngoscopy and cephalometry in the diagnosis of hyperplasia of the pharyngeal tonsils. Int Arch Otorhinolaryngol. 2012;16(2):209-16.
47. Li AM, Wong E, Kew J, et al. Use of tonsil size in the evaluation of obstructive sleep apnoea. Arch Dis Child. 2002;87(2):156-9.
48. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012;130(3):576-84.
49. Kaditis A, Kheirandish-Gozal L, Gozal D. Pediatric OSAS: Oximetry can provide answers when polysomnography is not available. Sleep Med Rev. 2016;27:96-105.
50. Katz ES, Greene MG, Carson KA, et al. Night-to-night variability of polysomnography in children with suspected obstructive sleep apnea. J Pediatr. 2002;140(5):589-94.
51. Markov D, Jaffe F, Doghramji K. Update on parasomnias: a review for psychiatric practice. Psychiatry (Edgmont). 2006;3(7):69-76.
52. Howell MJ. Parasomnias: an updated review. Neurotherapeutics. 2012;9(4):753-75.
53. Parrino L, Halasz P, Tassinari CA, Terzano MG. CAP, epilepsy and motor events during sleep: the unifying role of arousal. Sleep Med Rev. 2006;10(4):267-85.
54. Licis AK, Desruisseau DM, Yamada KA, et al. Novel genetic findings in an extended family pedigree with sleepwalking. Neurology. 2011;76(1):49-52.

Paediatric tracheostomy

Morad Faoury[1], **Andrea Burgess**[2] and **Hasnaa Ismail-Koch**[3]

[1]Morad Faoury MD, Academic fellow, University Hospital Southampton NHS Foundation Trust

[2]Andrea Burgess FRCS ORL-HNS, Consultant ENT Surgeon with a specialist interest in Paediatrics, Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust and Hampshire Hospitals NHS Foundation Trust

[3]Hasnaa Ismail-Koch DM, DLO, FRCS ORL-HNS, Consultant ENT Surgeon with a specialist interest in Paediatrics, Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust

Correspondence:
Hasnaa Ismail-Koch DLO, FRCS ORL-HNS,
Department of Paediatric Otorhinoloaryngology
Southampton Children's Hospital, University Hospital Southampton, Tremona Road, Southampton SO16 6YD
Email: hasnaa@doctors.org.uk

Abstract

Paediatric tracheostomy is a procedure that all registered otorhinolaryngologists should be able to perform at least in an emergency situation. This review article examines how this procedure has changed over the years. It considers the indications, preoperative surgical checks, counseling, tracheostomy tubes, surgical technique, complications and outlines health care needs at home for children with long-term tracheostomies.

J ENT Masterclass 2016; 9 (1): 57 - 63.

Key words

paediatric tracheostomy, tracheostomy tube, tracheostomy techniques, tracheostomy complications

Introduction

The first paediatric tracheostomy was undertaken in 1620[1]. Most early tracheostomies were performed as emergencies for relief of upper airway obstruction due to infection. In 1833 Trousseau performed around 200 tracheostomies due to the diphtheria epidemic[2].

The indications for the procedure expanded when Galloway undertook tracheostomy during the poliomyelitis epidemics of the early 1950s, promoting the use of tracheostomy for positive-pressure ventilation. This highlighted the potential use of tracheotomy in optimising ventilation in other situations such as post cardiac surgery, high-grade burns, and in the care of preterm infants[3].

Nowadays, the majority of tracheostomies in the paediatric age group are not performed in the emergency situation. They are inserted for chronic non-infective upper airway obstruction or long-term ventilation[4,5,6,7]. Airway obstruction can be congenital or acquired (table 1).

One study showed that the most common indications necessitating paediatric tracheostomy were; long-term ventilation (20%), craniofacial abnormality causing airway obstruction (18%) and subglottic stenosis (14%)[8]. With improved intensive care techniques, children with more complex respiratory and neuromuscular conditions are surviving longer thus increasing prevalence of tracheostomies for prolonged ventilation. With advances in medical and surgical treatments such as balloon dilatation and laryngotracheal reconstruction, there has been a reduction in tracheostomies performed for

Table 1: Congenital and acquired causes of upper airway obstruction

Congenital	Acquired
Nasal	Infection
Oropharyngeal obstruction (e.g. Pierre Robin sequence and other craniofacial abnormalities)	Trauma (e.g. physical, intubation, burns, chemical, occurring at any level)
Supraglottic (e.g. laryngomalacia)	
Glottic (e.g. congenital vocal fold paralysis, laryngeal web)	
Subglottic e.g. subglottic stenosis, subglottic haemangiomas)	
Tracheobronchial	
(e.g. tracheobronchomalacia)	
Tumours/ Malignancy	
Neurological/ Neuromuscular	

obstructive conditions such as subglottic haemangiomas, subglottic stenosis and laryngeal clefts[9] .

Preoperative counseling

Looking after a child with a tracheostomy is life changing and has a huge impact on the carers including; practical issues of tube management, worries about tube safety and social stigma. Where the tracheostomy is planned, preoperative counseling is essential and includes:

1. Multidisciplinary meetings
2. Reassurance about voice issues, swallowing and feeding
3. Educational material, videos and meeting other parents of children with a tracheostomy

As with any surgical procedure, the surgeon must have a clear and honest discussion with the family concerning the benefits, risks, and alternatives to tracheostomy.

Preoperative checks

In cases of airway obstruction, a full dynamic and static evaluation of the airway including laryngotracheo-bronchoscopy is performed. This is to assess anatomy, function and to determine whether any endoscopic surgical intervention could avoid the need for tracheostomy.

Prior to tracheostomy routine blood tests and a coagulopathy screen should be undertaken. A chest x-ray is mandatory to evaluate the respiratory system and may also be helpful in establishing the position of trachea.

There are various anatomical differences between adult and paediatric airways and these should be considered when undertaking a paediatric tracheostomy (table 2).

Tracheostomy tubes

The selection of an optimal tracheostomy tube depends on the clinical indication and the size of the airway[10]. Both the diameter and length should be considered. The internal diameters of paediatric tracheostomy tubes range from 2.5-5.5 mm and the lengths range from 30-36 mm for neonates and 39-56 mm for paediatric patients[10]. The diameter of the tracheostomy tube can be calculated on the basis of the size (the inner diameter) of the child's endotracheal tube. Great Ormond Street Hospital has produced a chart to aid tube selection[11]. Neonatal tubes are equal to pediatric tubes in their both inner and outer diameters[12]. As a result of their small size, paediatric tracheostomy tubes are only single-lumen.

Regarding tracheostomy tube length, a child under 12 months of age requires a shorter 'neo' tube; whereas a child over 12 months of age requires a longer 'paed' tube[13].

Paediatric tubes were initially cuffless but low-pressure cuffed models have become available over the last few years to aid ventilation. Using too large a tube diameter or overinflation of a cuffed tube may result in tracheal injury due to vascular compromise resulting in; pressure necrosis, ulceration fibrosis and eventually stenosis.

As children grow they generally require progressively larger tracheostomy tubes to avoid nocturnal desaturations whilst allowing for speech[14,15].

Table 2: The anatomical airway differences between children and adults that should be considered when undertaking a neonatal or paediatric tracheostomy

Anatomical Differences
The paediatric larynx has a higher position in the neck
The neck is shorter
The cricoid and thyroid cartilages are difficult to palpate
The subcutaneous fat is more prominent
The paediatric laryngeal structures and trachea are more pliable
The pleura extends into the neck, therefore is more susceptible to injury

Open surgical tracheostomy technique

The procedure is ideally undertaken on an intubated child under general anesthesia.

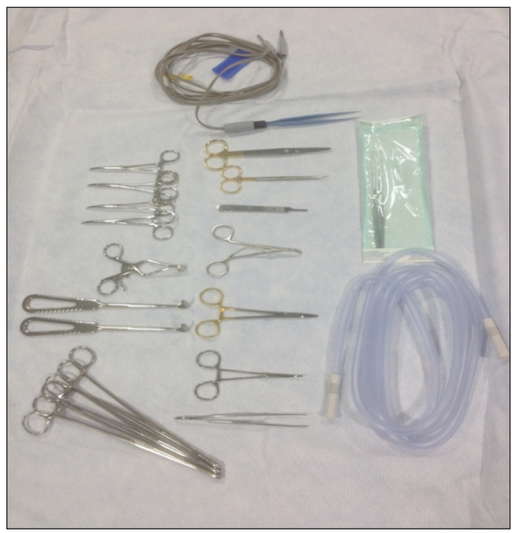


Figure 1: *Equipment set up for a paediatric tracheostomy*

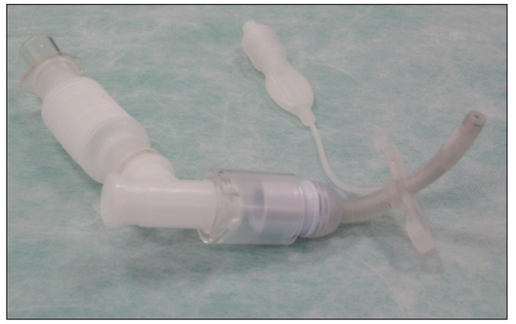


Figure 2: *Tracheostomy tube attached to anaesthetic connector*

1. Set up equipment

Figure 1 shows the equipment set up for a paediatric tracheostomy.

2. Check Tracheostomy Tube size

It is necessary to check the tracheostomy tube size and ensure one size smaller is available. If a cuffed tube is used the cuff should be checked prior to commencing the procedure. The anaesthetic connectors connecting the tracheostomy tube to the anaesthetic circuit should also be checked (figure 2). The tracheal suction length should be measured by placing an appropriately sized tracheal suction catheter into the tracheostomy tube with the suction catheter tip just visible beyond the tracheostomy tube.

3. Position the child

The child is positioned with the head extended using a shoulder roll and head ring. Excessive hyperextension should be avoided in children as this may result in mediastinal structures presenting in the neck and therefore making them vulnerable to injury. The head is then stabilised in the midline position using surgical tape placed across the chin attached to the operating table(figure 3). In certain cases neck extension may be contraindicated due to the risk of atlantoaxial subluxation e.g. with Trisomy[21] (Down's syndrome) or achondroplasia[13].

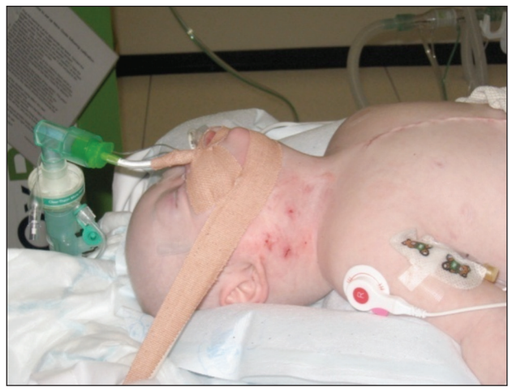


Figure 3: *Positioning the child with a shoulder roll, head ring and chin tape*

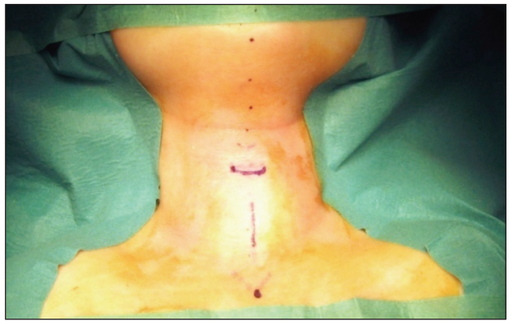


Figure 4: *Surface landmarks: The incision is placed halfway between the cricoid cartilage and suprasternal notch*

4. Skin Incision

The skin incision should be marked. A vertical or horizontal incision is made in the midline midway between the expected position of the cricoid cartilage and suprasternal notch (figure 4). The lateral limits of a horizontal incision are the anterior borders of the sternocleidomastoid muscles. Local anesthetic 2% 'lignospan special' (2%

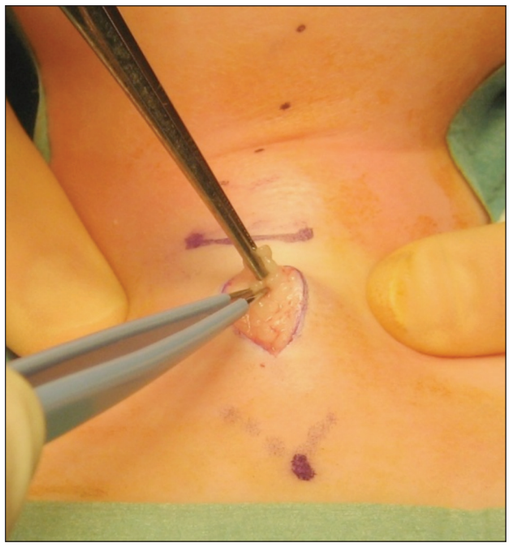


Figure 5: *Removal of subcutaneous fat using bipolar dissection*

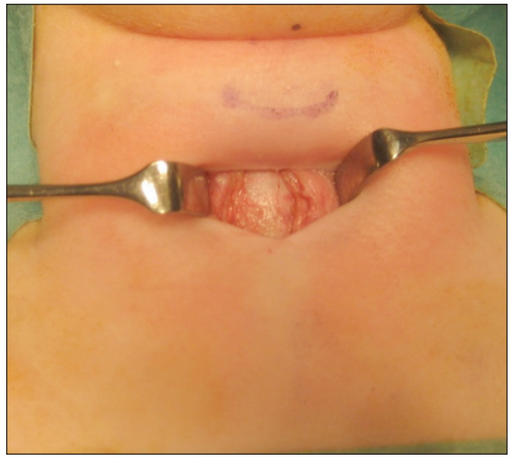


Figure 6: *Skin and subcutaneous tissue retracted to expose the strap muscles and trachea*

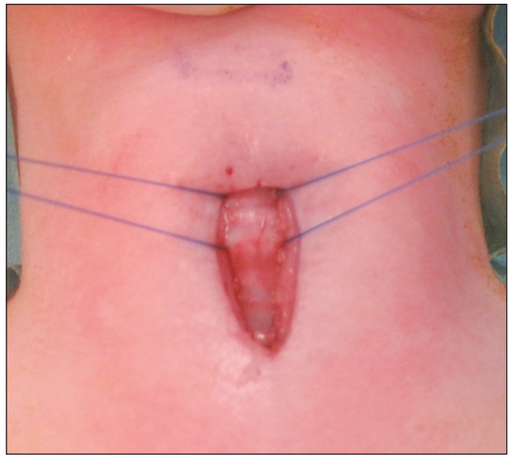


Figure 7: *Bilateral prolene stay sutures in the tracheal wall on either side of the planned tracheal incision*

Lidocaine with 1:80,000 adrenaline) is infiltrated into the area of the planned incision. Alternatively in small neonates, 1 ml of 1 in 1,000,000 adrenaline can be used. A vertical skin incision is the preferred technique for emergency tracheostomies when preoperative ventilation and intubation is not possible and a surgical airway is urgently required.

5. Removal of subcutaneous fat, dissection and identification of trachea

The skin incision is continued through into the subcutaneous fat. The fat is debulked around the incision site using bipolar diathermy (figure 5). The removal of subcutaneous fat aids the placement of maturation sutures. In an emergency tracheostomy, where timing is critical, this is not necessary. The midline cervical fascia between the strap muscles is identified and divided (figure 6). The strap muscles can then be divided in the midline using bipolar diathermy or blunt dissection, maintaining meticulous haemostasis throughout. The strap muscles are retracted laterally to expose the thyroid isthmus. The thyroid isthmus is divided using bipolar diathermy to identify the trachea. It is essential to stay in the midline at all times particularly in neonates where the apex of the lung dome extends from the thorax into the root of the neck[16]. The cricoid cartilage and tracheal rings are identified. It is essential to avoid injury to the first tracheal ring as this may lead to subglottic stenosis. A saline soaked pledget may prove useful in gently clearing the anterior tracheal wall to improve exposure of the trachea. Caution should be exercised when dissecting the lower trachea as the innominate artery normally passes below the 5th tracheal ring.

6**. Insertion of stay sutures**

Non-absorbable 3/0 or 4/0 prolene stay sutures are placed through the tracheal rings 3-5 on either side of the planned midline tracheal incision (figure 7). Stay sutures are beneficial in applying upward and lateral pull on the trachea, bringing it to the surface, and can be lifesaving during accidental decannulation.

7. Tracheal incision and maturation sutures

A vertical tracheal incision is made through two tracheal rings between the stay sutures (usually between the 3rd -5th). In a non-emergency situation, maturation sutures are recommended and are placed prior to tracheostomy tube

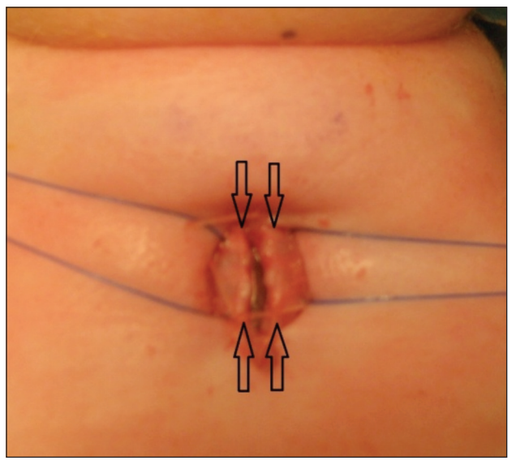


Figure 8: *Tracheal stoma with four maturation sutures in place (arrows)*

insertion. These are 4/0 vicryl absorbable sutures between the trachea and skin connecting the trachea directly to the skin, creating a safer stoma. These are placed superiorly and inferiorly on either side of the skin (figure 8). The inferior maturation sutures are the most crucial. Whilst applying the maturation sutures the endotracheal tube remains in place (access can be improved by withdrawing the tube slightly and/ or deflating the cuff if present). In order to prevent anaesthetic gases escaping and to support ventilation the tracheal incision can be intermittently occluded with a small pledget or by carefully crossing over the stay sutures.

8. Tracheostomy tube insertion

Once the maturation sutures have been applied the tracheostomy tube can be inserted under direct vision (figure 9). The position of the tracheostomy tube may be checked intraluminally using a flexible endoscope. The distal end of the tube should ideally be situated above the carina.The tracheostomy ties are then applied and knotted; the tube should be well secured with the head flexed to avoid accidental dislodgement, but not too tight so as to cause vascular compromise and skin breakdown.The tube should not be sutured to the skin, as paediatric skin is very elastic therefore, should the tube dislodge reinsertion of a sutured tube would be more difficult. The stay sutures are then taped to the chest and labelled‘RIGHT’, ‘LEFT’, and ‘DO NOT REMOVE’ (figure 10). The purpose and use of the stay sutures should be explained to all involved in the care of the child prior to the first tracheostomy tube change.

Postoperative care

Chest X-ray is required to exclude a pneumothorax, surgical emphysema and reconfirm the position of the tracheostomy tube. Paediatric or neonatal intensive care unit stay may be required in some instances until the first tracheostomy tube change. The child may be sedated and paralysed for 48 hours if necessary. Antibiotic prophylaxis may be indicated postoperatively. A tracheostomy box should be set up at the patient’s bedside containing a same size and smaller tube, lubricant, saline, suction catheters, scissors, ties, dressings.

Careful suctioning and humidification is essential especially in the first 3 days. The tracheocutaneous tract is usually well established at 72 hours[17]. Nursing staff should be informed regarding the correct suction length in order to avoid any distal tracheal injury and granulations. The skin of the neck and stoma should also be checked on a daily basis.

The first tracheostomy tube change should be considered at 6-7 days, but may be performed earlier. The surgeon

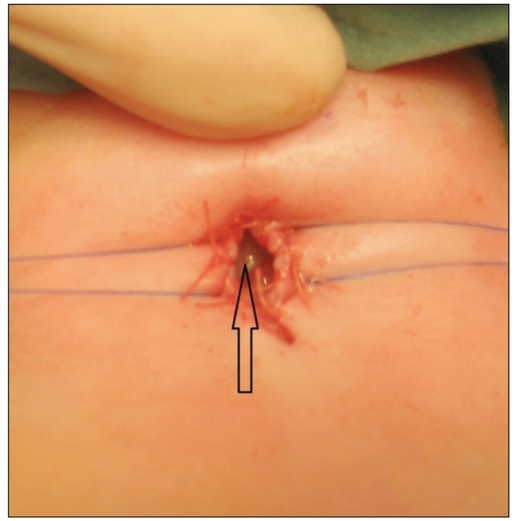


Figure 9: *Endotracheal tube visible in stoma (arrow)*

determines the exact timing of the first tracheotomy tube change. This should be performed in a safe environment where emergency reintubation is possible. Following tube change and conformation of correct positioning the tube is secured. Finally the stay sutures are removed.

Laryngotracheobronchoscopy with review of the tracheal stoma and the original indication for tracheostomy by the multidisciplinary team should be undertaken at regular intervals. This may range from six monthly to yearly, however an individual case based approach should be employed.

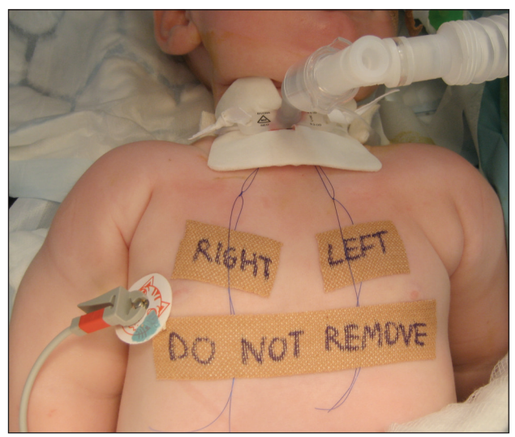


Figure 10: *Tracheostomy tube in situ with stay sutures taped to the chest and labelled*

Complications

The risks of tracheostomy can be classified as early postoperative and long-term complications.

Early complications

Complications directly related to the procedure itself include; losing airway control, insufficient ventilation, bleeding, pneumothorax and oesophageal injury. Many paediatric patients requiring tracheostomy have complex medical co-morbidities, which also increases the risks of cardiac arrest and death[18]. The incidence of tracheostomy tube occlusion has been reported to be as high as 72% in premature and newborn children decreasing to 14% in paediatric patients older than 12 months[19]. The higher rate of blockage in the younger age group is attributed to the narrower diameter of tracheostomy tubes and bronchopulmonary dysplasia resulting in viscous bronchial secretions in premature infants[19].

Accidental decannulation is a serious complication in paediatric patients. The National Tracheostomy Safety Project details algorithms on how to manage new and established blocked tracheostomy tubes[20].

Using the correct tracheostomy tube and ensuring that the wound is not closed too tightly can minimise subcutaneous emphysema.

Late complications

Failure of decannulation can be related to different factors. Pre-decannulation laryngotracheobronchoscopy is generally recommended if the tracheostomy has been in place for longer than 3 months to look for granulomas, tracheomalacia and vocal cord movement[21]. Decannulation attempts should be undertaken within the six weeks following this laryngotracheobronchoscopy.

If decannulation fails, despite optimal conditions, further laryngotracheobronchoscopy should be performed to diagnose any stomal or tracheal granulations. Tracheal granulomas frequently seen in very young patients are caused by either trauma from the distal tube end or excessive suctioning. Infective factors from the skin and airway may also contribute to granulation formation.

These may be removed either endoscopically using bronchoscopes with cold steel, KTP laser techniques or externally by intubating the trachea with an endotracheal tube and excising the granuloma through the stoma using a skin hook[22]. Any other structural or dynamic pathology such as suprastomal collapse, subglottic and tracheal stenosis must be addressed prior to further decannulation attempts.

Tube dislodgment and blockage remain important complications which increase in frequency as a child becomes more mobile.

The reported mortality rate for paediatric tracheostomy is 0.7%[23].

The rate of persistent tracheocutaneous fistula following decannulation is 13-43%[24]. Small pinpoint tracheocutaneous fistulas may be managed with silver nitrate cautery to the tract. Larger fistulas should be sealed over and it is sensible to undertake polysomnography to ensure that the child is not using the fistula for ventilatory purposes. The tracheocutaneous fistula can be repaired if polysomnography is normal and airway assessment is adequate.

Tracheostomy impacts speech and language development. Earlier decannulation results in improved speech and language developmental outcomes[25,26].

A multidisciplinary approach to management optimising initial hospital care and promoting effective communications has been shown to improve outcomes and avoid complications[27]. This includes weekly care conferences, consensus guidelines, educational initiatives, care plans, and regular follow up with endoscopic assessment.

Home care preparation

Pre-discharge family and home environment planning are essential. During the hospital stay the child's family or guardians undertake a structured and detailed training program, requiring the achievement of competencies and providing the necessary skills to manage the long-term care at home. Although complications can occur, several studies report a low rate of documented accidents and high carer satisfaction rates when managing the children at home with appropriate support[28,29].

Conclusion

Paediatric tracheostomy continues to have a significant role in paediatric airway management. There have been many changes in indications, tubes and surgical modifications over the years. The main development however has been the multidisciplinary approach to tracheostomy management and the increasing role of the parents in caring for their children at home.

References

1. Fraga JC, de Souza JCK, Kruel J. Pediatric tracheostomy. Jornal de Pediatria. 2009; 85(2):97–103
2. Rajesh O, Meher R. Historical Review of Tracheostomy. The Internet Journal of Otorhinolaryngology 2005; 4(2)
3. de Trey L, Niedermann E, Ghelfi D et al. Pediatric tracheotomy: a 30-year experience. J Pediatr Surg. 2013; 48(7):1470-1475
4. Trachsel D, Hammer J. Indications for tracheostomy in children. Paediatr Respir Rev. 2006; 7(3):162-168
5. Kilic D, Findikcioglu A, Akin S et al. When is surgical tracheostomy indicated? Surgical "U-shaped" versus percutaneous tracheostomy. Ann Thorac Cardiovasc Surg. 2011; 17(1):29-32
6. Alibrahim IJ, Kabbani MS, Abu-Sulaiman R et al. Outcome of tracheostomy after pediatric cardiac surgery. J Saudi Heart Assoc. 2012; 24(3):163-168
7. Overman AE, Liu M, Kurachek SC et al. Tracheostomy for infants requiring prolonged mechanical ventilation: 10 years' experience. Pediatrics 2013; 131(5):1491-1496
8. Douglas CM, Poole-Cowley J, Morrissey S et al. Paediatric tracheostomy-An 11 year experience at a Scottish paediatric tertiary referral centre. Int J Pediatr Otorhinolaryngol. 2015; 79(10):1673-1676
9. Hadfield PJ, Lloyd-Faulconbridge RV, Almeyda J et al. The changing indications for paediatric tracheostomy. Int J Pediatr Otorhinolaryngol. 2003; 67(1):7-10
10. Mathur NN, Meyers AD. Pediatric Tracheostomy 2016. Available at http://emedicine.medscape.com/article/873805-overview (accessed 28 May 2016).
11. Tweedie DJ, Skilbeck CJ, Cooke J, Wyatt ME. Choosing a paediatric tracheostomy tube: an update of current practice. J Laryngol Otol. 2008; 122(2):161-169
12. Deutsch ES. Tracheostomy: Pediatric Considerations. Respiratory Care 2010; 55(8):1082–1090
13. Ismail-Koch, Jonas N. Paediatric tracheostomy. In: Open Access Atlas of Otolaryngology, Head & Neck Operative Surgery, Editor Fagan J. Available at https://vula.uct.ac.za/access/content/group/ba5fb1bd-be95-48e5-81be-586fbaeba29d/Paediatric%20tracheostomy.pdf (accessed 28 May 2016).
14. Watt JW, Fraser MH. The effect of insufflation leaks in long-term ventilation. Waking and sleeping transcutaneous gas tensions in ventilator-dependent patients with an uncuffed tracheostomy tube. Anaesthesia 1994; 49(4):328-330
15. Behl S, Watt JW. Prediction of tracheostomy tube size for paediatric long-term ventilation: an audit of children with spinal cord injury. Br J Anaesth. 2005; 94(1):88-91
16. Genther DJ, Thorne MC. Utility of routine postoperative chest radiography in pediatric tracheostomy. Int J Pediatr Otorhinolaryngol. 2010; 74(12):1397-1400
17. Abdullah VJ, Mox JS, Chan HB et al. Paediatric tracheostomy. H K J Paediatr. 2003; 8:283-289
18. Mahadevan M, Barber C, Salkeld L et al. Pediatric tracheotomy: 17 year review. Int J Pediatr Otorhinolaryngol. 2007; (71):1829-1835
19. Davis MG. Tracheostomy in children. Paediatr Respir Rev. 2006; 7(Suppl):S206-S209
20. The National Tracheostomy Safety Project Paediatric emergency algorithms. Available at http://www.tracheostomy.org.uk/Templates/NTSP-Paeds.html (accessed 28 May 2016).
21. Sasaki CT, Gaudet PT, Peerless A. Tracheostomy Decannulation. Am J Dis Child. 1978; 132:266-269
22. Ismail-Koch H, Vilarino-Varela J, Harker H, Hore I. The use of endotracheal tubes in the excision of troublesome paediatric suprastomal granulomas. Clin Otolaryngol. 2011; 36(4):403-404
23. Carr MM, Poje CP, Kingston L et al. Complications in Pediatric Tracheostomies. The Laryngoscope 2001; 111:1995–1998
24. Tasca RA, Clarke RW. Tracheocutaneous fistula following paediatric tracheostomy--a 14-year experience at Alder Hey Children's Hospital. Int J Pediatr Otorhinolaryngol. 2010; 74(6):711-712
25. Jiang D, Morrison GA. The influence of long-term tracheostomy on speech and language development in children. Int J Pediatr Otorhinolaryngol. 2003; 67(Suppl):S217-120
26. Rane S, Shankaran S, Natarajan G. Parental perception of functional status following tracheostomy in infancy: a single center study. J Pediatr. 2013; 163(3):860-866
27. Abode KA, Drake AF, Zdanski CJ et al. A Multidisciplinary Children's Airway Center: Impact on the Care of Patients With Tracheostomy. Pediatrics 2016; 137(2):1-9
28. Reiter K, Pernath N, Pagel P et al. Risk factors for morbidity and mortality in pediatric home mechanical ventilation. Clin Pediatr (Phila). 2011; 50(3):237-243
29. Joseph RA. Tracheostomy in infants: parent education for home care. Neonatal Netw. 2011; 30(4):231-242

Paediatric vocal cord paralysis

Virginia Fancello[1], **Matthew Ward**[2], **Hasnaa Ismail-Koch**[3] and **Kate Heathcote**[4]
[1]MD, Laryngology Fellow, Poole Hospital NHS Foundation Trust.
[2]DM, FRCS ORL-HNS, Senior Registrar ENT, Poole Hospital NHS Foundation Trust.
[3]DM, DLO, FRCS ORL-HNS, Paediatric Consultant ENT Surgeon, University Hospital Southampton NHS Foundation Trust.
[4]FRCS ORL-HNS, Consultant ENT surgeon, Poole Hospital NHS Foundation Trust.

Correspondence:
Kate Heathcote, ENT Department, Poole General Hospital, Longfleet Rd, Dorset BH15 2JB
Email: kate.heathcote@gmail.com

Abstract
Vocal cord palsy in children may occur in isolation or in association with other pathologies. It may be unilateral or bilateral, temporary or permanent and may present in a number of ways.This includes ill-defined feeding difficulties, weak cry or in an emergency situation with stridor. The advent of flexible nasolaryngoscopes has greatly improved our ability to diagnose these conditions. In infants and toddlers the primary concerns are focused on the airway and aspiration risk. Whereas the full impact of the vocal disability only reveals itself as the child gets older, effecting social and educational development. The focus of this review is to give an up-to-date approach to diagnosis and management of both unilateral and bilateral vocal cord palsy in children.

J ENT Masterclass 2016; 9 (1): 64 - 68.

Key words
vocal cord palsy, laryngeal electromyography, laryngeal reinnervation

Acknowledgement
Andrea Burgess, Paediatric Consultant ENT Surgeon, University Hospital Southampton NHS Foundation Trust. Who contributed to the clinical cases and development of the management approach described.

Introduction
The term “vocal cold paralysis” (VCP) refers to the absence of vocal cord movement, typically due to lower motor neurone dysfunction[1]. It may be unilateral (UVCP) or bilateral (BVCP) and be due to a central lesion or, more commonly, as a result of vagal or a recurrent laryngeal nerve (RLN) impairment.

In recent decades the prevalence of paediatric VCP seems to have increased[2].This is likely to be, at least in part, due to an increase in diagnosis as more units routinely use paediatric flexible nasolaryngoscopes (FNL). Another important factor is the improved survival rates among pre-term infants. However, the true incidence of VCP in children remains unknown.

Aetiology
In 2006 Smith proposed a classification system whereby the causes of paediatric VCP can be identified as congenital, hereditary or acquired[3]. Their prevalence of the different aetiologies varies widely between studies and over the decades, showing interesting changes in recent years[4]. (Tab. 1)

UVCP is most frequently iatrogenic[1,2]. As the survival rate of premature infants increases, accordingly so does the requirement for cardiac surgery. Patent ductus arteriosus (PDA) ligation has a particularly high complication rate of VCP of up to 23% in babies under 1 kg[6]. Pre- and post-operative evaluation of the larynx in children undergoing high risk surgery should be the gold standard.This facilitates early diagnosis and treatment thus preventing aspiration and is wise from a medicolegal standpoint.

Intraoperative monitoring of the RLN may be a useful adjunct to decrease nerve damage. Unfortunately, there are no commercially available tubes of appropriate size for newborns at present[7].

BVCP is predominantly of idiopathic or neurological origin. Arnold Chiari Malformation is the most frequent central nervous system defect associated with BVCP[1,2,6,9,10].

Fortunately, antibiotic therapies and mass vaccination campaigns have greatly reduced infectious causes of VCP[11].

Traumatic birth, in particular forceps and breach delivery, can cause both unilateral and bilateral VCP due to traction injury of the vagus or RLN[1]. This is less and less described, most likely due to the increase rate of caesarean section.

Tabl1 1: Aetiology of VCP in children[1,3,4,9,10,11]

CONGENITAL	ACQUIRED
Cerebral agenesis	Neoplastic (brain, neck and mediastinal)
Corpus callosum agenesis	Cerebral vascular accidents
Nucleus ambiguous dysgenesis	Traumatic
Arnold-Chiari malformation	Birth injury
Hydrocephalus	Postsurgical correction of cardiovascular
Encephalocele	or oesophageal abnormalities
Meningomyelocele	Neck surgery
Meningocele	Ortner’s syndrome
Congenital myasthenia gravis	INFECTIVE
Cardiomegaly	Mediastinitis
Interventricular septal defect	Pertussis encephalitis
Tetralogy of Fallot	Polyneuritis
Vascular ring	Polioencephalitis
Dilated aorta	Diphtheria
Double aortic arch	Rabies
Patent ductus arteriosus	Syphilis
Transposition of great vessels	Herpes encephalitis
Aberrant innominate artery	Tetanus
Cystic Hygroma	Botulism
Acute foetal suffering	Tuberculosis
Neonatal benign hypotonia	Congenital Varicella Zoster
ASSOCIATED WITH OTHER CONGENITAL ANOMALIES	Congenital Rubella
Laryngeal abnormalities	Epstein Barr Virus infection
(subglottic stenosis, laryngomalacia, laryngeal cleft, laryngeal haemangioma)	Guillian-Barrè Syndrome
Bronchogenic cyst	NEUROTOXIC
Oesophageal cyst, duplication, atresia	Vincristine/Vinblastine
Cricopharyngeal stenosis	Heavy metal poisoning
HEREDITARY	
Autosomal dominant	
Autosomal recessive	
X-linked	
Isolated mutation	
Associated with other hereditary syndromes (e.g. Pelizaeus Merzbacher syndrome, Cri du chat disease, Charcot Marie Tooth disease, Neurofibromatosis)	

Diagnosis
A meticulous history with a careful physical examination is crucial.This should focus on symptoms of VCP, for example, abnormalities in the voice or cry, feeding difficulties, and stridor or cyanotic episodes.It is also important to establish any risk factors as discussed above.

FLN is an essential tool for assessing the dynamic movement of the larynx. A 2.8mm paediatric fibreoptic scope is reasonably tolerated by children. In newborns swaddling can be a helpful technique to ensure that the child remains still. Similarly, children older than 3-4 years can usually tolerate FLN after careful explanation of the technique. Between the ages of 1-2 years, awake FLN can be very difficult and is approached on a case by case basis.

Microlaryngobronchoscopy under general anaesthesia plays a fundamental role in differentiating VCP from other laryngeal defects such as cricoarytenoid joint fixation, interarytenoid scar or vocal fold fusion, and to exclude associated laryngeal abnormalities for example subglottic stenosis.

Magnetic Resonance Imaging, and in selective cases Computer Tomography, may be necessary to investigate the aetiology and associated pathologies.

The clinical manifestations must be carefully evaluated before any surgical procedure is considered in view of the potential long-term impact some may have on voice. Direct observation of breathing and oxygen saturation monitoring are essential to plan the management. When feeding difficulties are present, a videofluoroscopy may be used to investigate silent aspiration, particularly in cases with cardiorespiratory co-morbidities.

Laryngeal Electromyography (LEMG) introduced into clinical practice by Hirano and Ohala in 1969, is a useful examination in children with vocal cord immobility[13]. It can help to plan treatment in cases where the differentiation between paralysis and fixation may be difficult to make. Moreover, in children with BVCP it can be valuable in predicting recovery.

Laryngeal ultrasound was proposed by Friedman in 1997 as a way to assess vocal cord mobility[14]. This technique is non-invasive, painless and requires neither sedation nor general anaesthesia. It may be of use as a screening tool to exclude VCP rather than to investigate a suspected case.

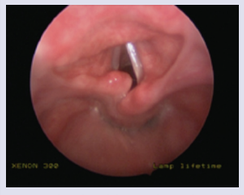
Clinical features and management
VCP is the second commonest cause of stridor in neonates and infants after laryngomalacia and accounts for more than 10% of laryngeal anomalies in children[15]. Children with concurrent cardiac or neurological pathologies are particularly vulnerable to cyanotic episodes, intercostal recession, and apnoeas.Thus, tracheostomy is more likely

to be required as well as in those with obstructive sleep apnoea due to conditions such as micro/retrognathia.

UVCP

In neonates UVCP may present as a weak cry or choking episodes. Intermittent stridor may also be a feature and has been reported to occur in up to 77% cases[1,2,9]. If stridor is present it is usually mild and well tolerated.As a result, microlaryngoscopy may not, at first glance, appear indicated. However, it is vital to distinguish UVCP from arytenoid dislocation which may be caused by intubation. The appearance of both can be very similar, especially as patients with UVCP often have marked arytenoid prolapse. If dislocation is present, the dislocated arytenoid needs to be relocated as soon as possible in an attempt to prevent permanent ankylosis. During microlaryngoscopy the mobility of the cricoarytenoid joint should be checked. In palsy the joint is mobile whereas in dislocation the arytenoid is firmly in place and the joint must be forcibly reduced in an attempt to restore function and prevent ankyloses with permanent fixation. Intra-operative Laryngeal Electromyography (LEMG) may be helpful in this differential. (Case 1)

Case 1: Untreated Arytenoid Dislocation



As a premature baby this 20-year-old was intubated for a significant length of time. She was subsequently diagnosed with a unilateral vocal cord palsy and no treatment was offered. She struggled with her voice throughout her education and when she came to us she had just abandoned her degree course with depression. We performed a microlaryngoscopy but the prolapsed arytenoid was completely fixed in position and the vocal cords lying at disparate levels. LEMG showed normal innervation of the muscles on that side. In conclusion she had never had a palsy but a traumatic dislocation of her arytenoid.

In infancy the primary concern with UVCP is aspiration, in which instance an injection augmentation is indicated. Hyaluronic acid is probably the most suitable injectable currently available as it requires low injection pressures and distributes evenly within the cord.It is more rapidly reabsorbed than other substances with a duration of effectiveness of only about 3 months. However, spontaneous recovery is a possibility, so this duration of action is not inappropriate.The injection may be repeated if necessary.

As the child grows, the dysphonia will become an increasing issue.The child's school and social life can be greatly affected by their inability to raise or project their voice, for example to ask or answer a question in the classroom. There may also be airway compromise at extremes of exercise as the flaccid arytenoid is drawn into the airway. The traditional solution is a Type 1 Thyroplasty with insertion of a silastic or gortex implant through a window cut into the thyroid lamina. Concurrent arytenoid adduction may also be required to reposition the cartilage. Unlike in adults, it is not possible to perform the procedure under local anaesthetic. It is thus harder to size an implant or tension an arytenoid suture, as it cannot be based on functional effect. It is also particularly difficult to get the vocal cords to meet on the same horizontal level when performing a thyroplasty in a child. In addition, as the laryngeal framework grows the implant will become ineffective and may become displaced requiring revision. Laryngeal framework surgery may also compromise the growth of the cartilage and. In reality many of these children are left untreated unless they are aspirating. At the time of PDA surgery in a premature baby the obvious concern to all is the life threatening pathology. Looking at parent forums however, it is interesting to see how many were not counselled regarding the significant lifelong impact of vocal cord palsy in addition to the immediate aspiration risk.

An alternative treatment for UVCP is non-selective reinnervation[16]. In this technique a branch of the ansa cervicalis is anastomosed with the recurrent laryngeal nerve. This reinnervates the muscles of the hemi-larynx and can restore muscular tone and improve arytenoid position. There is no restoration of movement coordinate with respiration and phonation, hence "non-selective". One advantage of this technique is that the laryngeal framework is not disrupted in any way and so the larynx will continue to grow without interruption or the need for revision of the procedure. The reinnervation may not be effective for up to 6 months, while axonal ingrowth occurs, and so injection augmentation with a temporary substance should be performed simultaneously. (Case 2)

Speech therapy is of benefit in all age groups.Feeding techniques may avoid aspiration and in older children voice exercises can improve compensation from the contralateral vocal cord[17].

Tracheostomy is reported in less than 20% and these cases are mainly children with comorbities and sleep apnoea[1]. It is occasionally used in life-threatening aspiration.

BVCP

In BVCP the VCs usually lie in adduction and so the cry is preserved with stridor being the main feature. A common scenario presenting to ENT is of an intubated infant who has failed extubation. The first step is to distinguish between BVCP and glottic fixation due to posterior scarring from prolonged intubation. We have found that microlaryngoscopy with tubeless, Total Intravenous Anaesthesia (TIVA) and spontaneous respiration provides optimum conditions for examination and palpation of the larynx. We also use Simultaneous LEMG to help determine prognosis.

Case 2: UVCP Treated with Reinnervation

This teenager had a UVCP as a result of resection of a cystic hygroma when he was 2 years old. At the time of surgery, it was not possible to find any remaining branches of the ansa cervicalis on the ipsilateral side. The contralateral ansa was therefore mobilised and anastomosed with the RLN via a cable graft. This table shows pre and post-operative result at 9 months follow up.

	Endoscopic findings	GRBAS	VHI-10*	Shimmer (%)	Jitter	MPT (sec)
Pre op	Incomplete closure with significant prolapse of the arytenoid	G2R1B2A1S1	19	15.7	3.1	6.1
Post op (9 months)	Full glottic closure with mucosal wave	G1B0R0A1S0	11	4.6	0.6	12.5

* voice handicap index 10

For patients in whom the palsy is iatrogenic, the surgeon may well have an impression as to the state of the nerves and the likelihood of spontaneous recovery.If recovery is going to occur in iatrogenic cases, signs of co-ordinate movement would be expected by 3 months post injury. In idiopathic cases the time frame is much less predictable and recovery has been reported to occur many years later[1,2]. Recovery rates in children with BVCP of idiopathic and neurological aetiology are higher than those of iatrogenic origin[7]. (Case 3)

Case 3: BVCP post Tracheo-oesophageal fistula repair

This neonate was found to be stridulous following repair of a tracheo-oesophageal fistula. A diagnosis of BVCP was made and the infant intubated. A trial of extubation a week later was unsuccessful and so after 2 weeks a microlarygoscopy with LEMG was performed. The ET tube was removed in theatre and the TIVA was lightened to observe respiratory effort and laryngeal movement. It could be seen that the vocal cords were being passively drawn in by the Bernoulli effect on inspiration. EMG electrodes were inserted, under direct vision, into the thyroarytenoid and posterior cricoarytenoid muscles to look at neuromuscular status during inspiration and phonation/cry. We used concentric needles held in place with crocodile forceps but hook-wire electrodes can be used and left in place as the child wakes. At this 2 week post injury LEMG, we ascertained that there was no spontaneous activity/fibrillation that would indicate axonal damage. Therefore, the decision was made to keep the child intubated rather than to proceed with tracheostomy as full recovery was likely. The microlarygoscopy and LEMG was repeated 2 weeks later and recovery of movement coordinate with respiration and absence of synkinesis was found. This gave us the confidence that extubation would be successful. The child made a full recovery, avoiding tracheostomy.

Tracheostomy is frequently performed in children with BVCP, with reported rates of between 68% to up 80% of BVCP[1,2]. Despite the difficulties in managing a tracheostomy, in our opinion this option is often preferable to procedures that are destructive to the laryngeal structures such as cordotomy, arytenoidectomy and vocal cord lateralisation. These procedures result in permanent degradation of voice which may be avoided if recovery occurs or if Selective Laryngeal Reinnervation, as described by Professor Jean-Paul Marie, is successful[18]. The aim of this technique is to restore physiological vocal cord movement that is coordinated with respiration and phonation. The upper root of the phrenic nerve on one side is diverted via a cable graft to innervate both posterior cricoarytenoid (PCA) muscles thus achieving inspiratory abduction of the vocal cords. The adductor muscles are reinnervated from a small branch of the hypoglossal nerve that supplies the thyrohyoid muscle on either side. This nerve is not active in inspiration and so does not antagonise the action of the PCAs. Professor Marie has performed this technique in children of all ages, with excellent success rates.We are currently introducing the technique in to the UK[19].

Conclusion

VCP has an associated mortality rate due to respiratory compromise and complications from aspiration. Treatment is imperative to prevent mortality and morbidity. Technological developments have improved the diagnostic rate and new techniques, such as reinnervation, have the potential to improve outcomes.

References:

1. DayaH, HosniA, Bejar-SolarI et al.Pediatric vocal fold paralysis: a long-term retrospective study. Arch Otolaryngol Head Neck Surg. 2000; 126(1):21-25
2. Jabbour J, Martin T, Beste D, Robey T. Pediatric Vocal Fold Immobility:Natural History and the Need for Long-Term Follow-up. JAMA Otolaryngol Head Neck Surg. 2014;140(5):428-433
3. Smith ME. Vocal Fold Paralysis in Children. In: Lucian Sulica, Andrew Blitzer editors, Vocal Fold Paralysis: Springer 2006; pp 225-235
4. Cohen SR, GellerKA, BirnsJW, ThompsonJW. Laryngeal paralysis in children: a long-term retrospective study. Ann Otol Rhinol Laryngol. 1982; 91:417-424
5. Smith ME, King JD, Elsherif A et al. Should all newborns who undergo patent ductus arteriosus ligation be examined for vocal fold mobility? Laryngoscope 2009; 119(8):1606-1609
6. Zbar RI, Chen AH, Behrendt DM et al. Incidence of vocal fold paralysis in infants undergoing ligation of patent ductus arteriosus. Ann Thorac Surg. 1996; 61:814–816
7. King EF1, Blumin JH. Vocal cord paralysis in children. Curr Opin Otolaryngol Head Neck Surg. 2009 Dec; 17(6):483-487
8. Oestreicher-Kedem Y, DeRowe A, Nagar H et al. Vocal fold paralysis in infants with tracheoesophageal fistula. Ann Otol Rhinol Laryngol 2008; 117:896–901.
9. De Gaudemar I, Roudaire M, FrançoisM, NarcyP.Outcome of laryngeal paralysis in neonates: a long term retrospective study of 113 cases. Int J Pediatr Otorhinolaryngol. 1996; 34(1-2):101-110

10. Emery PJ, FearonB. Vocal cord palsy in pediatric practice: a review of 71 cases. Int J Pediatr Otorhinolaryngol. 1984; 8(2):147-154
11. Dedo DD. Pediatric vocal cord paralysis. Laryngoscope 1979; 89(9 Pt 1):1378–1384
12. Silva-Munhoz Lde F, Bühler KE, Limongi SC. Comparison between clinical and videofluoroscopic evaluation of swallowing in children with suspected dysphagia. Codas. 2015; 27(2):186-192
13. Hirano M, Ohala J. Use of hooked-wire electrodes for electromyography of the intrinsic laryngeal muscles. J Speech Hear Res. 1969; 12(2):362-373.
14. FriedmanEM. Role of ultrasound in the assessment of vocal cord function in infants and children. Ann Otol Rhinol Laryngol. 1997; 106:199-209
15. Holinger PH, Brown WT. Congenital webs, cysts, laryngoceles and other anomalies of the larynx. Ann Otol Rhinol Laryngol. 1967; 76(4):744-752
16. Marie JP. Nerve reconstruction. In: Remacle M, Eckel HE, editors. Surgery of Larynx and Trachea. Heidelberg: Springer; 2010. pp. 279–294
17. Schindler A, Bottero A, Capaccio P et al. Vocal improvement after voice therapy in unilateral vocal fold paralysis. J Voice 2008; 22:113–118
18. Marie JP, Verin E, Woisard V et al. Successful reinnervation of congenital bilateral vocal cord paralysis. Paper presented at IX Congress of European Society of Pediatric Otorhinolaryngology 2006; June18-21, Paris, France
19. Marina MB1, Marie JP, Birchall MA. Laryngeal reinnervation for bilateral vocal fold paralysis. Curr Opin Otolaryngol Head Neck Surg. 2011; 19(6):434-438

Transoral laser surgery for advanced laryngeal cancer

Isabel Vilaseca[1-2] and **Manuel Bernal-Sprekelsen**[1-2]
[1]Department of Otolaryngology. Hospital Clínic. Barcelona. Spain
[2]University of Barcelona, Medical School. Barcelona. Spain

Correspondence:
Dr. Isabel Vilaseca, MD, PhD,
Otolaryngology Department
Hospital Clínic. Barcelona. Catalunya. Spain
c/ Villarroel 170. 08036-Barcelona
Email: ivila@clinic.ub.es

Abstract
Surgical treatment of laryngeal cancer has evolved progressively towards transoral resections. In early tumours, local control with transoral laser microsurgery (TLM) has proved to be as good as in open surgery and fully comparable to that achieved under radiation protocols, but at a lower cost. Consequently, TLM is presently considered a first line treatment in early laryngeal cancer.

These good oncological and functional results have pushed TLM indications to intermediate and advanced carcinomas. In this article we review the outcomes of TLM in the treatment of locally advanced tumours of the larynx, putting special emphasis on difficulties, appropriate patient selection and different technical considerations.

The oncologic outcomes published in the literature suggest that TLM is comparable to other treatment alternatives in appropriately selected patients. From the functional point of view, TLM reduces patient morbidity, provides faster recovery and avoids tracheotomy in a high number of patients.

J ENT Masterclass 2016; 9 (1): 69 - 74.

Key words
transoral laser microsurgery, advanced carcinoma, laryngeal cancer, CO2 laser

Conflicts of interest
The authors declare no conflicts of interest.

Acknowledgements
To Dr. José Luis Blanch and to all the members of the Hospital Clínic ENT Department.

Introduction
In the last decades, TLM has changed the concept of laryngeal cancer surgery. The possibility to remove the tumour transorally, in a concept of minimally invasive surgery, has reduced postoperative morbidity, with a more rapid recovery for patients and avoiding a tracheostomy in most of them. From the oncologic point of view, TLM has proved to be as good as open surgery and totally comparable to radiation protocols in early laryngeal cancer, but at a much lower cost[1]. Thus in many centres, where external approaches or radiation therapy were established as a first line treatment, the treatment protocols have been reconsidered.

Subsequently, such good results obtained in early tumours have pushed the indications of TLM to intermediate-advanced laryngeal cancers. In that scenario, TLM shares a leading role with chemoradiation strategies and open surgery. According to the literature, there is increasing evidence that in appropriate cases, comparable oncological results can be achieved with TLM also for locally advanced tumours, with a substantial decrease in morbidity and a very good postoperative quality of life[2-4]. Unfortunately, no randomized studies have been conducted in this area, and the decision process is in part dependent to the learning curve and to the availability of treatment alternatives.

The goals of TLM include the oncologic cure, the organ preservation with an acceptable voice, a regular swallowing recovery, and avoiding a permanent tracheostomy or gastrostomy. There are currently no absolute recommendations regarding the indications or contraindications for TLM in advanced laryngeal tumours. An appropriate selection of ideal candidates needs to foresee that after the final tumour resection the patient has

all odds of an aspiration-free deglutition or a good chance of swallowing rehabilitation.

Authors with experience in TLM essentially include T3 laryngeal tumours and, exceptionally, selected T4a cases (usually with limited involvement of the tongue base, growth towards the membranous pyriform sinus or minimal extralaryngeal extension). Bilateral involvement of the posterior commissure, cricoid cartilage infiltration, extensive subglottic involvement and marked extralaryngeal tumour extension are considered as contraindications[5-8].

Controversies for TLM in locally advanced tumours

Exposure of the tumour

Adequate exposure of the tumour is always needed to achieve a complete oncologic sound resection. A useful approach requires a suitable anatomy, an experienced surgeon, adequate instruments (different size and types of laryngoscopes, forceps, etc) and the knowledge of tricks about how to improve the tumour view .

Piazza et al. have recently published a predictive scoring system "the laryngoscore" which is based on eleven anatomic variables, and permits to anticipate the difficulties with the exposure of the larynx before a transoral approach[9]. The laryngoscore may help in preoperative planning and counselling. According to the authors, it also seems to be related to the risk of close or positive margins[10].

During surgery, initial debulking with the laser in scan mode may be necessary to progressively improve exposure in large tumours. External pressure is extremely helpful in the anterior commissure and the ventricle. The pressure has to be exerted on the cricoid cartilage, to verticalize the larynx and to facilitate the perpendicular cut with the laser. Under these conditions, and after repositioning the laryngoscope many times, most advanced tumours can be resected. A recent analysis of the exposure in 1.109 consecutive patients treated with TLM in our center showed that advanced tumours were more difficult to expose than early ones, but overall, only in 23 patients (2.07%) the resection was not possible (unpublished data). Exposure according to location and extension of the tumours is expressed in Table 1.

Assessment of the margins

Margins assessment is another key point of TLM since it may condition local relapse and the need for adjuvant treatment. Usually, tumour resection in a single piece is not possible in advanced tumours, requiring the tumour to be divided into multiple blocks. It is difficult then to obtain representative and assessable surgical margins throughout the entire resection. Moreover, when the number of samples sent for pathological study is very high, its final interpretation is complicated and may lead to confusion.

There are certain tips that can be used in advanced TLM to decrease the possibility of uncertain margins. One is to seek a resection plane which is set away from the tumour boundary in those areas where a wider resection will not lead to a functional impairment. In laryngeal tumours, especially in advanced supraglottic or lateral glottic cases, this plane is often (identified with) the thyroid perichondrium. The blunt detachment of this inner perichondrium and inspection of an undamaged thyroid wing facilitates the obtainment of a deep, tumour-free margin. Thus, for those advanced glottic tumours, a subperichondric dissection is recommended. For advanced supraglottic tumours, the advice is to completely remove the thyroepiglottic fat of the affected area. By contrast, in other superficial or deep areas far from the thyroid lamina, TLM should be supported by an intraoperative study of samples, usually obtained from the resection area.

The presence of focal infiltration of the thyroid cartilage represents an additional difficulty for the surgeon. The extent of the infiltration to be considered a T3 is not clearly specified in the TNM classification, and the efficiency of imaging techniques to adequately assess incipient cartilage infiltration is between 60-85%, which supposes a limitation in the preoperative workup[11-12]. Focal cartilage infiltration is often an intraoperative finding, accompanied by the impossibility of conducting intraoperative cartilage biopsies for confirmation. Removal of a cartilage window or extensive ablation of the affected cartilage is recommended. For more extended infiltrations, the likelihood that tumour cells circulate within the marrow should not be underestimated. Thus, limited resection of the area of focal involvement may be insufficient and the possibility of an open partial approach should be considered.

Even in the best scenario, there are many postoperative situations in which the margin may be considered "uncertain". These are given when the specimen sent for the pathology analysis presents a wide area of carbonization, when the laser reaches the cartilage and the certainty of infiltration remains unclear, or when the surgeon has enlarged the resection by means of additional vaporization. The attitude to be adopted in this clinical situation varies according to each author.

Table 1: Exposure according to tumour location and tumour size.

	Good	Difficult
All tumours (T1-T4a)		
Supraglottic	273/311 (87.8%)	38/311 (11.2%)
Glottic	556/535 (87.6%)	79/635 (12.4%)
Anterior commissure (vertical plane)	123/163 (75.5%)	40/163 (25.4%)
T3-T4a		
Supraglottic	109/131 (83.2%)	22/131 (16.8%)
Glottic	47/55 (85.5%)	8/55 (14.5%)
Anterior commissure (vertical plane)	26/33 (78.8%)	7/33 (21.2%)

Table 2: Oncologic results after TLM for advanced supraglottic tumours (T3-T4)

	n	TNM	Local control with TLM	Final local control	DSS / DFS	OS
Iro et al., 1998[19]	48	T3-T4	83.3%	–	–	–
Rudert et al., 1999[20]	17	T3-T4	–	–	–	47%
Ambrosch et al, 2001[21]	50	T3	86%	91%	71%	–
Motta et al., 2004[22]	18	T3	77%	–	81%	81%
Davis et al., 2004[23]	46	28 T2 18 T3	97%	–	–	63%
Cabanillas et al., 2008[24]	15	T3	70%	–	80%	–
Vilaseca et al., 2010[18]	96	T3	69.8%	91.7%	61.8%	45.8%
Peretti et al., 2010[25]	20	T3	83%	–	–	–
Canis et al., 2014[3]	104	T3	77.3%	–	84.2%	66.5%
Canis et al., 2013[5]	48	T4a	–	–	62.9%	49.9%
Vilaseca et al., 2016[2]	154	129 T3 25 T4a	73.8%	93.9%	67.6%	55.6%
Pantazis et al., 2015[7]	24	T3	77.5%	–	91.7%	87.5%
Peretti et al., 2016[26]	22	T3	95.4%	–	76.3%	59.3%

Table 3: Oncologic results after TLM for advanced glottic tumours (T3-T4)

	n	TNM	Local control with TLM	Final local control	DSS / DFS	OS
Motta et al., 1997[27]	37	T3	–	–	67% DSS	55%
Ambrosch et al., 200[21]	70	T3	68%	87%	62% DFS	–
Motta et al., 2005[28]	51	T3	65%	–	72% DSS	64%
Hinni et al., 2007[29]	41	27 T3 14 T4	74%	–	68% DSS	55%
Grant et al., 2007[30]	10	5 T3	45%	–	40% DSS	62%
		5 T4				
Peretti et al., 2010[16]	11	T3	71.6%	–	100% DSS 40.9% DFS	–
Vilaseca et al., 2010[18]	51	T3	47.1%	88.2%	86.3% DSS	73.1%
Canis et al., 2013[5]	31	T4a	66.6%	–	75.4% DSS 62.2% DFS	65.3
Canis et al., 2014[3]	122	T3	71.5%	–	84.1% DSS 57.8% DFS	58.6%
Breda et al., 2015[8]	40	T3-T4	–	72.%	90.8% DSS	–
Pantazis et al., 2015[7]	19	T3	52.7%	–	63.2% DSS	63.2%
Peretti et al,. 2016[26]	34	T3	70%	–	72.9% DFS	65.2%

Table 4: Functional results after TLM for advanced supraglottic tumours (T3-T4)

	n	TNM	LPR	LFS	FPR	Gastrostomy (definitive)	Tracheotomy (definitive)
Ambrosch et al., 2001[21]	50	T3	–	–	–	0%	0.02%
Motta et al., 2004[22]	18	T3	93.7%	–	–	0%	–
Cabanillas et al., 2004[31]	15	T3	86%	–	–	–	–
Vilaseca et al., 2010[18]	96	T3	–	76.6	74.5%	–	–
Peretti et al., 2010[25]	20	T3		88.2%	–	0%	0%
Canis et al., 2013[5]	48	T4a	–			8%	8.3%
Canis et al., 2014[3]	104	T3	92%		–	–	2%
Pantazis et al., 2015[7]	24	T3	91.7%			0%	0%
Peretti et al., 2016[26]	22	T3	95.4%			0%	0%
Vilaseca et al., 2016[2]	154	129 T3 25 T4a		75.2%		1.3%	2.6%

LPR: laryngeal preservation rate; LFS: laryngectomy-free survival; FPR: function preservation rate.

Blanch et al. classify the status of the margins in three groups; affected, non-affected or uncertain[13]. The inclusion in the latter group is made according to the pathology report together with the subjective impression of the surgeon during the surgery and the postoperative endoscopic aspect of the resection site. Systematic enlargement is recommended only in the case of affected margins and a policy of watchful waiting is adopted in case of uncertain and non-affected margins.

Other authors only rely the status of the margins on the pathology report. In a series of head and neck carcinomas of different locations Jackel et al. recommended surgical review in all cases of positive or uncertain margins[14]. The authors also suggested postoperative radiation when clear negative margins could not be assessed. On the contrary, Karatzanis et al., based on a series of laryngeal cases, concluded that the final prognosis depends on achieving negative margins, regardless of the number of laser sessions required to obtain it.

They found no advantage in the administration of adjuvant radiotherapy compared to those monitored closely[15]. Finally, Peretti et al. propose the subdivision of margins

Table 5. Functional results after TLM for advanced glottic tumours (T3-T4)

	n	TNM	Site	LPR	LFS	FPR	Gastrostomy (definitive)	Tracheotomy (definitive)
Ambrosch et al., 2001[21]	167	T2b-T3	G	–	–	–	0%	0.5%
Motta et al., 2005[18]	51	T3	G	80.5%	–	–	0%	–
Hinni et al., 2007[29]	117	T2-T4	41 G 65 S	86%	51%	–	7% survivors	3% survivors
Grant et al., 2007[30]	10	T3-T4	G	–	–	–	10%	10%
Olthoff et al., 2009[32]	39	T3-T4	S+G	–	–	89.7%	30% survivors	10% all series 0% survivors
Vilaseca et al., 2010[18]	51	T3	G	–	58.9	51%	–	–
Peretti et al., 2010[16]	11	T3	G	72.7%	–	–	–	–
Blanch et al., 2011[17]	26	T3	LAC	–	65.5%	–	0%	0%
Canis et al., 2013[5]	31	T4a	G					
Canis et al., 2014[3]	122	T3	G	83%				0%
Breda et al., 2015[8]	40	T3-T4	G	69.2%				
Pantazis et al., 2015[7]	19	T3	G	73.7%			0%	0%
Peretti et al,. 2016[26]	34	T3	G	85.3%			0%	0%

LPR: laryngeal preservation rate; LFS: laryngectomy-free survival; FPR: function preservation rate; LAC: laryngeal anterior commissure.

into negative, positive on the surface and positive in depth, only accepting a "wait and see" attitude in cases with superficial involvement[16].

Local control

One of the weak points in TLM for advanced laryngeal cancers is the local control, which in some sublocations is lower than for external partial laryngectomies. This is especially true in very extended supraglottic tumours, in tumours where the vertical plane of the anterior commissure is involved and when the thyroid cartilage is widely infiltrated.

In a recent review of the literature, Peretti et al. evaluated the limits of TLM and concluded that in lesions of the entire larynx with limited deep invasion toward the anterior and lateral visceral compartments, a high rate of success in terms of oncological and functional outcomes can be achieved and reproduced by the vast majority of dedicated head and neck surgeons[10]. In such cases, TLM should be considered a first line treatment. We totally agree with the authors that supraglottic tumours with limited infiltration of the pre-epiglottic space are between the best indications to be treated by TLM. However, we also consider that the size is not "per se" a limitation for TLM if the tumour is well defined, being the exposure and the impact of the removed extension on functional aspects the only true limits for transoral resection[2,6].

By contrast, those lesions involving the vertical plane of the anterior commissure or the anterior paraglottic space, are among the most difficult to treat. An advanced learning curve in TLM and standardized resection is formally recommended to avoid incomplete resections and improve the outcomes[17]. We recommend wide excision in a horseshoe-shape, with a top-to-down approach which systematically includes resection of the base of the epiglottis, the ventricular folds and some of the inferior preepiglottic fat. This superior wide approach does not only enable a better identification of possible in-depth infiltration, but also facilitates subsequent fiberendoscopic control during the follow-ups.

Because of a higher local control, supracricoid laryngectomy is considered in many centers a first line treatment in the anterior commissure. However, the indications are limited by the patient age and pulmonary status. The great advantage of TLM is that it may be performed, at any age, avoiding the need for tracheotomy and feeding tube in the vast majority. Moreover, in case of a relapse, salvage therapy by open surgery and/or non-surgical treatment protocols are still an option, maintaining a respectable rate of functional preservation. Under such assumptions, we consider TLM as a first line treatment.

Finally, the involvement of the posterior paraglottic space with invasion of the crico-arytenoid joint and infiltration of the laryngeal framework may negatively influence both oncological and functional results, thus limiting the value of TLM. A complete approach of the superior and inferior paraglottic space requires resection of the arytenoid. It is often necessary to load the anaesthesia tube in an anterior position and support it on a rigid laryngoscope. Further exploration of the posterior commissure and posterior subglottis with laryngeal endoscopes helps to delineate the resection. However, wide excisions at this level often involve functional limitations, with secondary aspirations postoperatively that are difficult to treat. Thus, preoperatively individual decision should be taken with the patient after evaluating pros and cons of partial surgery, organ preservation protocols and even total laryngectomy.

Adjuvant treatment

The assumption of close margins in the tumour site after TLM may push to administrate systematically adjuvant (chemo) radiation therapy in advanced laryngeal cancer. Ideally the indications should be the same that those considered after open partial approaches, that means, it should mainly be reserved for T4 cases, for advanced nodal disease or for tumours displaying perineural or angiolimphatic infiltration. In general, TLM should be considered a curative treatment per se and postoperative treatment restricted to a few cases with potential adverse prognosis as listed above.

The administration of adjuvant treatment after TLM in advanced laryngeal carcinomas has not been discussed properly in the literature. A higher local control after TLM, for large T3-T4a supraglottic tumours treated with TLM and adjuvant treatment has been reported, without jeopardizing functional outcomes[2,5-6]. By contrast, in advanced glottic tumours adjuvant treatment is usually not recommended since it may limit seriously functional outcomes and quality of life[18].

Outcome of TLM for advanced laryngeal cancer

The oncologic and functional results of locally advanced laryngeal carcinomas treated with TLM include series from a limited number of institutions. In general, patients treated with TLM represent a subgroup of selected patients and a number of them (usually in the supraglotis) will receive additional adjuvant treatment because of the nodal status. Overall and disease specific survival are expressed in Tables 2-3.

Although functional status has not been the main objective of most studies, it is noteworthy that TLM leads to faster

functional recovery compared to existing (mainly open) surgical techniques, with reduced hospital stay and a very marked decrease in the number of temporary tracheotomies. Moreover, in the majority of publications, age and respiratory functional status are not an exclusion criteria to undergo TLM. Functional outcomes for advanced supraglottic and glottic cancers treated by TLM are reported in Table 4-5.

Conclusions

Present reports in the literature suggest that, in expert centers, TLM is a very good alternative for advanced laryngeal carcinomas, with functional and oncological outcomes, totally comparable to those of other therapeutic alternatives in adequately selected patients. Compared with other surgical techniques, TLM reduces the morbidity for the patients, provides a faster functional recovery and the possibility to avoid a tracheostomy in a very high number of cases.

Further studies are still necessary to assess the reproducibility of the technique between centers and to define the need of adjuvant treatment after TLM. These aspects should help to definitively establish the role of this technique in the treatment of locally advanced laryngeal tumours.

References

1 Suárez C, Rodrigo JP, Silver CE, et al. Laser surgery for early to moderately advanced glottic, supraglottic, and hypopharyngeal cancers. Head Neck. 2012;34:1028-35.
2 Vilaseca I, Blanch JL, Berenguer J, et al. Transoral laser microsurgery for locally advanced (T3-T4a) supraglottic squamous cell carcinoma: Sixteen years of experience. Head Neck. 2016;38:1050-7.
3 Canis M, Ihler F, Martin A, et al. Results of 226 patients with T3 laryngeal carcinoma after treatment with transoral laser microsurgery. Head Neck. 2014 ;36:652-9.
4 Vilaseca I, Ballesteros F, Martínez-Vidal BM, et al. Quality of life after transoral laser microresection of laryngeal cancer: a longitudinal study. J Surg Oncol. 2013 ;108:52-6.
5 Canis M, Ihler F, Martin A, et al. Organ preservation in T4a laryngeal cancer: is transoral laser microsurgery an option? Eur Arch Otorhinolaryngol. 2013;270:2719-27.
6 Canis M, Martin A, Ihler F, et al. Results of transoral laser microsurgery for supraglottic carcinoma in 277 patients. Eur Arch Otorhinolaryngol. 2013;270:2315-26.
7 Pantazis D, Liapi G, Kostarelos D, et al. Glottic and supraglottic pT3 squamous cell carcinoma: outcomes with transoral laser microsurgery. Eur Arch Otorhinolaryngol 2015;272:1983-90.
8 Breda E, Catarino R, Monteiro E. Transoral laser microsurgery for laryngeal carcinoma: Survival analysis in a hospital-based population. Head Neck. 2015;37:1181-6.
9 Piazza C, Mangili S, Bon FD, et al. Preoperative clinical predictors of difficult laryngeal exposure for microlaryngoscopy: the Laryngoscore. Laryngoscope 2014;124:2561-7.
10 Peretti G, Piazza C, Mora F, et al. Reasonable limits for transoral laser microsurgery in laryngeal cancer. Curr Opin Otolaryngol Head Neck Surg. 2016;24:135-9.
11 Adolphs AP, Boersma NA, Diemel BD, et al. A systematic review of computed tomography detection of cartilage invasion in laryngeal cancer. Laryngoscope 2015;125:1650-5.
12 Taha Ms, Hassan O, Amir M, et al. Diffusion weighted MRI in diagnosing thyroid cartilage invasion in laryngeal carcinoma. Eur Arch Otorhinolaryngol 2014;271:2511-6.
13 Blanch JL, Vilaseca I, Bernal-Sprekelsen M, et al. Prognostic significance of surgical margins in transoral CO2 laser microsurgery for T1-T4 pharyngo-laryngeal cancers. Eur Arch Otorhinolaryngol. 2007;264:1045-51.
14 Jäckel MC, Ambrosch P, Martin A, Steiner W. Impact of reresection for inadequate margins on the prognosis of upper aerodigestive tract cancer treated by laser microsurgery. Laryngoscope. 2007;117:350-6.
15 Karatzanis AD, Waldfahrer F, Psychogios G, et al. Effect of repeated laser microsurgical operations on laryngeal cancer prognosis. Head Neck. 2010;32:921-8.
16 Peretti G, Plazza C, Cocco D, et al. Transoral CO2 laser treatment for Tis-T3 glottic cancer: the Brescia experience on 595 patients. Head Neck 2010;32:977-83..
17 Blanch JL, Vilaseca I, Caballero M, et al. Outcome of transoral laser microsurgery for T2-T3 tumours growing in the laryngeal anterior commissure. Head Neck. 2011;33:1252-9.
18 Vilaseca I, Bernal-Sprekelsen M, Luis Blanch J. Transoral laser microsurgery for T3 laryngeal tumors: Prognostic factors. Head Neck. 2010;32:929-38.
19 Iro H, Waldfahrer F, Altendorf-Hofmann A, et al. Transoral laser surgery of supraglottic cancer. Arch Otolaryngol Head Neck Surg 1998;124:1245-1250.
20 Rudert HH, Werner JA, Höft S. Transoral carbon dioxide laser resection of supraglottic carcinoma. Annal Otol Rhinol Laryngol 1999;108:819-827.
21 Ambrosch P, Rödel R, Kron M, et al. Transoral laser microsurgery for cancer of the larynx. A retrospective analysis of 657 patients (in German). Onkologe 2001;7:505-512.
22 Motta G, Esposito E, Testa D, et al. CO2 laser treatment of supraglottic cancer. Head Neck. 2004;26:442-6.
23 Davis RK, Hadley K, Smith ME. Endoscopic vertical partial laryngectomy. Laryngoscope 2004;114:236-240.
24 Cabanillas R, Rodrigo JP, Llorente JL, et al. Oncologic outcomes of transoral laser surgery of supraglottic carcinoma compared with transcervical approach. Head Neck. 2008;30:750-5.
25 Peretti G, Piazza C, Ansarin M, et al. Transoral CO2 laser microsurgery for Tis-T3 supraglottic squamous cell carcinomas. Eur Arch Otorhinolaryngol. 2010;267:1735-42.
26 Peretti G, Piazza C, Penco S, et al. Transoral laser microsurgery as primary treatment for selected T3 glottic and supraglottic cancers. Head Neck. 2016;38:1107-12.
27 Motta G, Esposito E, Cassiano B, et al. T1-T2-T3 glottic tumors: fifteen years experience with CO2 laser. Acta Otolaryngol Suppl 1997;527:155-9.
28 Motta G, Esposito E, Motta S, et al. CO2 laser surgery in the treatment of glottic cancer. Head Neck 2005;27:566-574.
29 Hinni M, Salassa JR, Grant DG, et al. Transoral Laser Microsurgery for Advanced Laryngeal Cancer. Arch Otolaryngol Head Neck Surg 2007;133:1198-1204.
30 Grant DG, Salassa JR, Hinni ML, et al. Transoral laser microsurgery for untreated glottic carcinoma. Otolaryngol Head Neck Surg 2007;137:482-486.
31 Cabanillas R, Rodrigo JP, Llorente JL, et al.. Functional outcomes of transoral laser surgery of supraglottic carcinoma compared with a transcervical approach. Head Neck 2004;26:653-9.
32 Olthoff A, Ewen A, Wolff HA, et al. Organ function and quality of life after transoral laser microsurgery and adjuvant radiotherapy for locally advanced laryngeal cancer. Strahlenther Onkol 2009;185: 303-9.

Open partial surgery for primary and recurrent laryngeal cancer

Giuseppe Spriano MD**, Giuseppe Rizzotto*** MD**, Andy Bertolin*** MD, **Giuseppe Mercante** MD, **Antonio Schindler**† MD, **Erika Crosetti**† MD, **and Giovanni Succo**† MD
Otolaryngology Dept – IRCCS IRE, National Cancer Institute "Regina Elena", Rome, Italy
*Otolaryngology Dept – Vittorio Veneto Hospital, Treviso, Italy
†Biomedical and Clinical Science Dept "L. Sacco" – University of Milan, Milan, Italy
†Head and Neck Oncology Service – IRCCS FPO Candiolo Cancer Institute, Turin, Italy
†Otolaryngology Dept – Oncology Dept University of Turin, San Luigi Gonzaga Hospital, Turin, Italy

Correspondence:
Erika Crosetti MD
Head and Neck Oncology Service, IRCCS FPO, Candiolo Cancer Institute
Strada Provinciale 142 Km 3.95, 10060 Candiolo, Italy
Email: erikacro73@yahoo.com

Abstract

The evolution of treatment for advanced laryngeal carcinoma is focusing on maintaining locoregional control while also maintaining a functional larynx. Open partial horizontal laryngectomies may be a viable option for intermediate and selected advanced laryngeal carcinoma while maintaining laryngeal functions. Strict selection criteria, based on locoregional tumour extent as well as on patient's general condition, allow excellent oncological outcomes. Whereas, albeit slightly worse, but similar, outcomes are also obtained in radiorecurrent patients, these procedures must be included as an option in selected patients with radiorecurrent laryngeal cancer.

J ENT Masterclass 2016; 9 (1): 75 - 82.

Key words

Partial laryngectomy, laryngeal cancer, supracricoid laryngectomy, supratracheal laryngectomy, salvage surgery

Introduction

The last two decades have gradually witnessed a paradigm shift in the treatment of laryngeal cancer with the primary focus now on organ and function preservation[1,2].

Several approaches are available for the treatment of laryngeal cancer at the different primary tumour (T) and nodal (N) stages, with comparable rates of overall survival, locoregional control and laryngectomy-free survival.

The non-surgical approaches, primary radiotherapy[3] (RT) for early stages (I-II) and concurrent chemoradiotherapy[2] (CT-RT) or induction chemotherapy followed by radiotherapy[1] (IC-RT) for advanced stages (III-IV), have demonstrated that larynx preservation is feasible, even though the disappointing long-term results[4] of CT-RT deserve further evaluation and investigation[5].

On the other hand, surgery can be offered to patients as a valuable method to preserve part of the larynx and its functions, avoiding the negative physical and psychosocial impact of a permanent tracheostomy[6]. Open partial horizontal laryngectomies[7] (OPHL) and transoral laser microsurgery (TLM)[8] have been used extensively, with excellent results, as upfront treatment in early (I-II) as well as in more advanced stages (III). Even in the latter case, OPHLs have shown very good oncological outcomes, high laryngectomy-free survival, relatively low morbidity and mortality rates, and finally acceptable functional outcomes, as long as a careful selection of patients is carried out (good general and functional conditions, cN0, patient compliance to an intensive rehabilitation protocol, different subcategories based on local T extent)[9,10]. After an appropriate selection, based essentially on pre-treatment and post-treatment tumour extent, OPHLs can also be used as salvage procedures in radiorecurrent[11] and laser-recurrent[12] laryngeal cancer, achieving comparable survival rates, an acceptable (although higher) morbidity, effective swallowing and a sufficiently intelligible voice.

Based on this scenario, a review of recent English language literature was carried out in an attempt to assess the changes which are occurring, based on indications, strategies and technique refinements. We focused only on OPHLs since vertical partial laryngectomies have now largely been replaced by TLM.

History and current classification

In the late nineteenth century, surgeons began to think about how to save part of the larynx and its functions[13], but it was only in the second half of the last century that these interventions became established as an effective weapon in the treatment of laryngeal cancer, untreated or radiorecurrent in an intermediate stage and also in selected advanced stages.

Buck and Solis-Cohen in the USA, and Hautant and Leroux-Robert in France were the pioneers of vertical partial laryngectomies. Supraglottic laryngectomy, described by Alonso in 1947, opened the era of horizontal partial laryngectomies[14] (HSL), and later Bocca et al.[15] popularized and extended the indications for this excellent procedure.

The concept of applying the idea of a horizontal, drawer-like resection to non-supraglottic carcinomas, i.e. to glottic and subglottic tumours, was first suggested by Mayer and Rieder in Vienna[16] and became popular through routine application to intermediate categories of tumours in France[17,18] and in Italy[19,20], and later in USA in 2001[21]. Finally, under the impulse of Laccourreye and colleagues[22], these interventions, usually referred to as "supracricoid partial laryngectomies" (SCPL), have gained major importance for the treatment of intermediate and selected advanced laryngeal carcinomas.

In 2014, the European Laryngological Society proposed a classification[23] of the more commonly adopted procedures according to extent of resection, including three types of OPHL: type I – supraglottic, type II – supracricoid, and type III – supratracheal. This proposal attempted to establish a comprehensive yet straightforward classification system of these surgical procedures, to aid in teaching this surgery to residents and novices and in interpreting and comparing the post-operative results achieved by different institutions.

In particular, OPHL type III expands the indications of the type II procedures to some problematic glottic cT3 (i.e. subglottic extensions towards the cricoarytenoid joint) and with great caution in a very limited number of cT4a cases with minimal anterior extralaryngeal extension, when it is reasonable to expect it to be an exclusive treatment[24].

OPHLs as upfront treatment

Following its recent widespread diffusion, particularly in many European and South American countries, OPHLs are today addressing the upfront treatment of laryngeal carcinoma in early and intermediate stages (rarely T1, T2 and selected T3). The procedure has been shown to be effective, even in selected limited T4a disease[7,25-29].

With regard to supraglottic cancer, our literature review revealed that, if complete resection can be achieved, the oncologic results of TLM appear to be comparable to those of type I OPHLs.

Studies comparing OPHL type I vs TLM I have demonstrated equivalent oncologic results[30] (5-year disease-specific survival (DSS) 72% vs 80%, 5-year laryngeal preservation rate 80% vs 86%, and in both arms, all patients who survived for 5 years after the surgical treatment of tumours retained the larynx), but the comparison of functional outcomes[31] revealed that TLM had a significantly lower functional impact on swallowing than OPHL type I and was associated with lower morbidity and a shorter hospitalization time.

Supraglottic tumours are more difficult to control loco-regionally compared with glottic ones, given their presentation at a later stage and with a much higher incidence of cervical node metastasis[32].

Given these negative characteristics, and despite the good results obtained by transoral procedures (TLM and transoral robotic surgery (TORS)[33,34], the conservative management of early-intermediate supraglottic cancer can be safely achieved by type I and type IIb OPHLs with larynx preservation in the majority of patients (95% at 5 years)[35]. These procedures therefore retain their relevance, in particular, for patients who are difficult to manage endoscopically, due to the lack of exposure and in the case of bulky tumours.

The preoperative selection should focus on the patient's related exclusion criteria[10] as well as poor general condition, severe diabetes mellitus, severe bronchopulmonary chronic obstructive disease, neurological problems impairing the ability to expectorate and/or swallow or severe cardiac disease. Advanced age, an important cut-off for relative surgical indication, cannot be considered, in itself, an exclusion criterion[36].

Undoubtedly, analysing the recent scientific reports for laryngeal cancer, there is a substantial difference between English-speaking countries and some European countries such as Italy. National Comprehensive Cancer Network (NCCN) guidelines Version 1.2016[25] as well as the Italian Head and Neck Society (IHNS) guidelines for glottic/supraglottic cancer amenable to larynx preservation include the option of OPHL for selected T^3. In the current practice, the term "selected" means a patient in good general condition (prerequisite to cope successfully with probable and prolonged dysphagic sequelae) when it is reasonable to expect OPHL to be the exclusive treatment (T^2-T^3 N^0 tumours with anterior commissure or transglottic spread). The same principle has sometimes been applied, albeit with great caution, as the upfront option in very restricted pT4a cases, with minimal anterior extralaryngeal extent, when it is reasonable to expect an exclusive treatment[10,28].

Type II OPHLs (supracricoid partial laryngectomies) were first used for early laryngeal cancer and have recently been suggested for T^3 laryngeal cancer as well[22,27,37]. In patients with T^2 and select T^3 tumours, 5-year local control rates exceed 90% with disease-free survival (DFS) ranging between 70% and 90%[9,10,26,38-43]. The overall survival (OS) as pooled mean is about 79.7% and the rate of completion total laryngectomy due to a severe grade of aspiration is low (1–3%)[9,10,44].

In type II OPHL, the paraglottic space is resected and the hyoid bone is impacted onto the cricoid cartilage in order to reconstruct the larynx. Although the vocal cords are resected, speech and swallowing are retained without the need for term tracheostomy[6].

In 1972, Serafini[19] reported a new type of open partial laryngectomy called tracheohyoidoepiglottopexy aimed at managing laryngeal cancer with subglottic extension: this procedure entailed the preservation of the suprahyoid epiglottis as well as the pexy of the hyoid bone and the residual epiglottis to the first tracheal ring. Because of removal of both arytenoids, the resulting functional outcomes were poor and Serafini abandoned this technique in the early 1980s.

In the 1990s, Laccourreye et al.[45] reported a modification of conventional supracricoid partial laryngectomy (SCPL), removing the cricoid ring in the case of glottic tumours with anterior subglottic extension: this has opened the way for "functional" supratracheal partial laryngectomies (OPHL type III), whose current version was described in 2006 by Rizzotto et al.[20].

Nowadays, OPHL type III involves resection of the entire glottic and subglottic sites along the thyroid cartilage, sparing both or at least one functioning cricoarytenoid unit (i.e. half of the posterior cricoid plate, with the corresponding arytenoid and the intact inferior laryngeal nerve on the same side). Inferiorly, the limit of resection encompasses the cricoid reaching the first tracheal ring.

The oncological and functional results reported in the literature are still insufficient to attribute a specific role to type III OPHL. However, they are very interesting and deserve further investigation in larger multi-institutional series[20,24,45-47].

In patients affected by pT^3 cancer, the 5-year locoregional control (LRC) and DFS are 88.7% and 86.4%, respectively, while in patients with a pT4a, LRC drops to 64.8% and DFS to 52.7%. The functional results are comparable to those of the more studied type II OPHL.

Finally, a possible future role of type III OPHL could be that of a rescue intraoperative procedure if, during a type II OPHL, the resection margins are insufficient and thus allowing the surgeons to avoid shifting to an upfront total laryngectomy.

OPHL type II for recurrent laryngeal cancer after radiotherapy

In recent years, the treatment of laryngeal cancer has increasingly focused on tumour control as well as preservation of functionality. As a result, the attention given to function preservation and conservative approaches has meant that total laryngectomy has gradually been replaced as the primary treatment in favour of radiation, chemoradiation protocols, and conservative surgery[2,46,48].

The local recurrence rate after radiation therapy (RT) ranges from 5% to 13% for T^1 and from 25% to 30% for T^2 laryngeal cancer[49,50]. Recurrent laryngeal tumours often demonstrate aggressive behaviour, arise in a field where lymphatic drainage is unpredictable, and are associated with poor control rates[51]. Furthermore, diagnosis is more difficult because of the radiation sequelae such as oedema and the low specificity of conventional diagnostic tools. Different options have been proposed for the surgical treatment of laryngeal recurrences after RT failure: both endoscopic with laser excision[52-54], and with open partial laryngectomies, in particular, the horizontal procedures (OPHL)[55-65], and total laryngectomy[66-69]. However, even though the technique of total laryngectomy is the same in laryngeal recurrences as in previously untreated patients, it is associated with an increased risk of complications corresponding to a worse quality of life (QoL) for the patients.

The only validated therapeutic option in recurrences of laryngeal squamous cell carcinoma (LSCC) is total laryngectomy, however, several studies in the last decade have also evaluated different conservative surgical procedures and, in particular, OPHL type II.

OPHL type II (including both supracricoid partial laryngectomy with cricohyoidoepiglottopexy, SCPL–CHEP or OPHL type IIa, and supracricoid partial laryngectomy with cricohyoidopexy, SCPL–CHP or OPHL type IIb) can be adopted in many intermediate laryngeal cancers, strictly respecting tumour- and patient-related indications[58-60].

Some reports have documented the feasibility of OPHL type II in terms of local tumour control and functional results after radiotherapy. However, there is a bias related to the small number of cases and the low number of centres performing this type of surgery. Paleri et al. published an interesting meta-analysis on radiorecurrent laryngeal squamous cell carcinoma in 560 patients treated with open conservative laryngectomy but not focused on OPHL[70]. In their reports, different partial laryngectomy techniques have been considered.

Since the first report of OPHL type II after radiation failure, many centres worldwide have adopted this procedure as salvage surgery. Different papers by authors from different countries have confirmed the feasibility of the technique[55-64] and one was from Japan[65].

A meta-analysis of those papers shows that the majority of cases recur in a low to intermediate stage (rT1 27.5%, rT2 42.2%, rT3 23.1% and rT4 7.2%). The surgical procedures were OPHL type IIa or type IIb.

Local control at 24 months may vary from 70% to 95%[55-57,59-62,65] and DFS at 36 months ranged between 70% and 90%[55-59,61,65]. OS at 5 years has been reported between 70% and 90%[55-57,59,64,65].

Some cases require salvage or functional total laryngectomy because of re-recurrence or aspiration. The laryngeal preservation rate was 85.2%. The pooled mean decannulation rate was 92.1% based on data reported in the literature for over 200 patients. The incidence of laryngeal stenosis has to be considered to be a possible complication; this was described in 3.9% of cases and it may require further surgery to enhance airway patency and to facilitate tracheostomy decannulation. This event has been described in up to 8% of cases. An efficient swallowing was reported in over 90% of cases. The percutaneous endoscopic gastrostomy (PEG) dependence rate was 3.5%, while the aspiration pneumonia rate was 6.4% based on data reported for 221 patients.

Voice and speech outcomes are rarely reported in the literature, however, some data are available. In our earlier paper, we reported an 'acceptable quality of voice for most patients'[55]. Voice quality was definitively hoarse in all patients and maximum phonation time (MPT) ranged from 3 to 18 s (mean, 8.3 s). Marchese-Ragona et al. and Leon et al. reported 'satisfactory voice intelligibility in all cases'[56]. Similar results were also reported by Pellini et al. in a study in decannulated patients in which voice was evaluated as hoarse to varying degrees (19 patients grade 1, 49 grade 2, and 8 grade 3)[59]. MPT ranged from 2 to 18 s (mean, 7.9 s). Finally, Deganello et al. reported 'satisfactory voice production that allowed normal social interactions'[58].

Laryngeal recurrence represents the most salvageable area in head and neck with reported OS higher than 60% at 2 years[71]. Furthermore, it is more frequent in the primary site than in regional lymph nodes or distant sites[72,73]. Unfortunately, laryngeal salvage surgery corresponds to a decreased QoL and degradation of laryngeal function[71].

Diagnosis of laryngeal recurrence after radiotherapy can be challenging because of chronic oedema and, occasionally, arytenoid fixation. Difficulties in obtaining a representative biopsy are common due to oedema, chronic inflammation and fibrosis with higher chances of false negative results[51]. Furthermore, imaging has low specificity after radiation therapy.

Recurrent and persistent laryngeal cancer after radiotherapy is associated with aggressive growth patterns, high extralaryngeal spread and subglottic involvement, and intravascular and perineural invasion[51]. As a result, total laryngectomy is the most performed salvage procedure in the case of recurrent/persistent LSCC after radiotherapy. However, salvage total laryngectomy is associated with an increased risk of wound and systemic complications. In the review of the literature performed by Goodwin[71], major complications ranged from 5% to 48% while pharyngocutaneous fistula rates ranged from 30% to 80%[57,67,74,75]. In these scenarios, OPHLs have to be considered to be a valuable alternative for selected recurrent laryngeal cancers.

Published papers showed a very good local control rate which was over 90% at 24 months. rT stages reported in the literature may vary from rT1 to rT4 and the high rate of local control confirms that salvage OPHL type II can be a valuable treatment strategy in radiorecurrent tumours. The DFS rate at 36 months was 80%. This reflects the percentage of patients who are alive and without disease. Consequently, DFS evaluates not only local control but also regional control and distant metastases, and thus the global efficacy in terms of cancer cure of the treatment. The 5-year overall survival, which is related to the presence of comorbidities, synchronous/metachronous second primaries, and other diseases, was almost 80% confirming that OPHL type II represents a good alternative to total laryngectomy.

Functional results are good with 90% of patients recovering laryngeal function but some complications may occur, in particular, aspiration pneumonia (6.4%) and PEG dependence (3.5%).

Functional outcomes

When analysing OPHL outcomes, not only should safety of the surgical procedure and survival rates be considered but also functional outcomes. In fact, any treatment of laryngeal cancer severely impacts on several body functions, including respiration, swallowing, and voice, as well as quality of life (QoL)[76]. These functional outcomes may come into play when the treatment option is decided in conjunction with the patients and need to be fully discussed in preoperative counselling. The functional outcomes after OPHL which have been mainly investigated are a) length of hospital stay, time of feeding tube and tracheal cannula removal; b) swallowing functional outcome; c) voice functional outcomes; d) quality of life[77]. Most studies included patients after OPHL type II, but preliminary data suggest similar findings for OPHL type III[47,78].

The mean length of hospital stay varies from a minimum of 5 days to a maximum of 104 days[79,80]. Mean feeding-tube removal time shows high variability as well, ranging between 10 and 88 days[81,82]. Additionally, great heterogeneity was found in mean decannulation times, varying between 8 days and 105 days[79,83]. On the contrary, little variability exists in decannulation rates, which range between 85.7% and 100%[84,85], confirming good respiratory outcomes following OPHL.

Heterogeneous swallowing functional outcomes after OPHL are reported in the literature. By the first postoperative month, aspiration ranges from 30% to 100%[83,86], occurring more frequently with liquids than with solids and resolving spontaneously within 6 months in 15–80.4% of cases[44,87]. An unrestricted diet is safely achieved between the 6th postoperative month and the 1st postoperative year in 53–100% of patients[88,89]. In the long-term, between 12.9% and 67% of patients are reported to have occasional aspiration. However, a certain degree of chronic aspiration is demonstrated to be well tolerated in patients after OPHL[90], with a rate of aspiration pneumonia ranging between 0% and 21.7%. A moderate degree of pharyngeal retention of food, the presence of premature spillage and the necessity of multiple swallows per bolus are also often reported[88,89].

Voice impairment has been recognized as major complications in patients subjected to OPHL type II and III, and can significantly affect their physical and emotional condition. Thus, in OPHL type II and III patients, the voice is produced using a neoglottis that is inherently patent at rest and in turn demonstrated substantially less volitionally induced valving activity and resistance to airflow during voicing[91]. The loose and unstable neoglottic closure results in a significant loss of air during phonation that requires an increase in expiratory pressure and strength in the closure of the neoglottis in order to achieve rigidity and improve vibration.

The functional consequence is a strained, deep and asexualized voice, difficult to modulate and to raise; speech is composed of short sentences, because the patients are short of breath[92]. Maximum phonation time (MPT) implies adequacy of air support for speech and, in supracricoid laryngectomy (SCL) patients, is quite low, probably due to a lower resistance of the neoglottis with consequent air loss during phonation[85].

Thus, in order to compensate for the air wastage during phonation, the SCL patient needs to increase neoglottal resistance and subglottic pressure with consequent vocal fatigue because of the increased physiological effort required to phonate. Interestingly, MPT appears not to be significantly affected by arytenoid removal, suggesting well-tolerated recovery of the glottal closure after removal of the ipsilateral arytenoid and reconstruction of the neoglottis[93].

Only a few studies on functional outcome after OPHL included an assessment of QoL. Data are sometimes contradictory; it must be noted that QoL brings many factors into play, including the patient's psychosocial traits, cultural and ethnic backgrounds. Therefore, it is not surprising that different authors report different QoL scores on a small number of subjects studied in different countries. When swallowing-related QoL was analysed, data suggest that swallowing difficulties have only limited impact on daily living activities. Moreover, it is to be noted that between 80% and 90% of patients undergoing OPHL achieve the ability to eat out without restriction[80].

Self-assessment data revealed a moderate impact on voice related QoL (V-RQoL) in terms of speech after OPHL type II and III, on the emotional, physical and functional levels of the voice handicap index (VHI), even if some authors reported high degrees of vocal handicap[82,85]. Since the voice is mainly used for everyday verbal communication, it is possible that vocal QoL is perceived by the patients as not being very compromised, even if the voice per se is rather poor[94].

Conclusion

Multiple single and multi-institutional series support the evidence that open partial laryngectomies represent a valuable option for the treatment of laryngeal cancer in early, intermediate and also selected advanced stage, maintaining high OS, LRC and DFS as well as acceptable functional outcomes.

Whereas, albeit slightly worse, but similar, outcomes are also obtained in radiorecurrent patients, these procedures must be included as an option in selected patients with radiorecurrent laryngeal cancer.

References

1. The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med. 1991: p. 1685-1690.
2. Forastiere A, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. 2003: p. 2091–2098.
3. Mendenhall W, Werning J, Hinerman R, et al. Early laryngeal cancer. 2002: p. 3-9.
4. Forastiere A, Zhang Q, Webwr R, et al. Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. 2013 Mar 1: p. 845-852.
5. Denaro N, Russi E, Lefebvre J, Merlano M. A systematic review of current and emerging approaches in the field of larynx preservation. 2014 Jan: p. 16-24.
6. Tomeh C, Holsinger C. Laryngeal Cancer. 2014 Apr: p. 147-153.
7. Thomas L, Drinnan M, Natesh B, et al. Open conservation partial laryngectomy for laryngeal cancer: a systematic review of English language literature. 2012 May: p. 203-211.
8. Peretti G, Piazza C, Cocco D, et al. Transoral CO2 laser treatment for Tis-T3 glottic cancer: the University of Brescia experience on 595 patients. 2010 Aug: p. 977-983.
9. Succo G, Crosetti E, Bertolin A, et al. Benefits and drawbacks of open partial horizontal laryngectomies, Part A: Early- to intermediate-stage glottic carcinoma. 2016 Apr: p. E333-340.
10. Succo G, Crosetti E, Bertolin A, et al. Benefits and drawbacks of open partial horizontal laryngectomies, Part B: Intermediate and selected advanced stage laryngeal carcinoma. 2016 Apr: p. E649-657.
11. Marioni G, Marchese-Ragona R, Kleinsasser N, et al. Partial laryngeal surgery in recurrent carcinoma. 2015 Feb: p. 119-124.
12. Lucioni M, Bertolin A, Lionello M, et al. Open partial horizontal laryngectomy for salvage after failure of CO- laser-assisted surgery for glottic carcinoma. 2016 Jan: p. 169-175.
13. HB S. Case of larynx, successfully removed by laryngectomy: with an analysis of 50 cases of tumours of the larynx treated by operation. NY Med J. 1865: p. 110-126.
14. Alonso J. Conservative surgery of cancer of the larynx. Trans Am Acad Ophthalmol Otolaryngol. 1947: p. 633-642.
15. Bocca E, Pignataro O, Oldini C, et al. Extended supraglottic laryngectomy. Review of 84 cases. Ann Otol Rhinol Laryngol. 1987: p. 384-386.
16. Mayer E, Rieder W. Technique de laryngectomie permettant de conserver la permeabilité respiratoire (La cricohyoidepexie). Ann Otolaryngol Chir Cervicofac. : p. 677-681.
17. Labayle S, Bismuth R. La laryngectomie totale avec reconstruction. Ann Otolaryngol Chir Cervicofac. 1971: p. 219-228.
18. Piquet J, Desaulty A, Decroix G. La crico-hyoido-épiglotto-pexie. Technique opératoire et résultats fonctionnels. Ann Otolaryngol Chir Cervicofac. 1974: p. 681-690.
19. Serafini I. Reconstructive laryngectomy. Rev Laryngol Otol Rhinol. 1972: p. 23-32.
20. Rizzotto G, Succo G, Lucioni M, Pazzaia T. Subtotal laryngectomy with tracheohyoidopexy: a possible alternative to total laryngectomy. Laryngoscope. 2006: p. 1907-1917.
21. Weinstein G, El-Sawy M, Ruix C, et al. Laryngeal preservation with supracricoid partial laryngectomy results in improved quality of life when compared with total laryngectomy. Laryngoscope. 2001: p. 191-199.
22. Chevalier D, Laccourreye O, Brasnu D, et al. Cricohyoidoepiglottopexy for glottic carcinoma with fixation or impaired motion of the true vocal cord: 5-year oncologic results with 112 patients. Ann Otol Rhinol Laryngol. 1997: p. 364-369.
23. Succo G, Peretti G, Piazza C, et al. Open partial horizontal laryngectomies: a proposal for classification by the working committee on nomenclature of the European Laryngological Society. Eur Arch Otorhinolaryngol. 2014: p. 2489-2496.
24. Succo G, Bussi M, Presutti L, et al. Supratracheal laryngectomy: current indications and contraindications. Acta Otorhinolaryngol Ital. 2015 Jun: p. 146-156.
25. National Comprehensive Cancer Network. Clinical practice Guidelines in Oncology Version 1. ; 2016.
26. Mercante G, Grammatica A, Battaglia P, et al. Supracricoid partial laryngectomy in the management of T3 laryngeal cancer. Otolaryngol Head Neck Surg. 2013 Nov: p. 714-720.
27. Lima R, Freitas E, Dias F, et al. Supracricoid laryngectomy with cricohyoidoepiglottopexy for advanced glottic cancer. Head Neck. 2006 Jun: p. 481-486.
28. Laccourreye O, Brasnu D, Biacabe B, et al. Neo-adjuvant chemotherapy and supracricoid partial laryngectomy with cricohyoidopexy for advanced endolaryngeal carcinoma classified as T3-T4: 5-year oncologic results. Head Neck. 1998 Oct: p. 595-599.
29. Sessions D, Lenox J, Spector G. Supraglottic laryngeal cancer: analysis of treatment results. Laryngoscope. 2005 Aug: p. 1402-1410.
30. Cabanillas R, Rodrigo J, Llorente J, Suárez C. Oncologic outcomes of transoral laser surgery of supraglottic carcinoma compared with a transcervical approach. Head Neck. 2008 Jun: p. 750-755.
31. Peretti G, Piazza C, Cattaneo A, et al. Comparison of functional outcomes after endoscopic versus open-neck supraglottic laryngectomies. Ann Otol Rhinol Laryngol. 2007: p. 19-23.
32. Iro H, Waldfahrer F, Altendorf-Hofmann A, et al. Transoral laser surgery of supraglottic cancer. Arch Otolaryngol Head Neck Surg. 1998: p. 1245-1250.
33. Peretti G, Piazza C, Penco S, et al. Transoral laser microsurgery as primary treatment for selected T3 glottic and supraglottic cancers. Head Neck. 2016 Mar 11.
34. Ansarin M, Zorzi S, Massaro M, et al. Transoral robotic surgery vs transoral laser microsurgery for resection of supraglottic cancer: a pilot surgery. Int J Med Robot. 2014 Mar: p. 107-112.
35. Spriano G, Antognoni P, Piantanida R, et al. Conservative management of T1-T2N0 supraglottic cancer: a retrospective study. Am J Otolaryngol. 1997 Sep-Oct: p. 299-305.
36. Schindler A, Favero E, Capaccio P, et al. Supracricoid laryngectomy: age influence on long-term functional results. Laryngoscope. 2009 Jun: p. 1218-1225.
37. Dufour X, Hans S, De Mones E, et al. Local control after supracricoid partial laryngectomy for “advanced” endolaryngeal squamous cell carcinoma classified as T3. Arch Otolaryngol Head Neck Surg. 2004 Sep: p. 1092-1099.
38. Laccourreye O, Muscatello L, Laccourreye L, et al. Supracricoid partial laryngectomy with cricohyoidoepiglottopexy for “early” glottic carcinoma classified as T1-T2N0 invading the anterior commissure. Am J Otolaryngol. 1997 Nov-Dec: p. 385-390.
39. Akbas Y, Demireller A. Oncologic and functional results of supracricoid partial laryngectomy with cricohyoidopexy. Otolaryngol Head Neck Surg. 2005: p. 783-787.
40. Adamopoulos G, Yiotakis J, Stavroulaki P, Manolopoulos L. Modified supracricoid partial laryngectomy with cricohyoidopexy: series report and analysis of results. Otolaryngol Head Neck Surg. 2000: p. 288-293.
41. Ndiaye M, Dassonville O, Poissonnet G, et al. The supracricoid laryngectomy with cricohyoidopexy. Carcinological and functional results. 23 cases report of the Centre A Lacassagne (Nice). Rev Laryngol Otol Rhinol (Bord). 2004: p. 113-116.
42. Gallo A, Manciocco V, Simonelli M, et al. Supracricoid partial laryngectomy in the treatment of laryngeal cancer: univariate and maltivariate analysis of prognostic factors. Arch Otolaryngol Head Neck Surg. 2005: p. 620-625.
43. Schwaab G, Kolb F, Julieron M, et al. Subtotal laryngectomy with cricohyoidopexy as first treatment procedure for supraglottic carcinoma: Institut Gustave-Roussy experience (146 cases, 1974-1997). Eur Arch Otorhinolaryngol. 2001: p. 246-249.
44. Benito J, Holsinger F, Pérez-Martín A, et al. Aspiration after supracricoid partial laryngectomy: Incidence, risk factors, management, and outcomes. Head Neck. 2011 May: p. 679-685.
45. Laccourreye O, Brasnu D, Jouffre V, et al. Supra-cricoid partial laryngectomy extended to the anterior arch of the cricoid with tracheo-crico-hyoido-epiglottopexy. Oncologic and functional results. Ann Otolaryngol Chir Cervicofac. 1996: p. 15-19.
46. Rizzotto G, Crosetti E, Lucioni M, et al. Oncologic outcomes of supratracheallaryngectomy: Critical analysis. Head Neck. 2015 Oct: p. 1417-1424.
47. Schindler A, Fantini M, Pizzorni N, et al. Swallowing, voice, and quality of life after supratracheal laryngectomy: preliminary long-term results. Head Neck. 2015 Apr: p. 557-566.
48. Adelstein D, Li Y, Adams G, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J ClinOncol. 2003: p. 92–98.
49. Budach W, Hehr T, Budach V, et al. A meta-analysis of hyperfractionated and accelerated radiotherapy and combined chemotherapy and radiotherapy regimens in unresected locally advanced squamous cell carcinoma of the head and neck. BMC Cancer. 2006: p. 28.
50. Bonner J, Harari P, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. N Engl J Med. 2006: p. 567–578.
51. Zbären P, Nuyens M, Curschmann J, Stauffer E. Histologic characteristics and tumor spread of recurrent glottic carcinoma: analysis on whole-organ sections and comparison with tumor spread of primary glottic carcinomas. Head Neck. 2007 Jan: p. 26-32.
52. Steiner W, Vogt P, Ambrosch P, Kron M. Transoral car- bon dioxide laser microsurgery for recurrent glottic carcinoma after radiotherapy. Head Neck. 2004: p. 477– 484.
53. Quer M, Leon X, Orus C, et al. Endoscopic laser surgery in the treatment of radiation failure of early laryngeal carcinoma. Head Neck. 2000: p. 520–523.
54. Puxeddu R, Piazza C, Mensi M, et al. Carbon dioxide laser salvage surgery after radiotherapy failure in T1 and T2 glottic carcinoma. Otolaryngol Head Neck Surg. 2004: p. 84–88.
55. Spriano G, Pellini R, Romano G, et al. Supracricoid partial laryngectomy as salvage surgery after radiation failure. Head Neck. 2002: p. 759-765.
56. Marchese-Ragona R, Marioni G, Chiarello G, et al. Supracricoid laryngectomy with cricohyoidopexy for recurrence of early-stage glottic carcinoma after irradiation. Long-term oncological and functional results. Acta Otolaryngol. 2005: p. 91-95.
57. Piazza C, Peretti G, Cattaneo A, et al. Salvage surgery after radiotherapy for laryngeal cancer: from endoscopic resections to open-neck partial and total laryngectomies. Arch Otolaryngol Head Neck Surg. 2007 Oct: p. 1037-1043.
58. Deganello A, Gallo O, De Cesare J, et al. Supracricoid partial laryngectomy as salvage surgery for radiation therapy failure. Head Neck. 2008: p. 1064-1071.
59. Pellini R, Pichi B, Ruscito P, et al. Supracricoid partial laryngectomies after radiation failure: a multi-institutional series. Head Neck. 2008: p. 372-379.
60. De Vincentiis M, De Virgilio A, F B, et al. Oncologic results of the surgical salvage of recurrent laryngeal squamous cell carcinoma in a multicentric retrospective series: emerging role of supracricoid partial laryngectomy. Head Neck. 2015 Jan: p. 84-91.
61. Laccourreye O, Weinstein G, Naudo P, et al. Supracricoid partial laryngectomy after failed laryngeal radiation therapy. Laryngoscope. 1996: p. 495-498.
62. Makeieff M, Venegoni D, Mercante G, et al. Supracricoid partial laryngectomies after failure of radiation therapy. Laryngoscope. 2005: p. 353-357.
63. Leon X, Lopez M, Garcia J, et al. Supracricoid laryngectomy as salvage surgery after failure of radiation therapy. Eur Arch Otorhinolaryngol. 2007: p. 809-814.
64. Luna-Ortiz K, Pasche P, Tamez-Velarde M, Villavicencio-Valencia V. Supracricoid partial laryngectomy with cricohyoidoepiglottopexy in patients with radiation therapy failure. World J SurgOncol. 2009 Dec 19: p. 101.
65. Nakayama M, Okamoto M, Hayakawa K, et al. Clinical outcome of supracricoidlaryngectomy with cricohyoidoepiglottopexy: radiation failure versus previously untreated patients. AurisNasus Larynx. 2013 Apr: p. 207-210.
66. Jorgensen K, Godballe C, Hansen O, Bastholt L. Cancer of the larynx—treatment results after primary radiother- apy with salvage surgery in a series of 1005 patients. Acta Oncol. 2002: p. 69–76.
67. Weber R, Berkey B, Forastiere A, et al. Outcome of salvage total laryngectomy following organ preservation therapy: the Radiation Therapy Oncology Group trial 91- 11. Arch Otolaryngol Head Neck Surg. 2003: p. 44-49.
68. Johansen L, Grau C, Overgaard J. Nodal control and surgical salvage after primary radiotherapy in 1782 patients with laryngeal and pharyngeal carcinoma. Acta Oncol. 2004: p. 486-494.
69. Ganly I, Patel S, Matsuo J, et al. Results of surgical salvage after failure of definitive radiation therapy for early-stage squamous cell carcinoma of the glottic larynx. Arch Otolaryngol Head Neck Surg. 2006: p. 59–66.
70. Paleri V, Thomas L, Basavaiah N, et al. Oncologic outcomes of open conservation laryngectomy for radiorecurrent laryngeal carcinoma: a systematic review and meta-analysis of English-language literature. Cancer. 2011 Jun 15: p. 2668-2676.
71. Goodwin WJ. Salvage surgery for patients with recurrent squamous cell carcinoma of the upper aerodigestive tract: when do the ends justify the means? Laryngoscope. 2000 Mar: p. 1-18.
72. Jesse RH The evaluation of treatment of patients with extensive squamous cancer of the vocal cords Laryngoscope. 1975 Sep;85(9):1424-9
73. Shah JP, Loree TR, Kowalski L,Conservation surgery for radiation-failure carcinoma of the glottic larynx, Head Neck. 1990 Jul-Aug;12(4):326-31.
74. Johansen LV, Overgaard J, Elbrønd O,Pharyngo-cutaneous fistulae after laryngectomy. Influence of previous radiotherapy and prophylactic metronidazole Cancer. 1988 Feb 15;61(4):673-8
75. Sassler A, Esclamado R, Wolf G. Surgery after organ preservation therapy. Analysis of wound complications. Arch Otolaryngol Head Neck Surg. 1995 Feb: p. 162-165.
76. Weinstein G, Lacourreye O, Rassekh C. Conservation laryngeal surgery. In Otolaryngology head and neck surgery. St. Louis, Mosby: Cummings CW; 1998. p. 2200-2228.
77. Schindler A, Pizzorni N, Mozzanica F, et al. Functional outcomes after supracricoid laryngectomy: what do we not know and what do we need to know? Eur Arch Otorhinolaryngol. 2015 Nov 6.
78. Schindler A, Pizzorni N, Fantini M, et al. Long-term functional results after open partial horizontal laryngectomy type IIa and type IIIa: A comparison study. Head Neck. 2015 Nov 11.
79. Gonçalves A, Bertelli A, Malavasi T, et al. Results after supracricoid horizontal partial laryngectomy. Auris Nasus Larynx. 2010: p. 84-88.
80. Nakayama M, Okamoto M, Miyamoto S, et al. Supracricoid laryngectomy with cricohyoidoepiglotto-pexy or cricohyoido-pexy: experience on 32 patients. Auris Nasus Larynx. 2008: p. 77-81.
81. Woisard V, Puech M, Yardeni E, et al. Deglutition after supracricoid laryngectomy: compensatory mechanisms and sequelae. Dysphagia. 1996: p. 265-269.
82. Clayburgh D, Graville D, Palmer A, Schindler J. Factors associated with supracricoid laryngectomy functional outcomes. Head Neck. 2013: p. 1397-1403.

83. Laccoureye O, Brasnu D, Périé S, et al. Supracricoid partial laryngectomies in the elderly: mortality; complications, and functional outcome. Laryngoscope. 1998: p. 237-242.
84. Rizzotto G, Crosetti E, Lucioni M, Succo G. Subtotal laryngectomy: outcomes of 469 patients and proposal of a comprehensive and simplified classification of surgical procedures. Eur Arch Othorinolaryngol. 2012: p. 1635-1646.
85. Laccoureye O, Salzer S, Brasnu D, et al. Glottic carcinoma with a fixed true vocal cord: outcomes after neoadjuvant chemotherapy and supracricoid partial laryngectomy with cricohyoidoepiglottopexy. Otolaryngol Head Neck Surg. 1996: p. 400-406.
86. Lewin J, Hutcheson K, Barringer D, et al. Functional analysis of swallowing outcomes after supracricoid partial laryngectomy. Head Neck. 2008: p. 559-566.
87. Pinar E, Imre A, Calli C, et al. Supracricoid partial laryngectomy: analyses of oncologic and functional outcomes. Otolaryngol Head Neck Surg. 2012: p. 1093-1098.
88. Schindler A, Favero E, Nudo S, et al. Long-term voice and swallowing modifications after supracricoid laryngectomy: objective, subjective and self-assessment data. Am J Otolaryngol. 2006: p. 378-383.
89. Portas J, Queija D, Arine L, et al. Voice and swallowing disorders: functional results and quality of life following supracricoid laryngectomy with cricohyoidoepiglottopexy. Ear Nose Throat J. 2009: p. E23-30.
90. Simonelli M, Ruoppolo G, De Vincentiis M, et al. Swallowing ability and chronic aspiration after supracricoid partial laryngectomy. Otolaryngol Head Neck Surg. 2010: p. 873-878.
91. Laudadio P, Presutti L, Dall'olio D, et al. Supracricoid laryngectomies: long-term oncological and functional results. Acta Otolaryngol. 2006: p. 640–649.
92. Bron L, Pasche P, Brossard E, et al. Functional analysis after supracricoid partial laryngectomy with cricohyoidoepiglottopexy. Laryngoscope. 2002: p. 1289-1293.
93. Torrejano G, Guimarães I. Voice quality after supracricoid laryngectomy and total laryngectomy with insertion of voice prosthesis. J Voice. 2009: p. 240-246.
94. Schindler A, Mozzanica F, Ginocchio D, et al. Voice-related quality of life in patients after total and partial laryngectomy. Auris Nasus Larynx. 2012: p. 77-83.

Management of professional voice problems

A.S Takhar MBChB(Hons) MRCS DOHNS[1], **R. Awad** MBBCh MD[2], **A. Aymat** FRCS (ORL-HNS)[3] and **N. Gibbins** MD FRCS(ORL-HNS)[3]
[1]ENT Speciality Registrar
[2]Clinical Lead Speech Therapist
[3]Consultant ENT Surgeon
Voice Disorders Unit, Department of Otolaryngology, University Hospital Lewisham, Lewisham High Street, London, SE13 6LH

Correspondence:
Mr A S Takhar, Department of Otolaryngology, University Hospital Lewisham, Lewisham High Street, London, SE13 6LH.
Email: aruntakhar@doctors.org.uk

Abstract

Introduction: The term professional voice user encompasses a wide range of professionals for whom their occupation is dependant on having a functioning voice and is not limited to singers and actors.

Assessment: An adequate assessment of such patients with dysphonia requires a multi-disciplinary approach in a specialised voice clinic. A thorough history, clinical examination including video-strobo-laryngoscopy and perceptual evaluation of the voice is required to make an accurate and complete diagnosis as well as guiding treatment strategies.

Pathology: Causes of dysphonia can be broadly be categorised into functional or organic / structural; however in clinical practice patients often have multiple aetiologies contributing to their voice disorder. Data on 1393 new patients seen in our voice clinic demonstrated that functional voice disorders, cysts and inflammatory laryngeal disorders were significantly higher amongst a subset of 255 singers.

Management: Multi-disciplinary management is essential to successfully treat dysphonia in professional voice users. Surgery can be helpful for pathology confined to the epithelium or superficial lamina propria but should not be considered a treatment in isolation. It is essential to elicit contributory psychological elements, as well as the impact the voice disorder is having on the patients professional demands.

Conclusion: Professional voice users with dysphonia require multi-disciplinary assessment and management. Their dysphonia is often multi-aetiological and all contributory factors must be addressed by the voice team in order to expedite successful, individualised treatment and manage patient expectations.

J ENT Masterclass 2016; 9 (1): 83 - 89.

Key words
Dysphonia, Professional Voice, Hoarseness

Introduction

Traditional definitions of the professional voice user dictated that this was the high performing singer or actor, however, due to changes in patient demographics this should now encompass a much broader spectrum of professionals: essentially anyone for whom their income depends on their ability to have effective verbal communication. These include teachers, lawyers, solicitors, nurses, call centre workers, shop assistants; and of course, doctors. As of August 2015 over 13 million of the nearly 31 million people employed in the UK were employed as professionals, associate professional and technical occupations or as managers, directors and senior officials[1]. There are also significant numbers of occupations within the other fields listed in table 1 that also require a functional voice for their employment. This would suggest that in the present day approximately 75-85% of people in employment rely on their voice to work and contribute economically. This is a stark contrast to a century ago when many more people were employed in manufacturing and agriculture where a voice disorder could be seen to have less of an impact upon maintaining employment. Another important consideration is the increased retirement age in the UK meaning such professionals are more likely to experience a voice problem at some point during their working life. It is therefore imperative that any patient who depends on their voice for their occupation is treated as a professional voice user and this article will discuss the management of such patients as well as looking at some of the specific differences amongst singers.

Table 1: ONS Statistics, Employment in UK by type, August 2015[1].

Standard Occupation Classification	Total in Employment (in thousands)
Managers, Directors and Senior officials	3,182
Professional occupations	6,083
Associate professional and technical occupations	4,289
Administrative and secretarial occupations	3,337
Skilled trade occupations	3,352
Caring, leisure and other service occupations	2,891
Sales and customer service	2,354
Process, Plant and machine operatives	1,965
Elementary Occupations	3,377

Assessment Of The Professional Voice User

Ideally all professional voice users should be seen in a dedicated voice clinic, of which there are now around 100 around the UK[2]. As a minimum the patient will initially be assessed by an ENT surgeon with a special interest in voice along with a specialist speech and language therapist[3]. The clinic should also be equipped with a range of laryngeal imaging equipment, including stroboscopy[4]. The team can also include a singing teacher, physiotherapist or osteopath, voice scientist, psychiatrist and social worker[5]. There should also be established referral pathways to relevant medical specialties such as neurology and gastroenterology.

The comprehensive assessment required of the patient with a voice disorder is detailed in Table 2. One of the most important features for the otolaryngologist is comprehensive history taking which can lead to a likely principal diagnosis prior to clinical examination. Key features of the assessment for the otolaryngologist are discussed below:

Voice History

It is important to determine the onset, duration and severity of voice symptoms. Enquiring about vocal load, and for singers in particular the frequency and duration of singing in their current schedule can provide important information, as well as the type of singer they are. Any upcoming major performances or specific career goals can dictate the urgency and intensity of therapy that may be required. Singers will often be more aware of fine changes in their voice production so enquiring as to whether there is a particular vocal range where their voice is maximally affected can help both the speech therapist and vocal coach focus their therapy appropriately[6].

Table 2: Initial Assessment of Patient with a voice disorder[3].

Assessment	Approach
Joint Assessment Otolaryngologist & SLT	Visual examination Laryngeal imaging Laryngographically synchronised stroboscopy Rigid endoscopy Flexible fiberoptic/digital nasendoscopy Shimmer and jitter measurements
Perceptual Assessment	Study of the interrelation between speech subsystems Identification of parameters of voice contributing to the dysphonia Evaluation of each speech subsystem and potential for change Establishment of a baseline and a measure of overall severity
Instrumental Assessment	Aerodynamics Pitch Intensity Resonance Vibratory Cycle Vocal Quality
Palpation of the Extrinsic Laryngeal Musculature Assessment	Status of the extrinsic laryngeal musculature Position of the laryngeal cartilages at rest Position of the laryngeal cartilages during phonation Degree of muscle tension.
Client Self- assessment	Self- perception of voice Impact of the voice disorder and symptoms on their life Profile of voice use Questionnaire

Relevant Medical History

It is important to elicit any factors from the medical history that may be exacerbating the voice problem. These include:

- Preceding upper respiratory tract infection that may have triggered dysphonia.
- History of rhinitis, allergies, or chronic rhinosinusitis.
- History of gastro-oesophageal reflux disease or symptoms of laryngopharyngeal reflux.
- Smoking and alcohol history.
- Caffeine intake and hydration status.
- Stress, anxiety and psychiatric disorders.
- Musculoskeletal disease or trauma to the head and neck that may be affecting posture and muscle tension.

Examination

A general ENT examination should be performed to exclude contributory factors to the voice disorder such as tonsillar disease or nasal polyposis. Specifically examination of the neck should include palpation of the extrinsic laryngeal musculature to assess for muscle tension and tenderness. The supra and infra hyoid muscles should be palpated. It can also be useful to palpate and displace the cartilage framework of the larynx to assess for tension and tethering[7]. There is marked variability within published literature between these techniques with few validated objective tools to quantify degree of diagnostic accuracy[8] of palpation but despite this palpation can provide valuable information contributing towards the diagnosis and treatment strategies.

The voice itself needs to be perceptually analysed. There are patient-centred or clinician-centred scoring tools. There are many patient-centred questionnaires with the most common being the VHI-10. The most commonly used clinician-centred analysis of voice is the GRBAS scale[9] (Grade, Roughness, Breathiness, Asthenia, Strain).

Visual examination of the larynx is imperative to assess for structural pathology and the dynamic function of the larynx. In addition vibratory patterns of the vocal cords can be assessed during phonation when voice-synchronised stroboscopy is adopted. Despite some modern advances, video-strobo-laryngoscopy is considered the gold standard in laryngeal imaging[10] and can be performed using a 70° or 90° rigid stroboscope or a newer flexible chip-and-tip naso-laryngoscope, these have been shown to be nearly as good as the conventional rigid strobe-laryngoscopy[11].

Pathology

Just as is the case with the general population, professional voice users can present with a wide variety of underlying pathologies and diagnoses for their dysphonia. In the broadest sense these can be categorised as functional or organic[5]. It is important to also recognise that in many cases there may be more than one aetiological factor contributing to the voice problem.

The most common functional disorder that is seen is muscle tension dysphonia. This is a form of voice use / abuse / misuse that is characterised by excessive muscular effort and pressed phonation[12]. This can also be referred to as muscle tension imbalance or laryngeal hyperfunction. Other causes of functional dysphonia can include conversion and psychogenic dysphonia. Due to the lack of uniformed terminology it is difficult to ascertain accurate estimates of the prevalence of such conditions.

The term organic dysphonia refers to either structural, neurological, endocrinological or laryngeal diseases. Structural causes can include vocal cord polyps, cysts, nodules, granulomas and many more.

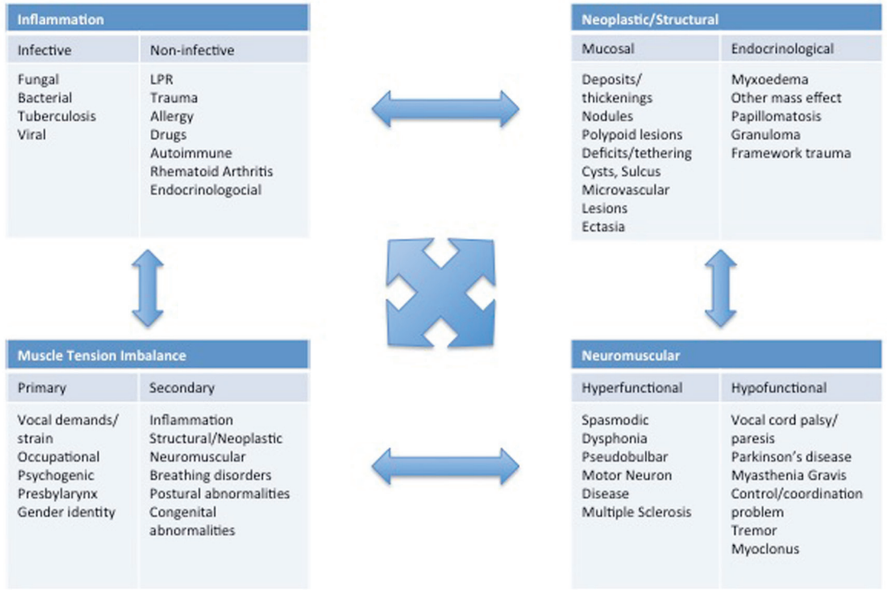
In clinical practice however it is clearly recognised that patients often have more than one pathology contributing to their voice problem and their dysphonia is a result of multiple aetiologies. According to work performed by Koufman and popularised by McGlashan[13] these can be broken down into inflammation, neoplastic / structural, neuromuscular, and muscle tension imbalance. There is very often complex interplay between aetiologies; for example the patient with a vocal fold polyp may then develop muscle tension imbalance as a compensatory mechanism. This categorisation and the interplay between pathologies are displayed in table 3.

Table 3. Aetiologies causing voice disorders and multifactorial causes – original figure – adapted from references detailed in separate table

There is a paucity of evidence in the literature detailing the prevalence of structural laryngeal disorders amongst the general population, let alone amongst professional voice users. Our voice disorders unit has kept a database of all patients seen in our voice clinic since 2010, and whilst this data is as yet unpublished, we have analysed the data of 1393 new patients seen between 2010-2015. Of these patients 449 (32.3%) were classified as professional voice users and 255 (18.3%) were singers. Our data demonstrated around half of all patients were diagnosed with functional disorders, and the other half with structural pathology. This rate was not significantly (p=0.87*) different amongst the subgroup of professional voice users. Interestingly though, in the subgroup of singers we found 65.9% had functional disorders with 34.1% having structural disorders. This was considered a significantly different distribution (p=0.0002*) and could be attributable to the differing expectations, training, and vocal ability in this group.

The most common pathology demonstrated in the whole cohort (19.1%) and amongst the subgroup of singers (33.3%) was vocal cord cysts (see figure 1) and this was significantly higher among singers (p=0.0031*). Inflammatory conditions including laryngitis, oedema and polypoidal degeneration of the cords represented 31.0% of patients in the singers group and was their 2nd most

Table 3. Aetiologies causing voice disorders and multifactorial causes[3,13]



popular pathology, whereas it only represented 11.5% amongst the whole cohort. In our series singers were significantly more likely (p=0.0001*) to have inflammatory pathology. There was no difference in the prevalence of vocal cord polyps (See Figure 2) between the two groups (p=0.4977*). Vocal cord nodules (see figure 3) represented only 4.08% of structural diagnoses in our series, with this rate being 9.2% amongst singers, and this difference was not quite considered significant (p=0.052*).

The relevant data is detailed in table 4. Overall vocal cord nodules were the 8th most common diagnosis in our series and this is much lower than expected based on the traditional thinking that nodules are the most common structural pathology, it may be that improvements in laryngeal imaging have meant that what was traditionally considered nodules on laryngoscopy are being more accurately diagnosed as unilateral cysts with contralateral oedema on stroboscopy. A wide variety of other pathologies were found in our case series and only the most salient and relevant features are presented in this article.

In summary, a wide-range of pathologies can contribute to dysphonia and often these will co-exist. Successful treatment of the voice disorder must incorporate management of all contributing elements.

*Assumed parametric data, calculated using Fishers exact test, two-tailed p-value

Management

The multidisciplinary approach to assessment of the professional voice user must also be employed in the management of their problem. Common exacerbating factors such as laryngopharygeal reflux should be treated with either a proton pump inhibitor[14] or liquid alginate suspension[15] and all other relevant lifestyle measures should be addressed. Speech and language therapy that

Table 4. Prevalence of principal voice disorder diagnoses in our case series

	Case Series	Professional Voice Users	Singers
Total	1393	449 (32.2%)	255 (18.3%)
Diagnosis			
Functional	707 (50.8%)	240 (53.5%)	168 (65.9%)
Structural	686 (49.2%)	209 (46.5%)	87 (34.2%)
• Cysts	131 (19.1%)		29 (33.3%)
• Polyps	44 (6.4%)		7 (8.1%)
•Nodules	28 (4.1%)		8 (9.2%)
•Inflammation**	79 (11.5%)		27 (31.0%)

**includes laryngitis, polypoidal degeneration, oedema

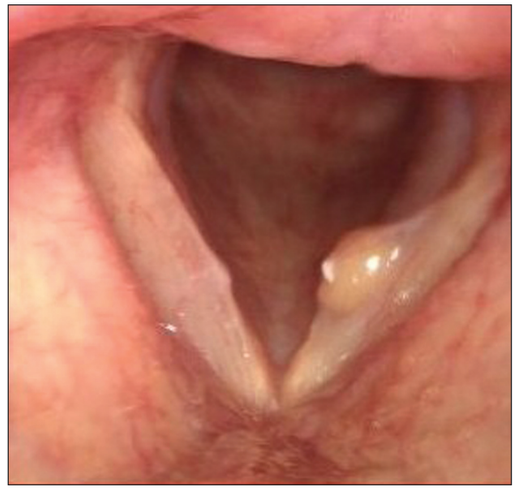


Figure 1: *Left vocal cord cyst with contralateral oedema (original with patient consent)*

involves a combination of education, vocal tract care and voice conservation will be appropriate in most cases; therapy can involve a direct (physiological) or indirect approach (psychosocial). Direct approaches involve techniques aimed at improving technical function of the voice whereas an indirect approach aims to address environmental, social and psychological elements underlying the dysphonia. Therapy should be tailored to the individual needs and can be curative, rehabilitative, facilitative or supportive[3].

The professional voice user may have much higher expectations of the treatment of their voice disorder due to the impact it may be having on their ability to work and the associated financial and professional implications.

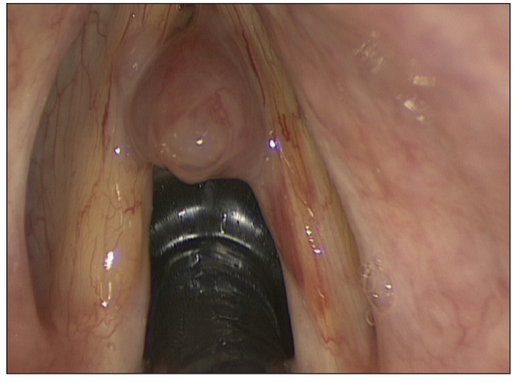


Figure 2: *Right vocal cord polyp (original with patient consent)*

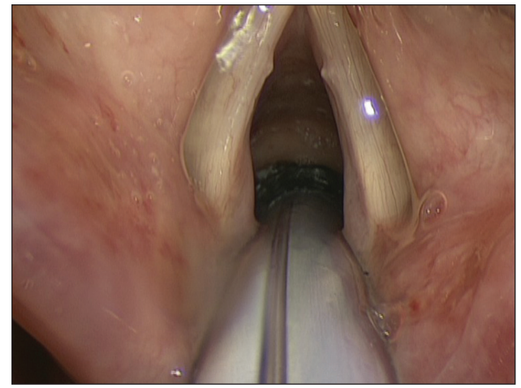


Figure 3: *Bilateral vocal cord nodules (original with patient consent)*

Eliciting expectations from the patient is vital to help tailor the timing and intensity of any therapy as well as giving sound advice to the patient. For example the professional singer with an active vocal cord haemorrhage who has a major performance in the coming days should be advised that voice rest is mandatory, and it may be necessary for them to cancel pressing rehearsals or performances. It is important to have an understanding of the types of singers and the vocal training they have and the vocal demands required of them. For example, classically trained singers are highly trained and often work on short term contracts using a vocal set that is largely the same whereas musical theatre singers will be required to produce many different qualities of voice, from ballad to rock. Other types of singers such as rock, pop and band singers may have little, if any, professional training and may be doing performances on a part time basis or as a hobby. Singers tend to be more 'in tune' with their voice than the non-professional voice user and so will notice any change immediately. This also has psychological implications as they will be very worried that any problem with their voice could permanently affect their career and what may ultimately be their true passion[7].

Structural problems with the larynx such as cysts and polyps that are confined to the epithelium and superficial layer of the lamina propria are the most amenable to surgical treatment with microlaryngoscopy and excision. Surgery confined to these layers should heal with no impact on vocal fold function, since the fibres of the lamina propria will re-establish in an orientation parallel to the epithelium[16]. However, surgery into deeper layers can cause scarring resulting in stiffness and reduction in the vocal wave, dramatically affecting the voice[6]. Surgery to lesions involving Reinke's space is best performed via a 'superior cordotomy' approach to avoid leaving a scar near

or on the free border of the vocal fold as this can cause tethering of the epithelium also affecting mucosal wave generation[7]. Microlaryngeal surgery should never be seen in isolation as a definitive treatment and must always be followed (and in some cases preceded) with speech and language therapy. The saying "the operation is the easy bit, the recovery is the hard bit" is a statement that rings true for such patients and the value of therapy must never me underestimated when managing patient expectations.

Conclusion

The term "professional voice user" now encompasses a broad spectrum of people for whom their occupation is dependant upon having a functional voice, included in this are singers who often have differing expectations with an increased psychological stressors. There is a huge range of underlying pathologies that can be attributable to the voice disorder and often they are multi-aetiological. The multi-disciplinary team is vital to ensure successful treatment and the 'voice clinic' where a joint assessment with speech therapist and surgeon working in synergy helps build trust, rapport and confidence in the diagnosis and treatment plan. It is imperative to understand and manage the expectations of the patient relevant to their professional demands and tailor care individually to try to meet these aims.

References

1. Office for National Statistics. Employment and employee types. 2016;Availableat:https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes. Accessed May 27, 2016.
2. British Voice Association. UK Voice Clinics. 2016; Available at: http://www.britishvoiceassociation.org.uk/free_voice-clinics.htm. Accessed May 27, 2016.
3. The Royal College of Speech and Language Therapists. RCSLT Resource Manual for Commissioning and Planning Services. 2009; Available at: https://www.rcslt.org/speech_and_language_therapy/commissioning/voice_plus_intro. Accessed May 29, 2016.
4. Casiano RR, Zaveri V, Lundy DS. Efficacy of videostroboscopy in the diagnosis of voice disorders. Otolaryngol Head Neck Surg 1992;107(1):95-100.
5. Mathieson L. The Voice and Its Disorders: 6th Edition. 6th ed. London: Whurr Publishers; 2001.
6. Benninger MS. The Professional Voice. J Laryngol Otol 2011;125:111-116.
7. Harris T, Harris S, Rubin JS, Howard DM. The Voice Clinic Handbook. London: Whurr Publishers; 1998.
8. Khoddami SM, Ansari NN, Jalaie S. Review on Laryngeal Palpation Methods in Muscle Tension Dysphonia: Validity and Reliability Issues. J Voice 2015;29(4):459-468.
9. Carding P, Carlson E, Epstein R, Mathieson L, Shewell C. Formal perceptual evaluation of voice quality in the United Kingdom. Logoped Phoniatr Vocol 200;25(3):133-138.
10. Bless DM, Hirano M, Feder RJ. Videostroboscopic evaluation of the larynx. Ear Nose Throat J 1987;66:289-296.
11. Singh A, Kazi R, Venkitaram R, Kapoor K, Nutting C, Clarke P, et al. Does flexible videostroboscopy compare with rigid videostroboscopy in the assessment of the neoglottis? A preliminary report. Clin Otolaryngol Allied Sci 2008;33(1):60-63.
12. Sataloff RT. Professional Voice: The Science and Art of Clinical Care. 3rd ed. San Diego: Pleural Publishing Inc; 2005.
13. McGlashan J, Costello D, Bradley PJ. Hoarseness and voice problems. In: Ludman H, Bradley PJ, editors. ABC of Ear, Nose and Throat. 5th ed.: Blackwell Publishing Ltd, Oxford; 2007. p. 71-77.
14. Franco RA, Andrus JG. Common Diagnoses and Treatments in Professional Voice Users. Otol Clin North Am 2007;40:1025-1061.
15. McGlashan JA, Johnstone LM, Sykes J, Strugala V, Dettmar PW. The value of a liquid alginate suspension (Gaviscon Advance) in the management of laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 2009;266(2):243-251.
16. Benninger MS, Alessi D, Archer S, Bastian R, Ford C, Koufman J. Vocal fold scarring: current concepts and managment. Otolaryngol Head Neck Surg 1996;115:474--82.

Management of head and neck sarcoma

Justin CL Yeo FRCS (ORL-HNS)[1], **Iain J. Nixon** PhD, FRCS (ORL-HNS)[2] and **Ioanna Nixon**[3] PhD, MPH, FRCReq
[1]ENT Registrar, St John'sHospital, Livingston
[2]Consultant ENT Surgeon, St John's Hospital, Livingston
[3]Consultant Clinical Oncologist, Head and Neck/Sarcoma, Clinical Lead Sarcoma,
Edinburgh Cancer Center, Edinburgh, UK

Correspondence:
Ioanna Nixon
Email: joanna.nixon@nhs.net

Abstract
Head and neck sarcomas are a rare diverse group of neoplasms arising within soft tissues or bones. In this rare tumour type, prospective trials are not feasible. Multimodality treatment plans including surgery, radiation and chemotherapy are often indicated. A multidisciplinary team (MDT) approach involving both sarcoma and head and neck MDTs is recommended for management of these tumours. This article provides an overview of the presentation, pathology and management of these lesions.

J ENT Masterclass 2016; 9 (1): 90 - 96.

Key words
Sarcoma, head and neck cancer, staging, management

Conflict of interest
None

Introduction
Head and neck sarcomas are a rare heterogeneous group of cancers which can arise in the mesenchymal tissues (bones or within the soft and connective tissues). They account for approximately 2% to 15% of all sarcomas, and represent approximately 1% of head and neck malignancies[1]. According to the National Cancer Intelligence Network (NCIN) data[2], between 1990 and 2010, 4796 head and neck sarcoma patients were diagnosed in England, of which 793 (17%) arose in bones of skull and face, and 4003 (83%) within the connective and soft tissue (ratio of approximately 1:5). This was a diverse group with over 30 different histological types.

The most common soft tissue sarcomas (STSs) are leiomyosarcoma, liposarcoma (Figure 1) and sarcoma not otherwise specified (NOS). The most common bone sarcomas (BSs) are osteosarcoma, chondrosarcoma and Ewing's sarcoma.

Due to the relative rarity of the condition, published data on management and outcomes of head and neck sarcomas are limited, based on small series of patients. Most of these studies report retrospective cohorts managed over a number of decades to obtain a sufficient numbers. Evolution of imaging, surgical technique and adjuvant therapies make conclusions from such small series difficult to interpret.

Guidelines from the British Sarcoma Group (BSG)3 and the European Society for Medical Oncology (ESMO)[4,5] have been published on sarcoma management. However, these are not specific to head and neck sites. In contrast to sarcomas elsewhere, wide surgical margins are more difficult to achieve and the cosmetic and functional impact of major head and neck resections are significant. A multidisciplinary team (MDT) approach involving both sarcoma and head and neck MDTs is recommended for management of these tumours.[6]

Aetiology
The majority STSs of the head and neck arise sporadically with no obvious cause. However, various familial syndromes, environmental carcinogens and oncogenic viruses along with previous exposure to ionizing radiation have been implicated. In patients with type 1 neurofibromatosis, there is up to a 10% cumulative lifetime risk of developing sarcoma, usually malignant peripheral nerve sheath tumour (MPNST)7. Li-Fraumeni syndrome predisposes the individual to developing STSs, osteosarcoma, pre-menopausal breast cancer, brain tumours and adrenocortical carcinoma[8]. Gardner syndrome, a subtype of familial adenomatous polyposis, has also been linked to STSs[9].

Radiation exposure is a recognised risk factor in the late development of secondary sarcoma. Overall, osteosarcoma is the most common radiation-induced sarcoma for all body sites. In the head and neck region, malignant fibrous histiocytoma is the most common subtypes seen after ionizing radiation exposure[10]. The latent period between initial radiation and diagnosis of sarcoma ranges from 9-45 years with a median of 17 years. Chemical agents such as vinyl chloride gas (plastics industry), chlorophenols (sawmill workers) and arsenic (vineyard work) have been implicated as possible causative factors[11]. Associations have also been shown between human immunodeficiency virus and human herpesvirus 8 in Kaposi sarcoma[12], and for Epstein-Barr virus and smooth muscle tumours in immuno-compromised patients[13].

Presentation
Head and neck sarcoma presentation is dependent on the involved primary site. Lesions arising from the subcutaneous tissues of the face, neck or scalp present with a superficial mass which may be painful. Lesions arising from the upper aero-digestive tract, paranasal sinus and orbit will cause symptoms related to these areas, such as dysphonia, dysphagia, odynophagia, nasal obstruction, proptosis and diplopia. Cranial nerve deficits may be seen in skull base lesions. The most frequently involved anatomical sites are the superficial neck and parotid, sinonasal tract and visceral spaces of the neck[14].

Most head and neck sarcomas present with localised disease. Regional lymph node involvement is unusual although is more frequently associated with specific histological subtypes including rhabdomyosarcomas and epithelioid sarcomas[15]. The most common site of distant metastasis is the lungs. Mehendall et al reported that in the absence of lung metastasis, the risk of metastasis to other distant sites is extremely low[16].

Investigation
The evaluation of suspected head and neck sarcomas involves cross-sectional imaging and biopsy. Both computed tomography (CT) and magnetic resonance imaging (MRI) provide information regarding loco-regional extension, assessment of tissue composition and the presence of distant disease[4,5]. Although CT provides better bony detail, advantages of MRI include superior soft tissue resolution. In many cases the information provided is complimentary. Cross-sectional imaging is best performed before biopsy in order to maximise diagnostic accuracy. Chest CT is recommended to exclude pulmonary metastasis prior to definitive treatment in all cases[4]. 18F-flurodeoxyglucose positron emission tomography (18F-FDG-PET) is increasingly used in pre-treatment staging although it use is currently not considered standard[4].

Diagnostic tissue samples can be obtained using fine needle aspiration, core biopsy or open biopsy if required. The biopsy should be planned in a way that the tract can be safely excised at the time of definitive surgery in order to reduce the potential risk of tumour seeding.

Pathology & grading
Histological diagnosis should be based on the 2013 World Health Organisation (WHO) classification of tumours of soft tissue and bone[17]. Numerous changes have taken place in STS and BS classification, predominantly based on the identification of new genetic findings in different tumour types.

A range of outcomes are associated with histological subtypes of sarcoma. For example, all angiosarcomas are considered high grade and should be treated as such. In contrast, many chondrosarcomas are associated with slow growth and low rates of metastasis. Histological subtyping therefore remains critical in predicting the biological behaviour of tumours.

The malignant grade should also be provided in all sarcoma cases for the purpose of prognostication. The "Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system is generally used in STS, which distinguishes three malignancy grades based on differentiation, necrosis and mitotic rate[18] (Table 1). Again, grading should be performed prior to treatment as neoadjuvant medical therapies may affect these findings and limit the usefulness of grading of a subsequent resection specimen.

The ESMO guidelines do not provide a specific recommendation for BS histological grading[5]. Instead, BSs are graded according to the cell type and differentiation of the stromal component of the tumour. Less differentiated tumours are given higher grades. Chondroblastic and fibroblastic tumours are usually of lower grade (grade 1 or 2). An absence of cartilaginous lobulation and the presence of spindle cell forms are characteristics of high-grade (grade 3) lesions and are associated with poorer prognosis. Ewing's sarcoma is always classified as high grade[5].

Five-year overall survival is better in low-grade tumour and poor outcome is associated with positive surgical

Table 1: Federation Nationale des Centres de Lutte Contre le Cancer histological grading criteria

Tumour differentiation	Necrosis (macro and micro)	Mitotic count (n/10 high-power fields)
1: Well	0: Absent	1: n<10
2: Moderate	1: <50%	2: 10-19
3: Poor	2: >50%	3: n≥20

The sum of the scores of the three criteria determines the grade of malignancy
Grade 1: 2 and 3; Grade 2: 4 and 5; Grade 3: 6, 7 and 8.

margins[19]. As for histological subtypes, angiosarcoma and rhabdomyosarcoma have poor overall survival whilst pleomorphic sarcoma, fibrosarcoma, leiomyosarcoma and liposarcoma have better prognosis[20].

Staging

The most widely used staging systems for STSs and BSs are the International Union Against Cancer's (UICC) TNM staging system[4,5,21]. Due to the rarity and heterogeneity of these lesions (over 30 recognised histological subtypes of variable grade), it has been difficult to establish a working system to accurately stage all forms of this heterogeneous disease. Tumour size and histological grade are primary determinants of clinical stage. For STSs, the tumour size is further sub-staged into "a" (superficial tumour arising outside the investing fascia) and "b" (tumour is either beneath the fascia or invading the fascia). The UICC staging system for BSs considers the maximum lesion size (with a breakpoint at 8cm) and the presence of discontinuous tumours in the same bone without other distant metastasis. (Table 2 and 3)

Management

The primary modality of treatment for most head and neck sarcomas is surgery. Resection with clear margins is the aim in order to maximise the chance of local control. The role of adjuvant therapy is less clear and will depend on tumour type and resection status. Radiotherapy is commonly used in the post-operative setting. Chemotherapy has also been recommended by many groups. Timing of chemo-radiation is controversial. Some use neo-adjuvant therapy in order to help achieve a negative surgical margin, whereas others recommend post-operative adjuvant therapy. (Flow chart 1)

Table 2: TNM classification for Soft Tissue Sarcoma

Primary tumour (T)	
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour ≤ 5 cm in greatest dimension
T1a	Superficial tumour
T1b	Deep tumour
T2	Tumour > 5 cm in greatest dimension
T2a	Superficial tumour
T2b	Deep tumour
Regional lymph nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No regional node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

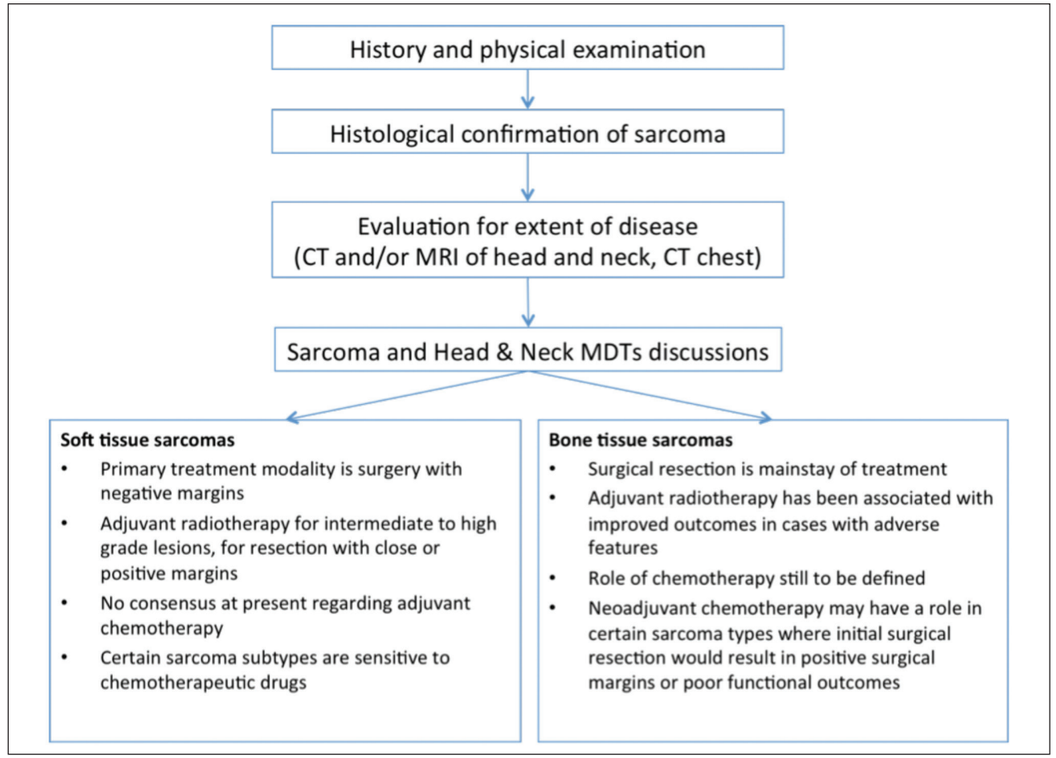
Management - STSs

The primary treatment modality for STSs is surgery aiming to achieve a wide excision with negative margins. Although there is no consensus regarding margin width, a 2cm margin is considered acceptable[4]. This presents a challenge in head and neck due to the need to preserve critical structures, functional anatomy and in order to minimise cosmetic defects. Hence, head and neck STSs tend to have lower local control rates and worse survival when compared to extremity STSs. Elective treatment of the neck is rarely indicated due to the low rates of nodal disease[14].

Adjuvant radiotherapy should be considered in cases with intermediate to high grade, lesions with >5cm, and for resections with close or positive margins 4. In addition, recurrence after surgical management alone will be considered for re-resection with post-operative radiotherapy. In low-grade cases, adjuvant radiotherapy may be avoided. However, the complexity of these cases means that each patient should be discussed in a MDT setting. Farhood et al reported that with head and neck STSs, a combined modality approach showed a local control rate of 90% versus 52% in those treated with surgery alone[22]. Similarly, Tran et al. published an 87% recurrence-free survival with adjuvant radiation therapy versus 45% with surgery alone[23]. In R^1 or R^2 resection margins, Barker et al. reported an increase in local control from 25% to 54% with adjuvant radiation therapy[19]. These results, while not conclusive, suggest a low threshold for recommending adjuvant radiotherapy is appropriate.

Table 3: TNM classification for Bone Sarcoma

Primary tumour (T)	
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour ≤ 8 cm in greatest dimension
T2	Tumour > 8 cm in greatest dimension
T3	Discontinuous tumours in the primary bone site
Regional lymph nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No regional node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1a	Lung only
M1b	Other distant sites



Flow chart 1: *A general overview of the management of head and neck sarcoma*

Radiotherapy alone may be the only option in management of select STSs where surgical resection is not achievable. However, the control rate for treatment with radiotherapy alone is reported to be approximately 25%24. The use of intensity modulated radiation therapy may allow higher doses for better control rate whilst limiting toxicity to normal tissue. As experience with proton therapy increases, the potential advantages of high dose delivery with minimal collateral tissue damage may define a role for this approach in selected cases.

There is no consensus on the current role of adjuvant chemotherapy[4]. The most commonly used chemotherapeutic drugs have been doxorubicin, dacarbazine and ifosfamide. Published study results have been conflicting. The Sarcoma Meta-analysis Collaboration (SMAC) published a meta-analysis reporting improved local control and metastasis-free survival with adjuvant chemotherapy, but no benefit in overall survival[25]. Hence, adjuvant chemotherapy is not standard treatment in adult-type STSs although some of the sarcomas seen more commonly in the paediatric and adolescent population such as Ewing's sarcoma, rhabdomyosarcoma of embryonal (Figure 2) and alveolar types are sensitive to these chemotherapeutic drugs[26].

Management - BSs

Surgical resection remains the mainstay of treatment for head and neck osteosarcoma. Adjuvant radiotherapy has been associated with improved outcomes for patients with adverse features such as large tumour size, extensive soft tissue infiltration and lymphovascular invasion[27]. However, osteosarcomas are relatively radio-resistant and doses in excess of 60Gy in conventional fractionation are recommended if feasible[28]. In the head and neck region, this is problematic due to close proximity to vital structures and therefore the risk of serious morbidity from treatment. Techniques such as 3D conformal radiotherapy and intensity-modulated radiation therapy could be utilised to overcome these issues. The role of chemotherapy is still ill-defined due to conflicting study results.

Data from Memorial Sloan Kettering Cancer Centre (MSKCC) for head and neck osteosarcoma did not

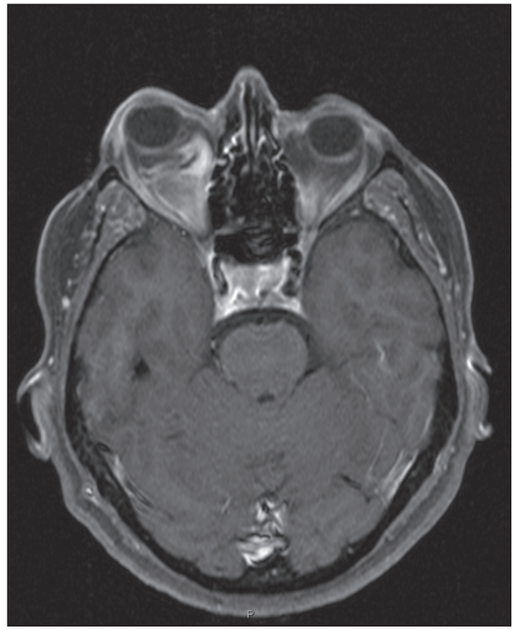


Figure 1: *An MRI scan showing liposarcoma of right orbit*

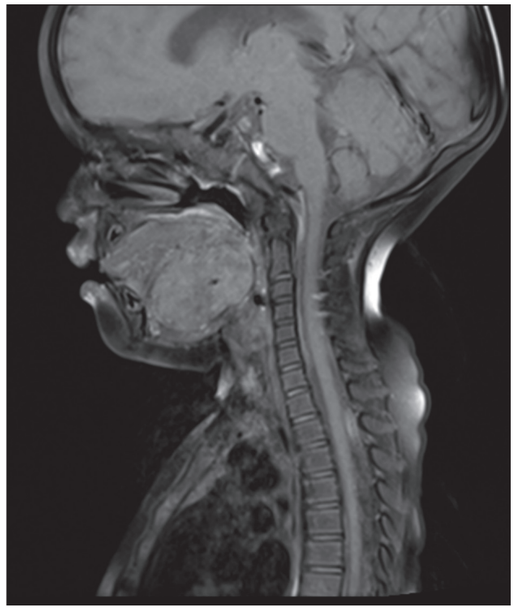


Figure 2: *An MRI scan showing embryonal rhabdomyosarcoma of the tongue base*

demonstrate improved local control or disease-specific survival with the addition of neoadjuvant chemotherapy to conventional management[29]. In contrast, Smeele et al reported that patients' overall and disease-free survivals were significantly improved by treatment with chemotherapy, both for patients who had complete and incomplete surgical removal of the tumour[30].

Obtaining negative surgical margins from complete surgical excision has been reported to be crucial not only for local control, but disease-specific survival. Survival rate has been reported to decrease from 75% to 35% in the presence of positive surgical margins[31]. Neoadjuvant chemotherapy may have a role in cases with high-grade head and neck osteosarcoma, rhabdomyosaroma or Ewing's sarcoma or with lesions where initial resection is likely to result in positive surgical margins or poor functional outcomes.

Chrondrosarcoma of the larynx is briefly described here as it is the most common sarcoma of the larynx (Figure 3). It makes up only 0.1% of all head and neck malignancies, and approximately 1% of malignant laryngeal tumours[32]. There is a 3:1 male preponderance[33]. Laryngeal chondrosarcoma tends to be locally invasive. However, it rarely displays regional or distant metastasis[32,33,34,35]. Historically, treatment usually entailed surgical excision in the form of total laryngectomy, as it is considered to be relatively radio-resistant. In a series of 592 cases of laryngeal chondrosarcoma, 1% of cases had non-surgical treatment[33]. Due to the relatively indolent disease course of most tumours, the majority of patients will now be considered for conservative surgical therapy. Serial transoral debulking of the tumour allows local disease to be controlled, often for many years. With such a treatment approach, salvage laryngectomy is reserved for cases where conservative management is unsuccessful. Disease-specific survival rates for 10 and 20 years have been reported at 82% and 68%[33].

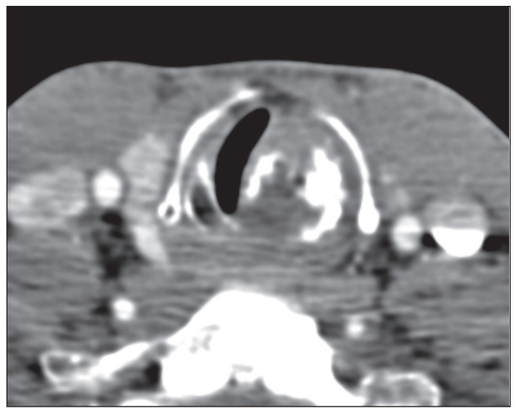


Figure 3: *A CT scan showing chondrosarcoma of the larynx involving the left cricoid cartilage*

Conclusion

Sarcomas of the head and neck are a rare and diverse group of mesenchymal tumours. The mode of presentation will vary with anatomical subsite and is similar to more common head and neck malignancies. All patients require cross sectional imaging (often both MRI and CT), which is ideally performed prior to biopsy.

The wide varieties of histological subtypes encountered are associated with a spectrum of outcomes, from aggressive lesions such as angiosarcoma to the more indolent behaviour of fibrosarcomas. Further prognostic information can be gained from standardised systems of histological grading.

Surgery remains the main therapeutic modality for head and neck sarcoma. Wide surgical margins are difficult to achieve, due to close proximity of vital structures, which may compromise outcome. Therefore, adjuvant radiotherapy may be recommended based on adverse tumour or surgical features in order to minimise the risk of local recurrence. Although chemotherapy has a well-defined role in certain tumour subtypes such as rhabdomyosarcoma, its role in adult sarcoma management is currently unclear.

Given the rarity and heterogeneity of this clinical entity, there is necessity for specialist treatment in a multidisciplinary context. In the UK, there are continuous improvements to normalise treatment pathways and standardise data collection for H&N STS, using the sarcoma network to allow meaningful interpretation of outcomes for this challenging patient group[6].

References:

1. Brockstein B. Management of sarcomas of the head and neck. Curr Oncol Rep. 2004;6(4):321-327.
2. http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/sarcomas/ (Last accessed 22/3/2016)
3. Grimer R, Judson I, Peake D et al. Guidelines for management of soft tissue sarcomas. Sarcoma. 2010;2010:506182. doi: 10.1155/2010/506182.
4. ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(S3):102-112.
5. ESMO/European Sarcoma Network Working Group. Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(S3):113-23.
6. Stavrakas M, Nixon I, Andi K, Oakley R, Jeannon JP, Lyons A, McGurk M, Urbano TG, Thavaraj S and Simo R. Head and neck sarcomas: Clinical and histopathological presentation, treatment modalities and outcomes. J Laryngol Otol. 2016;1:1-10. [Epub ahead of print]
7. Pollack IF, Mulvihill JJ. Neurofibromatosis 1 and 2. Brain Pathol. 1997;7:823–36.
8. Li FP, Fraumeni JF. Soft-Tissue Sarcomas, Breast Cancer, and Other Neoplasms: A Familial Syndrome? Ann Intern Med. 1969;71(4):747-52.
9. Johnson JG, Gilbert E, Zimmermann B et al. Gardner's syndrome, colon cancer, and sarcoma. J Surg Oncol. 1972;4(4):354-62.
10. Patel SG, See AC, Williamson PA et al. Radiation induced sarcoma of the head and neck. Head Neck. 1999;21(4):346-54.
11. Fingerhut MA, Halperin WE, Marlow DA et al. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. N Engl J Med. 1991;324(4):212-8.
12. Ensoli B, Barillari G, Gallo RC. Pathogenesis of AIDS-associated Kaposi's sarcoma. Hematol Oncol Clin North Am. 1991;5(2):281-95.
13. McClain KL, Leach CT, Jenson HB et al. Association of Epstein–Barr Virus with Leiomyosarcomas in Young People with AIDS. N Engl J Med. 1995;332(1):12-18.
14. Galy-Bernadoy C, Garrel R. Head and neck soft-tissue sarcoma in adults. Eur Ann Otorhinolaryngol Head Neck Dis. 2016 133(1):37-42.
15. Tallroth K. Lymphatic dissemination of bone and soft tissue sarcomas: a lymphographic investigation. Acta Radiol Suppl. 1976;349:1-84.
16. Mendenhall WM, Mendenhall CM, Werning JW et al. Adult head and neck soft tissue sarcomas. Head Neck. 2005;27(10):916-22.
17. Benz MR, Tchekmedyian N, Eilber FC et al. Utilization of positron emission tomography in the management of patients with sarcoma. Curr Opin Oncol. 2009;21(4):345-51.
18. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F (eds). WHO classification of tumours of soft tissue and bone. Lyon: IARC 2013.
19. Barker Jr JL, Paulino AC, Feeney S, McCulloch T, Hoffman H. Locoregional treatment for adult soft tissue sarcomas of the head and neck: an institutional review. Cancer J 2003;9(1):49–57.
20. Mücke T, Mitchell DA, Tannapfel A, Hölzle F, Kesting MR, Wolff KD, Kolk A, Kanatas A. Outcome in adult patients with head and neck sarcomas--a 10-year analysis. J Surg Oncol. 2010;102(2):170-4.
21. Sobin LH, Gospodarowicz MK, Wittekind CH (eds). TNM classification of malignant tumours, 7th Edition. Oxford: Wiley-Blackwell 2009.
22. Farhood AI, Hajdu SI, Shiu MH et al. Soft tissue sarcomas of the head and neck in adults. Am J Surg. 1990;160(4):365-9.
23. Tran LM, Mark R, Meier R, Calcaterra TC, Parker RG. Sarcomas of the head and neck. Prognostic factors and treatment strategies. Cancer 1992;70(1):169–77.
24. Kepka L, DeLaney TF, Suit HD, Goldberg SI. Results of radiation therapy for unresected soft-tissue sarcomas. Int J Radiat Oncol Biol Phys. 2005;63(3):852-9.
25. Sarcoma Meta-analysis Collaboration (SMAC). Adjuvant chemotherapy for localised resectable soft tissue sarcoma in adults. Cochrane Database Syst Rev. 2000;(4):CD001419.
26. Egas-Bejar D, Huh WW. Rhabdomyosarcoma in adolescent and young adult patients: current perspectives. Adolesc Health Med Ther. 2014;5:115-25.
27. Laskar S, Basu A, Muckaden MA, D'Cruz A, Pai S, Jambhekar N, Tike P, Shrivastava SK. Osteosarcoma of the head and neck region: lessons learned from a single-institution experience of 50 patients. Head Neck. 2008;30(8):1020-6.
28. Oda D, Bavisotto LM, Schmidt RA, McNutt M, Bruckner JD, Conrad EU 3rd, Weymuller EA Jr. Head and neck osteosarcoma at the University of Washington. Head Neck 1997;19:513–523.
29. Patel SG, Meyers P, Huvos AG, Wolden S, Singh B, Shaha AR, Boyle JO, Pfister D, Shah JP, Kraus DH. Improved outcomes in patients with osteogenic sarcoma of the head and neck. Cancer. 2002;95(7):1495-503.
30. Smeele LE, Kostense PJ, van der Waal I, Snow GB. Effect of chemotherapy on survival of craniofacial osteosarcoma: a systematic review of 201 patients. J Clin Oncol 1997;15:363–367.
31. Ha PK, Eisele DW, Frassica FJ, Zahurak ML, McCarthy EF. Osteosarcoma of the head and neck: a review of the Johns Hopkins experience. Laryngoscope. 1999;109(6):964-9.
32. Dubal PM, Svider PF, Kanumuri VV, Patel AA, Baredes S, Eloy JA. Laryngeal chondrosarcoma: a population-based analysis. Laryngoscope. 2014;124(8):1877-81.

33. Chin OY, Dubal PM, Sheikh AB, Unsal AA, Park RC, Baredes S, Eloy JA. Laryngeal chondrosarcoma: A systematic review of 592 cases. Laryngoscope. 2016 Jun 12. doi: 10.1002/lary.26068. [Epub ahead of print]
34. Thompson LD, Gannon FH. Chondrosarcoma of the larynx: a clinicopathologic study of 111 cases with a review of the literature. Am J Surg Pathol. 2002;26(7):836-51.
35. Rinaldo A, Howard DJ, Ferlito A. Laryngeal chondrosarcoma: a 24-year experience at the Royal National Throat, Nose and Ear Hospital. Acta Otolaryngol. 2000;120(6):680-8.

Transoral endoscopic ultrasonic surgery (TOUSS) as an alternative to TORS.

Mario M Fernández-Fernández MD, PhD[1], **Francesc X Avilés** MD, PhD[2], **Lourdes Montes-Jovellar** MD, PhD and **Marc Tobed** MD
[1]ENT Department. Hospital Universitario del Henares. Coslada. Madrid. SPAIN
[2]ENT Department. Hospital Universitario Joan XXIII. Tarragona. SPAIN
[3]ENT Department. Hospital Universitario Ramón y Cajal. Madrid. SPAIN
[4]ENT Department. Hospital Universitario Josep Trueta. Girona. SPAIN

Correspondence:
Mario Fernández-Fernández MD PhD
Address: Marques de Lozoya nº3-escC-9ºB
28007 – Madrid. SPAIN
Email: mmarcos.fernandezf@salud.madrid.org

Abstract
Transoral Ultrasonic Surgery (TOUSS) is a new endoscopic minimally invasive procedure to approach pharyngeal and laryngeal lesions without a robotic platform. The fundamental pillars of this procedure are the Feyh-Kastembauer retractor, the deflecting tip videoendoscope, that allows a high quality image with easy refinement of the endoscopic view, and the ultrasonic scalpel (Thunderbeat™). Besides de benign lesions, both early and locally advanced carcinomas are approachable with TOUSS. Many indications have been described, including the TOUSS-Total Laryngectomy technique, and first clinical experience has already been published. Further experience with the technique will show the benefits in terms of functional results and quality of life as well as the cost-eficacy compared with other treatment modalities, especially with other transoral endoscopic procedures that required expensive equipment as transoral robotic surgery (TORS). TOUSS is a low cost procedure that will easily spread the transoral endoscopic surgery to every patient and institution.

J ENT Masterclass 2016; 9 (1): 97 - 102.

Key words
TOUSS, TORS, Thunderbeat, transoral endoscopic surgery.

Disclosure
Dr. Mario Fernandez served as consultant for Olympus Europa SE & Co. KG.

Introduction
There is no doubt about the fact that minimally invasive surgery is the pathway that leads to the future of head and neck surgery. In this sense, transoral laser microsurgery (TOLM) was the most remarkable step forward in the last decades.[1-3] However, it seems that TOLM has touched the ceiling due to the limitations of the microscope as visualization instrument and the low coagulation capabilities of the laser. On the other hand, considerable progresses are seen in endoscopic head and neck surgery such as nasosinusal and cranial base surgery. The way for transoral endoscopic surgery was opened by Gregory Weinstein on de basis of a robotic procedure, and great advances are evident in the literature[4,5]. However, the high costs of acquisition, maintenance and disposables, are impairing the spread of the transoral endoscopic philosophy[6]. It is mandatory to design a more affordable procedure to let all surgeons and institutions start with the transoral endoscopic surgery.

This paper describes a novel endoscopic technique, TOUSS – TransOral Ultrasonic Surgery,[7] that combines ultrasonic energy, with high potential for cutting and coagulating, and high definition videoendoscopic imaging. The combination of both technologies allows the same output as robotic surgery for transoral approach of the upper aerodigestive way.

TOUSS set up
After general anesthesia, the intubation is done through the mouth to face posterior or lateral lesions. A nasopharyngeal intubation allows a more confortable procedure in laryngeal and the base of the tongue lesions. The patient is placed in supine position, without any elevation of the shoulders or neck extension.

The upper dental arch is protected with a plastic teeth protector. We prefer the Feyh-Kastembauer retractor (FK)

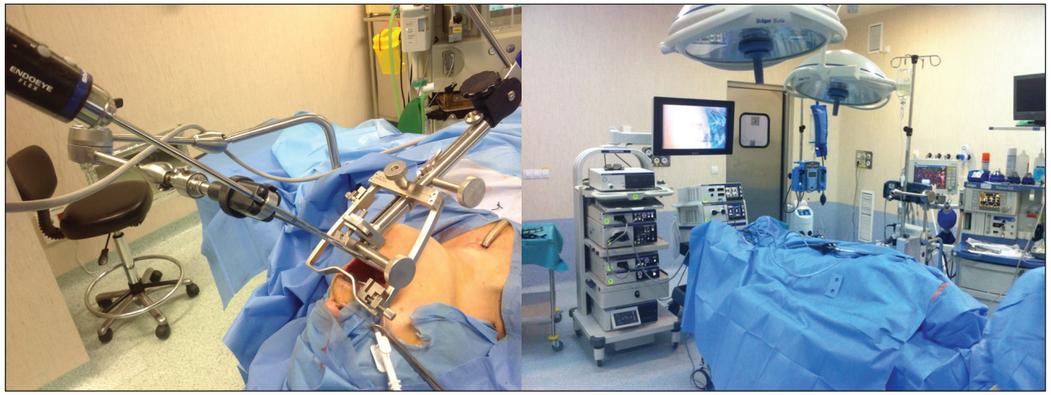


Figure 1, 2: *Disposition of FK retractor, scope holder and Videolaparoscope. The screen is located at the feet of the patient in an advanced position.*

to achieve a proper exposition of the laryngo-pharynx. The FK is fixed with a retractor holder with chest support that allows an easy releasing and refinement of its position during the procedure.[7])

The scope holder arm is attached to the left side of the table. The endoscopic view is obtained with a 5 mm videoendoscope that is fitted into the scope holder. Perhaps 3D imaging will demonstrate its advantages in order to a better space positioning, however we have no data related to this point yet. Olympus ENDOYE with the deflecting tip that allows an easy correction of the visualization up to 100º using the joysticks placed at the head the camera. (Figures 1,2)

The optimal exposition for each patient and each anatomical area should be reached with the correct combination of the appropriate FK blade and its anterior angulation.

In order to get a comfortable procedure and a clean surgical field, the ultrasonic scalpel is mandatory. The ultrasonic scalpel Thunderbeat™ incorporates also a bipolar vessel sealing system that increases the safety of the procedure, especially when vascular structures as lingual or laryngeal arteries are exposed within the pharynx. The 35cm pistol grip Thunderbeat™ allows stabilization of the instrument in the surgeon´s hand. This consideration is important as there are no structures like access ports to stabilize the instrument. Other grasping laparoscopic forceps are used to manipulate the tissues.

Surgical technique

The surgeon is standing up at the head of the patient with the patient positioned at the level of the surgeon´s elbows to get an ergonomic posture.[7]

One of the key aspects of the procedure is to take time for a correct exposition of the lesion with the FK retractor and the surgical planning of the resection. A lack of surgical planning can lead to the disturbance of the already resected tissue, and the inadequate endoscopic control of the surgical margins that force the surgeon to make a piecemeal resection. This concept is critical at the base of the tongue

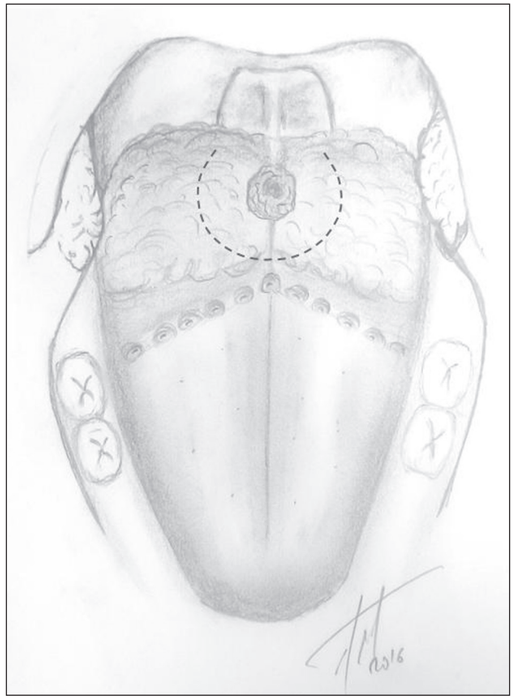


Figure 3: *Planification of the resection starting on the superior and lateral margins*

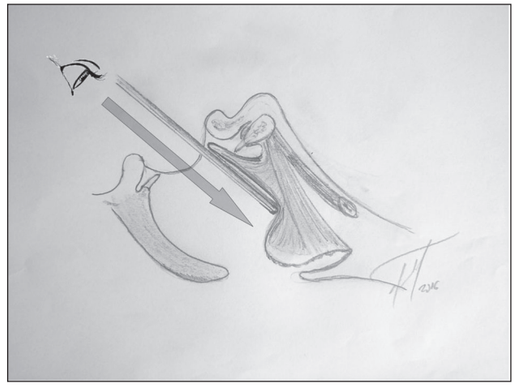


Figure 4: *Compression with the blade on the superior aspect of the tongue base will protrude the tissue and a straight access can be achieve*

due to the restrictions of the angle of approach. The resection should start from the superior and lateral mucosal limits. Afterwards the deep resection will release the lesion that will remain attached to the tongue only by the inferior margin. Now the mobility of the specimen will let finish the resection pulling the inferior border of the specimen with the forceps, allowing a vertical section of the inferior limit with the ultrasonic scalpel. (Figure 3, 4, 5).

The coagulation potential of the ultrasonic energy is not necessary at the level of the mucosa. Moreover, the thermal spread to the mucosal surgical margin should be avoided in order to preserve the quality of the specimen. The employ of monopolar tungsten tips to make the initial mucosal incision will let the retraction of the mucosa, and the subsequent use of the ultrasonic scalpel at the level of the peripherical margin will avoid its contact while it is activated. This aspect is critical to let the pathologist recognizes the oncological safety of the tumoral resection. The area of artefact in contact with the tumor will create doubts about the safety surgical margin, even with a good oncological resection. However, when there is a sector of normal mucosa between the artefact and the tumor, the artefact can be add to the normal mucosa to determine the safety distance between the tumoral front and the surgical margin. (Figure 6). A long suction cannula should be kept beyond the endoscope tip in order to avoid the smoke overclouds the endoscopic vision when the ultrasonic device is activated.

Indications

Regarding the pharynx, oropharyngeal and hypopharyngeal lesions are approachable with TOUSS.[7] The approach of posterior and lateral pharyngeal lesions is easy and

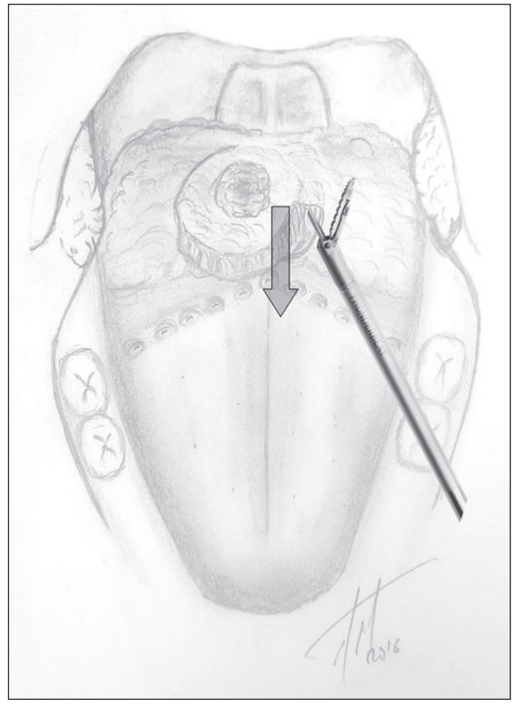


Figure 5: *After the deep resection, the traction on the inferior aspect of the specimen will face the inferior border of the lesion against de ultrasonic scalpel*

intuitive. The exposition does not play an important role in such anatomical areas. (Figure 7). The base of the tongue lesions are more dependent on the quality of exposition and the appropriate planning of the resection. It is not uncommon to reach the area of the entrance of the lingual artery at the base of the tongue. The pharyngeal lumen is a septic and wet cavity where the tightness of the vessel sealing line can be jeopardized. In this particular cases, the lingual artery can be easily identified and sealed safely with the Thunderbeat. The bipolar sealing system controls

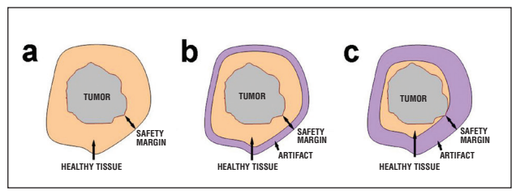


Figure 6. a: *Conventional surgical margin with cold knife;* **b:** *Surgical margin with artefact in ultrasonic scalpel. The artefact can be added to the surgical margin;* **c:** *Uncertain surgical margin. The artefact is in contact with the tumor and no possibility to ensure the safety of the resection*

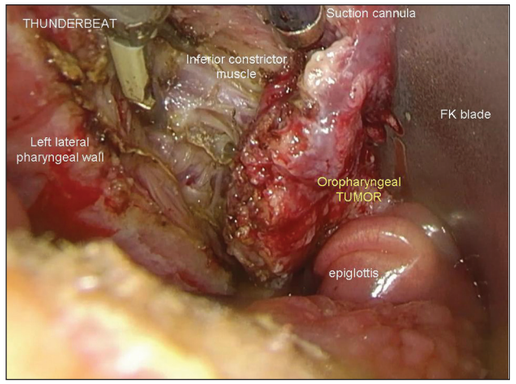


Figure 7: *Resection of an oropharyngeal carcinoma. The access to the lateral wall of the oropharynx is very easy and intuitive. The Thunderbeat allows a bloodless procedure and an optimal control of the anatomy*

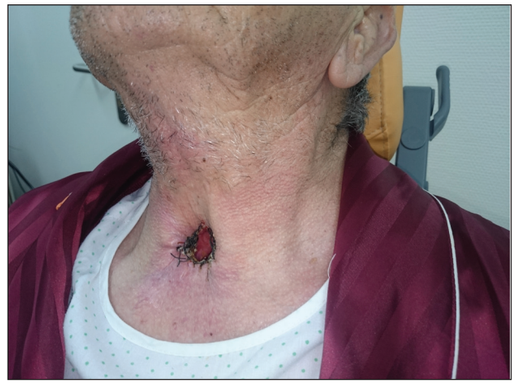


Figure 8: *10 days postop after a TOUSS Total Laryngectomy. Notice the absence of neck scars and the good shape of the cervical tissues*

the amount of energy that it is needed to deliver on the vessel in order to get a safe closure[8].

Related to the larynx, our current limitation is the procedures that involves the vocal folds. The high coagulation potential of the ultrasonic scalpel is too aggressive and not necessary in the glottic plane. Additionally, in this area, the surgical margin can be as low as 2 mm[9] to ensure the local control. So, there are other energies on more delicate instruments that can preserve much better the remaining normal mucosa. The TOUSS supraglottic laryngectomy is feasible, but proximity to the vocal folds should be taken into account. A tungsten tip monopolar instrument can be useful to refine the surgical margin in such a delicate area when preservation of the vocal fold mobility is possible. The first clinical experience with the technique is already published[7] and currently there is a multiinstitutional study is being conducted to analyse the surgical results and the benefits in terms of functionality and quality of life of the patients with head and neck cancer

Transoral Ultrasonic Total Laryngectomy (TOUSS-TL)

Perhaps Transoral Total Laryngectomy is the indication where the big potential of this concept can be better shown. TOUSS-TL consists in the complete removal of the larynx through a combined transoral and trans-stomal endoscopic cervical approach. The surgical steps are already described on the basis of the cadaver lab[10]. The hypothesis of preserving the vascularization of the tissues of the anterior aspect of the neck, avoiding the approach through external neck incisions will improve the neck dysesthesia of the patients, the complications rate and the management of postoperative complications. (Figure 8) The first two patients have been reported[10], and 6 patients have been already treated with TOUSS-TL. The surgery was complete in all cases and we do not registered any aborted case due to a lack of adequate exposition or intraoperative complication. Only two fistulas were registered, both of them in the two previously radiated patients. Both cases were treated satisfactorily with conservative treatment and no additional surgical treatment was necessary. The benefits in terms of oncological and functional results and quality of life will be reported in the long run.

Discussion

TOLM has entered our specialty in the 80s and indications have been developed gradually to establish itself as an alternative to open partial laryngeal surgery[1]. The approach of pharyngeal lesions was equally feasible from this microscopical approach.[2,3]. The success of TOLM relies on the possibility of the resection of the lesions without any damage to healthy tissue. However the limitations of the laser as a coagulation tool are evident as we move upwards from glottic plane to more vascular areas or larger vessels are exposed.[11]

Minimally invasive surgery has one of its development fronts in thoracic and abdominal laparoscopic surgery. This systematic has been exported to the neck by Gagner to approach thyroid and parathyroid glands[12,13]. Gagner´s setup has not been very successful, however it has opened the door to a new concept in neck surgery that is minimally invasive transcutaneal endoscopic surgery, using the endoscope as a visualization tool for neck surgery.

Endoscopic vision represents an advance over the microscopic, as it allows to get closer to the pathology, as well as the possibility to have the whole surgical field on focus. The deflecting tip of new videolaparoscopes leads to easy and precise refinements of the endoscopic vision which can be done with the joystick at the head of the camera.

Finally, we found in the ultrasonic scalpel the answer to the necessity for a better coagulation tool,[14] especially compared to the laser. It can cut tissue and coagulate up to 6 mm. The ultrasonic scalpel came into head and neck surgery from the hand of Paolo Miccoli as a cutting-coagulation tool for minimally invasive video-assisted thyroidectomy (MIVAT)[15] and it was the ideal instrument to step forward in developing a new systematic for transoral surgery. ThunderbeatTM incorporates a bipolar vessel sealing system that offers the highest safety in prevention of intraoperative and postoperative haemorrhagic complications.[8,16,17]

On this basis Transoral Ultrasonic Surgery (TOUSS) was developed as a transoral endoscopic technique, exporting to the head and neck surgery the concepts of laparoscopic surgery.[7] The philosophy, the concept and the technology used in laparoscopic surgery, especially in single-port laparoscopy, are now applied to neck surgery, considering the mouth as a single port

This concept has been previously developed by Gregory Weinstein since 2005, with the description of transoral robotic surgery (TORS) in an animal model[18]. However, the ultrasonic scalpel is not a bendable tool as a straight shaft is mandatory to transmit the piezoelectric energy to the tip of the instruments, so it is adaptable to a robotic arm but there is no possibility to take advantage of the robotic endowrist. The direct manipulation of the tissue with TOUSS keeps the tactile input, and it represents an additional advantage compared to TORS.

Besides the costs of acquisition and maintenance of a surgical robot, the doubts around the need of such degree of freedom inside the pharynx, makes transoral robotic surgery a questionable solution in short and medium term.

Now TOUSS offers a more powerful setup to reach the transoral removal of lesions in areas where TOLM have bleeding problems and complications.[11] The potential of TOUSS has allowed the transformation of open procedures like total laryngectomy in a transoral non-robotic endoscopic technique.[10] The advantages of TOUSS for the patients are related to the avoidance of open approaches through healthy tissue. This is especially remarkable in radiated patients. In such patients, the avoidance of a mandibulotomy has a positive impact in the patient quality of life.

The robotic equipment is unreachable for most of ENT departments and usually the cost-benefits studies are not encouraging[19,20]. TORS (transoral robotic surgery) was the first proposal for a transoral and endoscopic approach, but TOUSS is the first one that is feasible and reachable for most institutions. We believe that further cost-efficacy studios of TOUSS compared with TORS will show no doubt about its role in the present and the next future.

Conclusion

We have described TOUSS as a new feasible and intuitive procedure to approach transoral and endoscopically pharyngeal and laryngeal tumours. We believe that TOUSS that can play a significant role in the surgical treatment of pharyngeal and laryngeal cancer as well as other benign lesions, in the following years. Further experience with the technique will show us the long term results and the real benefits for the patients, in comparison with other treatment modalities.

References

1. Steiner W. Results of curative laser microsurgery of laryngeal carcinomas. Am J Otolaryngol. 1993 Mar-Apr;14(2):116-21.
2. Steiner W, Ambrosch P, Hess CF, Kron M. Organ preservation by transoral laser microsurgery in piriform sinus carcinoma. Otolaryngol Head Neck Surg. 2001 Jan;124(1):58-67.
3. Steiner W, Fierek O, Ambrosch P, et al Transoral laser microsurgery for squamous cell carcinoma of the base of the tongue. Arch Otolaryngol Head Neck Surg. 2003 Jan;129(1):36-43.
4. O'Malley BW Jr, Weinstein GS, Snyder W, Hockstein NG. Transoral robotic surgery (TORS) for base of tongue neoplasms. Laryngoscope. 2006 Aug;116(8):1465-72.
5. Weinstein GS, O´Malley BW Jr, Cohen MA, et al. Transoral robotic surgery for advanced oropharyngeal carcinoma Arch Otolaryngol Head Neck Surgery. 2010;136(11):1079-1085
6. Rudmik L, An W, Livingstone D, Matthews W, et al. Making a case for high-volume robotic surgery centers: A cost-effectiveness analysis of transoral robotic surgery. J Surg Oncol. 2015 Aug;112(2):155-63. doi: 10.1002/jso.23974. Epub 2015 Jul 14.
7. Fernández-Fernández MM, Montes-Jovellar L, Parente Arias PL, Ortega Del Alamo P. TransOral endoscopic UltraSonic Surgery (TOUSS): a preliminary report of a novel robotless alternative to TORS. Eur Arch Otorhinolaryngol. 2015 Dec;272(12):3785-91. doi: 10.1007/s00405-014-3423-6. Epub 2014 Dec 16.
8. Janssen PF, Brölmann HA, Huirne JA. Effectiveness of electrothermal bipolar vessel-sealing devices versus other electrothermal and ultrasonic devices for abdominal surgical hemostasis: a systematic review. Surg Endosc. 2012 Oct;26(10):2892-901. Epub 2012 Apr 27.
9. Alicandri-Ciufelli M, Bonali M, Piccinini A, et al. Surgical margins in head and neck squamous cell carcinoma: what is 'close'?. Eur Arch Otorhinolaryngol. 2013 Sep;270(10):2603-9. doi: 10.1007/s00405-012-2317-8. Epub 2012 Dec 28.
10. Fernández-Fernández MM, González LM, Calvo CR, et al. Transoral ultrasonic total laryngectomy (TOUSS-TL): description of a new endoscopic approach and report of two cases. Eur Arch Otorhinolaryngol. 2015 Oct 1.
11. López-Álvarez F, Rodrigo JP, Llorente-Pendás JL, Suárez-Nieto C. Transoral laser microsurgery in advanced carcinomas of larynx and pharynx. Acta Otorrinolaringol Esp. 2011 Mar-Apr;62(2):95-102. doi: 10.1016/j.otorri.2010.09.008.

12. Gagner M. Endoscopic subtotal parathyroidectomy in patients with primary hyperparathyroidism. Br J Surg. 1996 Jun;83(6):875.
13. Gagner M, Inabnet WB 3rd. Endoscopic thyroidectomy for solitary thyroid nodules. Thyroid. 2001 Feb;11(2):161-3.
14. W. J. Hodgson The ultrasonic scalpel. Bull N Y Acad Med. 1979 Nov; 55(10): 908–915.
15. Miccoli P, Berti P, Raffaelli M, et al. Impact of harmonic scalpel on operative time during video-assisted thyroidectomy. Surg Endosc. 2002 Apr;16(4):663-6. Epub 2001 Dec 10.
16. Seehofer D, Mogl M, Boas-Knoop S, et al. Safety and efficacy of new integrated bipolar and ultrasonic scissors compared to conventional laparoscopic 5-mm sealing and cutting instruments. Surg Endosc. 2012 Sep;26(9):2541-9. doi: 10.1007/s00464-012-2229-0. Epub 2012 Mar 24.
17. Tanaka R, Gitelis M, Meiselman D, et al. Evaluation of Vessel Sealing Performance Among Ultrasonic Devices in a Porcine Model. Surg Innov. 2015 Aug;22(4):338-43. doi: 10.1177/1553350615579730. Epub 2015 Apr 7.
18. Weinstein GS, O'Malley BW Jr, Hockstein NG. Transoral robotic surgery: supraglottic laryngectomy in a canine model. Laryngoscope. 2005 Jul;115(7):1315-9.
19. Byrd JK, Smith KJ, de Almeida JR, et al. Transoral Robotic Surgery and the Unknown Primary: A Cost-Effectiveness Analysis. Otolaryngol Head Neck Surg. 2014 Mar 21. [Epub ahead of print]
20. Dombrée M, Crott R, Lawson G, et al. Cost comparison of open approach, transoral laser microsurgery and transoral robotic surgery for partial and total laryngectomies. Eur Arch Otorhinolaryngol. 2014 Oct;271(10):2825-34. doi: 10.1007/s00405-014-3056-9. Epub 2014 Jun 7.

Management of occult primary in head and neck

Primož Strojan, PhD, MD

Correspondence:
Department of Radiotherapy
Institute of Oncology
Zaloška 2, SI-1000 Ljubljana
Slovenia
Email: pstrojan@onko-i.si

Abstract

Background. An occult primary tumor metastatic to cervical lymph nodes represents a rare clinical entity posing several diagnostic and therapeutic dilemmas.

Methods. Review of recent literature on diagnostic and therapeutic approaches in this clinical setting.

Results. Besides clinical examination, cross-sectional imaging and ipsilateral tonsillectomy are the mainstay of the diagnostic algorithm. Low-volume neck disease can be treated with either surgery or radiotherapy alone, whereas combined modality treatment is needed in more advanced disease. The rate of emerging mucosal primary tumors is comparable to the rate of metachronous primaries in patients with a known primary tumor which allows, in the majority of cases, treatment of the involved neck only. The impact of the p16/human papilloma virus status of metastatic nodes on treatment decisions and intensity will be defined in current treatment de-escalation clinical trials conducted in patients with a known primary.

Conclusions. After complete diagnostic workout the risk of missing an occult primary is low. Thus, treatment limited to the involved side of the neck is usually justified, with the advantage of lower toxicity and better prospects for salvage treatment when necessary.

J ENT Masterclass 2016; 9 (1): 103 - 108.

Key words

unknown primary tumor; cervical lymph node metastases; squamous cell carcinoma, therapy

Conflict of interest statement

The author declares that he has no conflict of interest.

Introduction

A cancer of unknown primary (CUP) site is defined as the presence of lymphatic or hematogenous metastases with no primary tumor discovered after rigorous diagnostic work-up. It represents a distinct clinical entity that accounts for up to 5% of patients with solid tumors.[1] The reasons for an unrevealed primary tumor can be numerous and multifactorial, starting with its small size to dormancy or involution as a result of immunologic and apoptotic processes.[2] Recently, the role of senescence, the microenvironment and tumor stem cells in impeding tumor growth has been suggested.[3,4]

Compared to extranodal involvement, the exclusively nodal presentation of metastases is less frequent. Neck lymph nodes are the most commonly involved nodal group with squamous cell carcinoma (SCC) as the predominant histologic type; adenocarcinoma prevails in other nodal regions.[5] In addition, CUP patients with SCC metastases to the neck nodes are granted a favorable prognosis, particularly when compared to those with metastases of other histologic backgrounds. The following discussion refers to CUP with cervical lymph node metastases of SCC histology.

Clinical presentation

Population-based incidence of CUP metastatic to neck nodes was reported to be around 3% and is influenced by the diagnostic algorithms used to reveal the hidden primary tumor.[6,7] According to reports of larger series and literature reviews, the typical patient is male in his 6th or 7th decade of life, a heavy smoker and a consumer of alcohol and presents with a level II neck node of N2a classification. A painless neck mass, first observed up to 5 months before setting the diagnosis, is usually reported.[8,9] In the era of a global epidemic of human papillomavirus (HPV)-associated oropharyngeal SCC this stereotype might be shifted toward a younger age, different lifestyle orientations and more advanced nodal disease at presentation.

Diagnostic workup

In the patient presented with a mass in the neck and no clinical signs or symptoms of a primary tumor or active

inflammation in the head or neck, the diagnostic procedure is focused on the verification of the mass and the systematic evaluation of upper aerodigestive tract mucosa to identify the primary tumor. Assessment for distant metastases is also an integral part of the diagnostic algorithm in CUP patients. If the mass is located in the lower neck or in the supraclavicular region, a primary is usually hidden below the clavicles and diagnostic efforts should be modified accordingly.

Identification of primary tumor (Fig. 1)

Fine-needle aspiration biopsy (FNAB) is the most elegant, safest and most cost-effective way to characterize an enlarged neck node: in experienced hands, and by using immunostaining, diagnostic sensitivity reaches 83-97% and specificity 91-100%.10 Determinations of p^{16}, HPV and Epstein-Barr virus (EBV) status of the biopsied node can be done in the FNAB specimen.[11,12] Ultrasonography guidance of the FNAB needle is particularly important in cases of cystic metastasis, where a high rate of false-negative results is frequently reported.[13] Core-needle biopsy or even open cervical lymph node biopsy are indicated only when repeated FNAB is non-diagnostic, or in patients with a high suspicion of lymphoma. Particularly, open biopsy is discouraged due to potential negative consequences (i.e. the risk of local recurrence and complications, systemic dissemination); when performed, it must follow non-invasive diagnostics and must be accomplished by adequate definitive treatment of the neck.[14,15]

Any attempt to identify a primary tumor starts with a detailed clinical examination and fiberoptic endoscopy of upper aerodigestive tract mucosa. With the advent of cross-sectional imaging a better presentation of areas traditionally difficult to examine by surgical endoscopy (e.g. hypopharynx, nasopharynx) was possible which successfully reduced the historically high rate of emerging primaries in these areas. Suspicious imaging findings direct subsequent biopsies: under these conditions Cianchetti et al. reported a primary tumor detection rate of >60% compared to 29.2% in patients with no suspicious findings on radiographic examinations.[16] Given the sensitivity of modern imaging, the majority of undiscovered primaries are hidden in crypts of tonsillar and lingual tonsils which makes random biopsy sampling obsolete.[17] In particular, this is the case in HPV-associated neck metastases which highlights the importance of p^{16}/HPV status determination in FNAB samples. The same relationship exists between EBV positivity of the involved neck node and the risk of an occult primary in the nasopharynx.[12]

In this context, directed biopsies (by clinical and imaging findings) and an ipsilateral palatine tonsillectomy, followed in cases of an unconfirmed primary with base of tongue resection, are indicated. Deep tonsil biopsy offers a significantly lower likelihood of finding an occult primary compared to a tonsillectomy (11.6% vs. 40.7%).[18] A bilateral procedure seems unnecessary, even if occult bilateral tonsillar tumors were reported in up to 23% of cases:[19] also in cases of a known early-stage tonsillar primary tumor treatment is usually unilateral.[20] Removal of the lingual tonsil in a manner comparable to a palatine tonsillectomy didn't become possible before the development of transoral base of tongue surgery. Combined or sequential (i.e. if no primary is found in the palatine tonsil on frozen sections) removal of both tonsils on the affected side resulted in notable rates of identified occult primaries, approaching 90%, especially in patients with p16/HPV positive neck metastasis.[21] It appears that the implementation of transoral base of tongue surgery into the diagnostic algorithms in CUP is the major contribution to the improved detection rate of occult primaries in these patients.

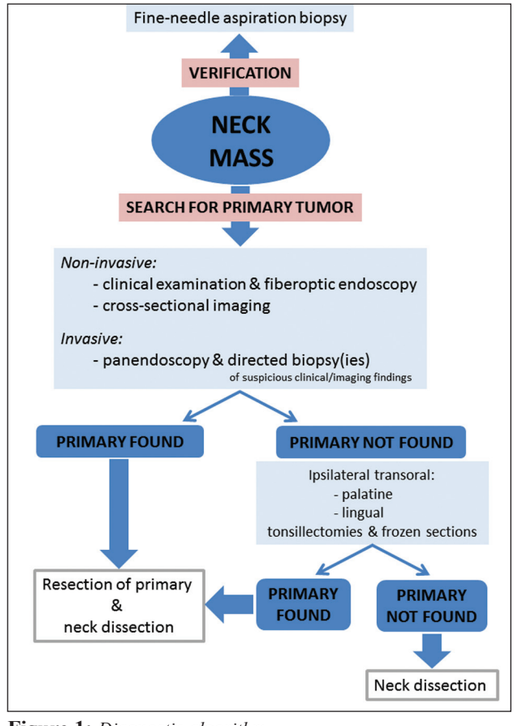


Figure 1: *Diagnostic algorithm*

At the moment, the added value of [18F]fluordeoxyglucose positron emission tomography and/or CT (FDG-PET/CT) in the search for hidden primary tumors in the head and neck seems to be marginal. The main reasons are the detection capability of the procedure which is limited to tumors ≥5 mm, basal uptake of FDG in normal lymphoid tissues, and salivary gland secretion of FDG that resulted in relatively high false-positive (up to 35%) but also false-negative rates (up to 31%).[22-25] Thus, a diagnostic biopsy cannot be avoided. Recent meta-analysis confirms these findings and observations: the authors reported a sensitivity and specificity of 0.97 (0.63-0.99) and 0.68 (0.49-0.83), respectively, a diagnostic odd ratio (DOR), positive likelihood ratio (PLR) and negative likelihood ratio (NLR) of 60 (3.2-1137), 3.1 (1.7-5.4) and 0.05 (0.003-0.76), respectively, whereas the primary tumor detection rate was 0.44 (0.31-0.58).26 Although an absolute cutoff is not defined, in good diagnostic tests the DOR should be >100, PLR >10 and NLR <0.1, which was not the case in this study.

Assessment for distant metastases

For M-staging, FDG-PET/CT proved to be a preferred diagnostic modality. Traditionally, a chest CT scan and abdominal ultrasound or CT are used to exclude systemic dissemination. Other tests (endoscopies, bone scintigraphy with technetium) are performed as clinically indicated. However, according to meta-analysis of studies comparing the diagnostic performance of integrated FDG-PET/CT, FDG-PET alone and/or CT alone for the overall assessment of distant metastases, integrated FDG-PET/CT has superior sensitivity (0.95 vs. 0.85 vs. 0.80) and similar specificity (0.96 vs. 0.95 vs. 0.94) to the other two modalities.[27] When used for the screening of distant metastases in head and neck cancer patients, interobserver agreement in FDG-PET was found to be markedly higher as compared to chest CT.[28]

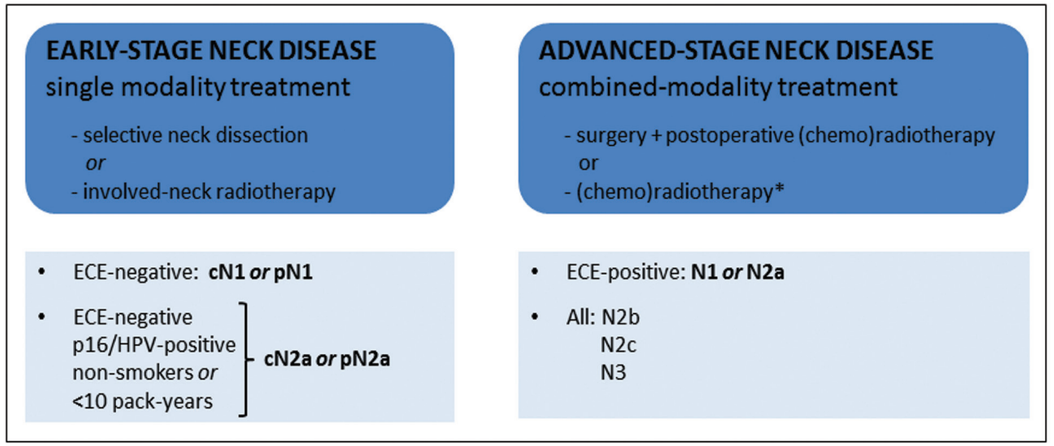
Treatment options

The intensity of treatment is guided by the extent of the neck disease and the patient's general condition and preferences, similar to patients with a known primary SCC of the head and neck (Fig. 2). The choice between up-front surgery and radiotherapy is usually biased by institutional practice; however, the advantage of the elimination of a gross tumor burden and potential micrometastases, together with the valuable information about the extent and aggressiveness of the neck disease (more accurate N-classification and recognition of extracapsular tumor spread) provided by the histopathological examination, gives preference to primary surgery in the majority of institutions. With an increasing number of CUP patients with p^{16}/HPV-associated neck metastases and their high sensitivity to radiotherapy and chemotherapeutics this may change.

The type of neck surgery is dictated by the extent of the nodal disease. All 5 neck levels are rarely at risk; thus, selective neck dissection is usually indicated.[29]

With regard to radiotherapy, two issues must be addressed: the extent of the radiation volume and the advantage of

Figure 2: *Treatment principles*



*salvage surgery in non-responders (evaluated with FDG-PET/CT 8-12 months after chemoradiotherapy)
ECE – extracapsular extension
HPV – human papillomavirus

modern radiotherapy techniques (i.e. intensity modulated radiotherapy, IMRT). Although many institutions practice comprehensive irradiation of pharyngeal and laryngeal mucosa,[30] no difference in the rate of emerging mucosal primary tumors was found after complete diagnostic workout when compared with radiotherapy limited to the involved side of the neck (around 10% in both groups).[31,32] Indeed, the risk of post-treatment occurrence of a mucosal primary above the clavicles in CUP patients was found to be comparable to the risk of a metachronous second primary tumor in patients cured of a known head and neck primary SCC.[33] The reason may lie in the radiation dose delivered during involved-field radiotherapy to the ipsilateral oropharyngeal and nasopharyngeal mucosa which is comparable to the dose used in more extensive radiation.[34] Also, the routine that incorporates diagnostic tonsillectomies may also be of importance, particularly in view of the fact that the oropharynx is expected to be the site of the primary tumor in more than 90% of cases.[16] Moreover, a significant difference between the two radiation approaches in the incidence and severity of acute but also late radiotherapy-related side effects should also be considered (Strojan, unpublished data).

The question on the need for elective radiation (or surgery) of the uninvolved contralateral neck is less clear. While the literature reviews suggest improvement in neck control after bilateral neck radiotherapy, many single-institution series analyzing outcome in patients with occult primary or known tonsillar tumor contradict this finding.[20,29] Inclusion bias (i.e. bilateral radiotherapy is mostly offered to patients with more extensive nodal disease) may contribute to this observation. There is no doubt, however, that bilateral radiotherapy is mandatory in N2c disease as well as in patients with a suspected midline primary tumor, e.g. in patients with p16/HPV-positive nodes after a palatine tonsillectomy not disclosing a primary tumor or in those with EBV-positive nodes and suspicious imaging studies but negative biopsy of the nasopharynx. On the other hand, the possibility of regular follow-up visits with periodic imaging checks of the neck and guided FNAB of suspicious lesions, together with potential morbidity and limitations for an eventual salvage procedure, speaks in favor of more limited intervention.

With the use of IMRT, the main benefit can be expected in the late toxicity profile of radiation, e.g. with improved xerostomia and dysphagia scores; it doesn't change acute toxicities, local control or survival.[35,36] When radiotherapy is limited to the involved side of the neck, no dosimetric advantage of IMRT can be anticipated over conventional 3-dimentional conformal radiation. Even the opposite is true: with the exposure of a larger volume of normal tissue to lower radiation doses, IMRT puts the patient at increased risk for the development of secondary malignancies.[37]

In CUP metastatic to the neck nodes, the addition of systemic therapy to radiation follows the premises set for patients with a known primary SCC. In a definitive and postoperative setting, concurrent administration of both modalities aimed to improve neck control in patients at higher risk for neck failure. In view of the increased sensitivity of p16/HPV-associated tumors to standard therapies and superior outcome,[38] the role of concurrent chemoradiation in this subgroup is yet to be defined. The results of currently conducted treatment de-escalation trials will be available in the coming years.[39] Another challenge was posed by questioning the prognostic importance of extracapsular tumor spread in p16/HPV-associated oropharyngeal tumors[40] and by the observation that binary assessment of extracapsular tumor spread (absent vs. present) provides inferior prognostic information to a more detailed description of extracapsular tumor extension.[41]

At present there is no evidence that concurrent administration of radiotherapy and systemic therapy affects the rate of subsequent systemic dissemination which goes up to 30% in some series.[42] This advocates for the use of effective adjuvant systemic therapy in patients at increased risk for distant metastases, such as those with multilevel/low neck metastases or large volume (N2c/N3) neck disease.[43] However, none of the induction/adjuvant systemic therapy regimens presently in routine use has ability to improve the survival of patients with a known primary SCC of the head and neck.[44]

Early-stage disease

For low-volume solitary nodal disease (N1) with no signs of extracapsular extension, surgery or radiotherapy alone was found to be equally effective.[45] In view of the excellent outcome in non-smokers with p16/HPV-associated N2a tumors of known origin treated with radiotherapy alone, unimodal treatment seems to be indicated also in patients with stage T0N2a p16/HPV-associated disease.[46] A combination of both modalities does not increase neck control or survival in these patients, only morbidity.[45] Especially in patients directed to radiotherapy, detailed pretreatment imaging examination of the neck is crucial to avoid undertreatment. For the same reason, in surgically treated patients a comprehensive clearance of the nodal regions in the neck and not only a simple excision of an enlarged lymph node are mandatory. Because neck staging and assessment of extracapsular extension are both more accurate after surgery than if evaluation is done only by imaging examinations, a selective neck dissection with its low morbidity and costs (compared to radiotherapy) appears to be the treatment of choice.

Advanced stage disease

For patients with determined extracapsular tumor spread and for those with N2 or N3 neck disease, a combined modality approach is indicated. Balaker et al. reported on a systematic review of 18 studies published from 1998 to 2010 that analyzed the treatment outcomes in CUP patients with neck metastases. No statistically significant difference in 5-year survival (52.4% vs. 46.6%, p=0.55) was found between patients treated with surgery and postoperative radiotherapy/chemoradiotherapy and those who underwent radiation/chemoradiation alone.[47] At the moment it is not known which of the two approaches is more effective and whether the integration of FDG-PET in the post-treatment evaluation of the irradiated neck (with surgical salvage in less than complete responders) have the potential to shift this balance toward a non-surgical option, particularly in the p16/HPV-positive group.

Conclusions

CUP with SCC metastases to the neck nodes constitutes up to 3% of head and neck SCCs. Clinical examination supplemented with cross-sectional imaging and the removal of the palatine and lingual tonsils minimize the risk of missing an occult primary. After comprehensive diagnostics the emergence rate of a mucosal primary equals the risk of a metachronous primary in patients cured of a known primary SCC of the head and neck. Under these conditions, the treatment of the involved neck only is justified in the majority of patients, which also offers better prospects for salvage therapy in cases of recurrence or new primary tumor in the head and neck area; it is also less toxic than more extensive treatment. Both primary surgery followed by (chemo)radiation or (chemo)radiation alone seem to be equally effective although the former provides valuable prognostic information that allows better adjustment of overall treatment intensity to the aggressiveness of the disease. The impact of the HPV status of metastatic nodes on treatment decisions and intensity is yet to be determined.

References

1. Pavlidis N, Briasoulis E, Hainsworth J, Greco FA. Diagnostic and therapeutic management of cancer of an unknown primary. Eur J Cancer 2003; 39: 1990-2005.
2. van de Wouw AJ, Jansen RL, Speel EJ, Hillen HF. The unknown biology of the unknown primary tumor: a literature review. Ann Oncol 2003; 14: 191-2+196.
3. Bissel MJ, Hines WC. Why don't we gt more cancer? A proposed role of the microenvironment in restreining ncer progression. Nat Med 2011; 17: 320-329.
4. Collado M, Serrano M. Senescence in tumours: evidence from mice and humans. Nat Rev Cancer 2010; 10: 51-57.
5. Hemminki K, Bevier M, Hemminki A, Sundquist J. Survival in cancer of unknown primary site: population-based analysis by site and histology. Ann Oncol 2012; 23: 1854-1863.
6. Grau C, Johansen LV, Jakobsen J, et al. Cervical lymph node metastases from unknown primary tumours: results from a national survey by the Danish Society for Head and Neck Oncology. Radiother Oncol 2000; 55: 121-129.
7. Strojan P, Ani-in A. Combined surgery and postoperative radiotherapy for cervical lymph node metastases from an unknown primary tumour. Radiother Oncol 1998; 49: 33-40.
8. Strojan P, Ferlito A, Medina JE, et al. Contemporary management of lymph node metastases from an unknown primary to the neck: I. A review of diagnostic approaches. Head Neck 2013; 35: 123-132.
9. Galloway TJ, Ridge JA. Management of squamous cell cancer metastatic to cervical nodes with an unknown primary site. J Clin Oncol 2015; 33: 3328-3337.
10. Layfield LJ. Fine-needle aspiration in the diagnosis of head and neck lesions: a review and discussion of problems in differential diagnosis. Diagn Cytopathol 2007; 35: 798-805.
11. Begum S, Gillison ML, Nicol TL, Westra WH. Detection of human papillomavirus-16 in fine-needle aspirates to determine tumor origin in patients with metastatic squamous cell carcinoma of the head and neck. Clin Cancer Res 2007; 13: 1186-1190.
12. Macdonald MR, Freeman JL, Hui MF, et al. Role of Epstein-Barr virus in fine-needle aspirates of metastatic neck nodes in the diagnosis of nasopharyngeal carcinoma. Head Neck 1995; 17: 487-493.
13. Goldenberg D, Begum S, Westra WH, et al. Cystic lymph node metastasis in patients with head and neck cancer: an HPV-associated phenomenon. Head Neck 2008; 30: 898-903.
14. McGuirt WF, McCabe BF. Significance of node biopsy before definitive treatment of cervical metastatic carcinoma. Laryngoscope 1978; 88: 594-597.
15. Ellis ER, Mendenhall WM, Rao PV, et al. Incisional or excisional neck-node biopsy before definitive radiotherapy, alone or followed by neck dissection. Head Neck 1991; 13: 177-183.
16. Cianchetti M, Mancuso AA, Amdur RJ, et al. Diagnostic evaluation of squamous cell carcinoma metastatic to cervical lymph nodes from an unknown head and neck primary site. Laryngoscope 2009; 119: 2348-2354.
17. Tanzler ED, Amdur RJ, Morris CG, et al. Challenging the need for random directed biopsies of the nasopharynx, pyriform sinus, and contralateral tonsil in the workup of unknown primary squamous cell carcinoma of the head and neck. Head Neck 2016; 38: 578-581.
18. Waltonen JD, Ozer E, Schuller DE, Agrawal A. Tonsillectomy vs. deep tonsil biopsies in detecting occult tonsil tumors. Laryngoscope 2009; 119: 102-106.
19. Kothari P, Randhawa PS, Farrell R. Role of tonsillectomy in the search for a squamous cell carcinoma from an unknown primary in the head and neck. Br J Oral Maxillofac Surg 2008; 46: 283-287.
20. Liu C, Dutu G, Peters LJ, et al. Tonsillar cancer: the Peter MacCallum experience with unilateral and bilateral irradiation. Head Neck 2014; 36: 317-322.
21. Fu TS, Foreman A, Goldstein DP, de Almeida JR. The role of transoral robotic surgery, transoral laser microsurgery, and lingual tonsillectomy in the identification of head and neck squamous cell carcinoma of unknown primary origin: a systematic review. J Otolaryngol Head Neck Surg 2016; 45: 28.
22. de Bree R. The real additional value of FDG-PET in detecting the occult primary tumor in patients with cervical lymph node metastases of unknown primary tumour. Eur Arch Otorhinolaryngol 2010; 267: 1653-1655.
23. Johansen J, Buus S, Loft A, et al. Prospective study of 18FDG-PET in the detection and management of patients with lymph node metastases to the neck from an unknown primary tumor. Results from the DAHANCA-13 study. Head Neck 2008; 30: 471-478.
24. Pereira G, Silva JC, Monteiro E. Positron emission tomography in the detection of occult primary head and neck carcinoma: a retrospective study. Head Neck Oncol 2012; 4: 34.
25. Lee JR, Kim JS, Roh JL, et al. Detection of occult primary tumors in patients with cervical metastases of unknown primary tumors:

comparison of (18)F FDG PET/CT with contrast-enhanced CT or CT/MR imaging-prospective study. Radiology 2015; 274: 764-771.
26. Zhu L, Wang N. 18F-fluorodeoxyglucose positron emission tomography-computed tomography as a diagnostic tool in patients with cervical nodal metastases of unknown primary site: a meta-analysis. Surg Oncol 2013; 22: 190-194.
27. Gao g, Gong B, Shen W. Meta-analysis of the additional value of integrated 18FDG PET-CT for tumor distant metastasis staging: comparison with 18FDG PET alone and CT alone. Surg Oncol 2013; 22: 195-200.
28. Senft A, de Bree R, Hoekstra OS, et al. Screening for distant metastases in head and neck cancer patients by chest CT or whole body FDG-PET: a prospective multicenter trial. Radiother Oncol 2008; 87: 221-229.
29. Strojan P, Ferlito A, Langendijk JA, et al. Contemporary management of lymph node metastases from an unknown primary to the neck: II. A review of therapeutic options. Head Neck 2013; 35: 286-293.
30. Richards TM, Bhide SA, Miah AB, et al. Total mucosal irradiation with intensity-modulated radiotherapy in patients with head and neck carcinoma of unknown primary: a pooled analysis of two prospective studies. Clin Oncol (R Coll Radiol) 2016 [Epub ahead of print].
31. Nieder C, Gregoire V, Ang KK. Cervical lymph node metastases from occult squamous cell carcinoma: cut down a tree to get an apple? Int J Radiat Oncol Biol Phys 2001; 50: 727-733.
32. Jereczek-Fossa BA, Jassem J, Orecchia R. Cervical lymph node metastases of squamous cell carcinoma of unknown primary. Cancer Treat Rev 2004; 30: 153-164.
33. Sinnathamby K, Peters LJ, Laidlaw C, Hughes PG. The occult head and neck primary: to treat or not to treat? Clin Oncol (R Coll Radiol) 1997; 9: 322-329.
34. Perkins SM, Spencer CR, Chernock RD, et al. Radiotherapeutic management of cervical lymph node metastases from an unknown primary site. Arch Otolaryngol Head Neck Surg 2012; 138: 656-661.
35. Marta GN, Silva V, de Andrade Carvalho H, et al. Intensity-modulated radiation therapy for head and neck cancer: systematic review and meta-analysis. Radiother Oncol 2014; 110: 9-15.
36. Paleri V, Roe JW, Strojan P, et al. Strategies to reduce long-term postchemoradiation dysphagia in patients with head and neck cancer: an evidence-based review. Head Neck 2014; 36: 431-443.
37. Hall EJ, Wuu CS. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys 2003; 56: 83-88.
38. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010; 363: 24-35.
39. Masterson L, Moualed D, Liu ZW, et al. De-escalation treatment protocols for human papillomavirus-associated oropharyngeal squamous cell carcinoma: a systematic review and meta-analysis of current clinical trials. Eur J Cancer 2014; 50: 2636-2648.
40. Sinha P, Lewis JS Jr, Piccirillo JF, et al. Extracapsular spread and adjuvant therapy in human papillomavirus-related, p16-positive oropharyngeal carcinoma. Cancer 2012; 118: 3519-3530.
41. Keller LM, Galloway TJ, Holdbrook T, et al. p16 status, pathologic and clinical characteristics, biomolecular signature, and long-term outcomes in head and neck squamous cell carcinomas of unknown primary. Head Neck 2014; 36: 1677-1684.
42. Ligey A, Gentil J, Créhange G, et al. Impact of target volumes and raiation technique on loco-regional control and survival for patients with unilateral cervical lymph node metastases from an unknown primary. Radiother Oncol 2009; 93: 483-487.
43. Wallace A, Richards GM, Harari PM, et al. Head and neck squamous cell carcinoma from unknown primary site. Am J Otolaryngol 2011; 32: 286-290.
44. Haigentz M Jr, Cohen EE, Wolf GT, et al. The future of induction chemotherapy for head and neck squamous cell carcinoma. Oral Oncol 2012; 48: 1065-1067.
45. Strojan P, Ferlito A, Langendijk JA, Silver CE. Indications for radiotherapy after neck dissection. Head Neck 2012; 34: 113-119.
46. O'Sullivan B, Huang SH, Siu LL, et al. Deintensification candidate subgroups in human papillomavirus-related oropharyngeal cancer according to minimal risk of distant metastasis. J Clin Oncol 2013; 31: 543-550.
47. Balaker AE, Abemayor E, Elashoff D, St. John MA. Cancer of unknown primary: does treatment modality make a difference? Laryngoscope 2012; 122: 1279-1282.

Fungal infections in rhinology

Yujay Ramakrishnan[1] (FRCS (ORL-HNS) and **Shahzada Ahmed**[2] BSc(Hons) DLO FRCS(ORL-HNS) PhD
[1]ENT Department, Queen's Medical Centre, Nottingham Derby Rd, Nottingham NG7 2UH
[2]ENT Department, University Hospitals Birmingham NHS Trust, Mindelsohn Way, Edgbaston, Birmingham B15 2GW

Correspondence:
Yujay Ramakrishnan, Consultant ENT and Skull Base Surgeon
Queen's Medical Centre, Nottingham
Derby Rd, Nottingham NG7 2UH
Email: yramakrishnan@nhs.net

Abstract
Fungal sinusitis is heterogenous consisting of both invasive and non-invasive subtypes. The clinical course can range from being indolent (eg fungal ball) to rapidly progressive (acute invasive fungal sinusitis). Due to overlap of symptoms with bacterial sinusitis, diagnosis can be delayed, sometimes with fatal consequences in immunocompromised patients. This article aims to give the reader an overview of the various fungal sinusitis subtypes, with particular emphasis on the clinical presentation and imaging subtleties, that would expedite and optimize management.

J ENT Masterclass 2016; 9 (1): 109 - 115.

Key words
Fungal sinusitis, fungal rhinosinusitis, invasive fungal sinusitis, non-invasive fungal sinusitis, granulomatous fungal sinusitis, allergic fungal rhinosinusitis, fungal ball

Fungal disease of the paranasal sinuses
Although fungi are ubiquitous within the environment, they rarely cause disease within the paranasal sinuses. The spectrum of disease is largely dependent on the immunological competence of the host. There is a great degree of heterogeneity in fungal sinusitis with respect to pathophysiology, type of population affected, response to treatment and prognosis.

The most commonly accepted classification of fungal sinusitis is based on the International Society for Human and Animal Mycology Group (2008) which categorizes fungal sinusitis into invasive (acute invasive, chronic invasive, and granulomatous) and non-invasive types (allergic fungal sinusitis and fungal ball) based on histopathologic evidence of tissue invasion[1].

Invasive fungal sinusitis

Acute Invasive Fungal Rhinosinusitis (AIFR)
AIFR is rare but can be rapidly progressive (<4 weeks) resulting in fatality within days. It is associated with angioinvasion and extrasinus extension through a combination of bony destruction, perineural and perivascular spread.

Two main patients are typically at risk: diabetics with ketoacidosis and patients who are immunocompromised (severe neutropenia, haematological malignancy, systemic chemotherapy, steroid therapy, bone marrow transplantation, AIDS). Common pathogens include Aspergillus sp (neutropenic patients) and members of the family *Mucoraceae (Mucor, Rhizopus, and Absidia)*[2]. Diabetic patients are particularly at risk from Zygomycetes (Rhizopus, Mucor) as these organisms have an active ketone reductase system and thrive in high glucose acidotic conditions.

Mortality rates of at least 50% have been reported[3]. As such, a high degree of clinical suspicion and subtle changes in imaging have to be identified to promptly diagnose and manage this condition.

Clinical Features
The clinical hallmark of AIFR is febrile neutropenia and facial pain with or without nasal congestion and orbital signs. Often however, the symptoms are non-specific (fever, headache, facial pain, rhinorrhea, and diplopia) and indistinguishable from bacterial sinusitis. The key is to have a low index of suspicion, particularly in immunocompromised patients. Serial nasoendoscopy, timely imaging +/- biopsy are critical[2] so that prompt treatment may be initiated.

Symptoms and signs occur rapidly, often within hours, reflecting the pattern of invasion into nearby structures. Nasal endoscopy often reveals discolouration/pallor of nasal mucosa progressing to ulceration and tissue necrosis. Spread to the orbit and intracranially can result in proptosis, diplopia, visual loss and neurological deficit (headaches, neurological deficit, seizures and coma). Extension of infection to the cavernous sinus via the orbital apex result in opthalmoplegia (cranial nerve palsies III, IV and VI) and orbital pain (ophthalmic division of trigeminal nerve involvement). Thrombosis of the cavernous section of the carotid artery inevitably results in brain infarction.

Interestingly, patients can present with advanced AIFR with orbital and cerebral complications with few signs or symptoms of rhinosinusitis and nasoendoscopy may be essentially normal[4]. This reinforces the need to have a high degree of suspicion in immunocompromised patients presenting with orbital or cerebral signs, with or without symptoms of sinus disease.

Diagnosis

Diagnosis often mandates imaging studies in conjunction with clinical and endoscopic examination as well as biopsies. Changes in mucosal appearance and/or sensation (anaesthesia) are typical on endoscopic examination. Mucosal pallor can progress to necrosis due to angioinvasion; black crusts, sloughing nasal mucosa and septal perforation may be evident. Biopsies should be taken from multiple sites, particularly the middle turbinate and septum in order to confirm the diagnosis and identify the causal fungal organism. The gold standard of diagnosis is pathological examination of permanent sections, prepared in potassium hydroxide. However, this process is time consuming and may delay the diagnosis and treatment. Frozen section is a technique that is useful in order to provide rapid evidence of invasion, and has been found to have a sensitivity of 84% and a specificity of 100% for the diagnosis of AIFR compared to permanent sections[5].

Both CT and MRI are complementary in the diagnosis of AIFR. CT allows detection of bony destruction while MRI is better at detecting mucosal, skin invasion, orbital or intracranial involvement. Non-contrast CT may show mucosal thickening in the affected sinuses, hyperattenuation within opacified sinuses (red flag for fungal aetiology), bony erosion and/or thickening of periantral fat planes. MRI is superior at evaluating extra-sinus disease, such as intracerebral and intraorbital spread. A unique early feature on MR imaging is the lack of enhancement of the affected mucosa of the turbinates, described as the ‘’black-turbinate sign”, reflecting tissue necrosis[6]. For similar reasons, there can be loss of contrast enhancement of the extraocular muscles[7].

Early orbital changes include inflammatory changes in orbital fat and extraocular muscles with resulting proptosis. There may be subtle obliteration of periantral fat within the pteryogopalatine fossa. Intracranial changes include leptomeningeal enhancement, cerebral infarction or subarachnoid haemorrhage secondary to thrombosis of the carotid artery +/-branches or mycotic aneurysm from angioinvasion[8].

Management

The mainstay of treatment is early aggressive surgical debridement, broad spectrum systemic anti-fungal treatment and reversing the underlying immunosuppression (eg diabetic ketoacidosis or neutropenia. Strict control of diabetes and reversal of neutropenia with granulocyte-colony stimulating factor[9] can lead to improved survival.

Surgical (endoscopic or open) debridement is carried out until clear, bleeding margins are observed. There is little evidence that radical resection, including orbital exenteration and radical maxillectomy, improves survival[3]. Indeed, endoscopic resection has been shown to lead to improved survival compared to those who undergoing open surgery[3]. This may partly be due to the fact that patients undergoing open surgery had far more advanced disease. A multidisciplinary approach involving ophthalmology, maxillofacial and neurosurgical expertise is paramount.

Broad-spectrum anti-fungal therapy eg amphotericin B deoxycholate should be commenced as soon as a diagnosis of AIFR is suspected. Due to the its nephrotoxic profile, safer lipid-formulations such as Amphotericin B lipid complex and liposomal amphotericin B have been developed. Fungal cultures are essential in determining sensitivity to anti-fungal agents. Once mucormycosis is ruled out, treatment may be changed to a less toxic azole which is more effective against Aspergillus compared to mucormycosis. Voriconazole is now recommended as first line treatment for invasive aspergillosis of the sinuses by the Infectious Disease Society of America. An alternative azole, posaconazole may be used as a step-down to oral treatment when clinical improvement is seen, to enable long term treatment.

Hyperbaric oxygen therapy (HBOT) has been proposed an adjunct to treatment of AIFR[10]. HBOT acts directly by increased production of oxygen-based free radicals and indirectly by reversing growth-promoting lactic acidosis and restoration of phagocytosis[11]. To date there is no clear evidence of the efficacy of HBOT in the treatment of AIFR.

Prognosis

In a recent systematic review by Turner et al[3], diabetic patients were found to have better prognosis, despite often more aggressive disease, possibly due to the fact that their underlying condition was more easily reversed than other conditions. Patients who have intracranial involvement, or who do not receive surgery as part of their therapy, have a poorer prognosis.

Chronic Invasive Fungal Rhinosinusitis

Chronic invasive fungal rhinosinusitis (CIFR) is rare. It is characterized by a slowly progressive invasive disease (>3 months). It tends to occur in immunocompetent individuals. It is differentiated from its chronic granulomatous invasive fungal sinusitis (CGIFS) counterpart by a lack of granulomas on histopathology and an association with diabetes mellitus.

Aspergillus spp. (fumigatus) or Mucor spp are the most common causative organisms[12]. The symptoms often mimic chronic sinusitis which is refractory to standard antibiotic treatment. As the disease advances, proptosis, orbital apex syndrome and neurological deficits may occur.

Diagnosis

The clinical work-up (nasoendoscopy, imaging and biopsy) is identical to AIFS. There can be nasal congestion and polyposis and evidence of fungal invasion on histology. Imaging features relatively similar to the acute counterpart except for the pattern of intrasinus calcification on CT.

In the AIFS, intrasinus calcifications shows a fine punctate appearance whilst in CIFS, as more calcium metabolites are deposited in the fungal mass, a more dense and coarse appearance is witnessed[13]. Localised erosion of the sinus walls are seen with extension into adjacent tissues, orbit and intracranial compartments.

Management

The treatment of CIFS is similar to AIFS i.e a combination of surgery followed by systemic antifungals. Systemic and topical amphotericin B should be started until cultures exclude Mucor species. Azole drugs such as voriconazole[14] and itraconazole are promising alternatives as they are effective via the oral route and are therefore easier and cheaper to administer for longer term treatment but are less effective against Mucor sp. A prospective randomised unblinded study compared Amphotericin B (conventional or liposomal) and itraconazole in the management of CIFR and found that both were equally efficacious[15].

Chronic Granulomatous Invasive Fungal Sinusitis

Chronic granulomatous invasive fungal sinusitis is rarely seen in the West and is more common in the North Africa, the Middle East and Asia. *Aspergillus flavus* is the most common causative fungi. It follows an indolent path and may be found in both immunocompetent and immunodeficient patients. Imaging features are nonspecific and similar to other forms of invasive fungal sinusitis. It is defined by the presence of non-caseating granulomas with Langhan’s type giant cells and fungal hyphae, although it may co-exist with other types of fungal sinusitis[16].

It is treated by surgery followed by antifungals. Antifungals like voriconazole instead of amphoteracin may be used as the disease is caused by Aspergillus flavus. Indeed, Rupa et al.[16] recommends postoperative treatment with either oral itraconazole or voriconazole for disease with limited extension and oral voriconazole for advanced disease extending to the brain. Amphotericin B was not recommended as first line therapy for CGFS.

Non-invasive fungal sinusitis

Allergic Fungal Rhinosinusitis

Allergic fungal rhinosinusitis (AFRS) is the most common form of fungal sinusitis. This condition shares similar histopathologic features with allergic bronchopulmonary aspergillosis (ABPA) and was first reported by Safirstein[17] in 1976.

AFRS consists of a non-invasive collection of eosinophilic mucin, resulting from a type I IgE-mediated allergic response to inhaled mould spores which colonize the sinus cavity. The fungi most commonly identified in the eosinophilic mucin include Alternaria, Bipolaris, Cladosporium, Curvularia, Drechslera and Helminthosporium from the dematiaceous family and Aspergillus species[18]. The importance of type I hypersensitivity in AFRS remains controversial as there are alternative hypothesis including humoral immunity, antibody-independent pathways and local sinonasal IgE production[19].

The typical patient with AFS is younger and atopic and immunocompetent. It is also more frequent in warm, humid environments and lower socioeconomic status[20].

Clinical Features

Symptoms mimic chronic rhinosinusitis which is refractory to medical treatment. They present often with unilateral, but sometimes bilateral nasal congestion, post nasal drip,

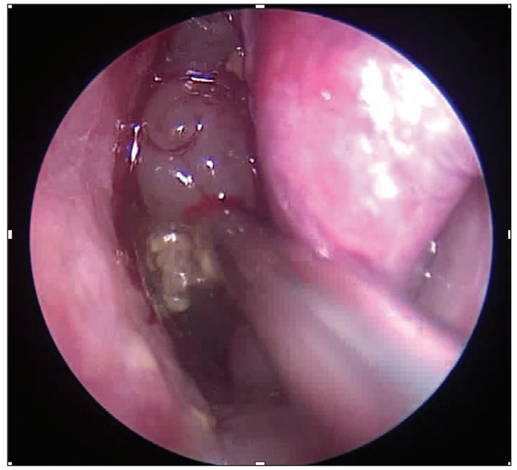


Figure 1: *Endoscopic findings of AFRS showing nasal polyposis and thick mucinous secretions*

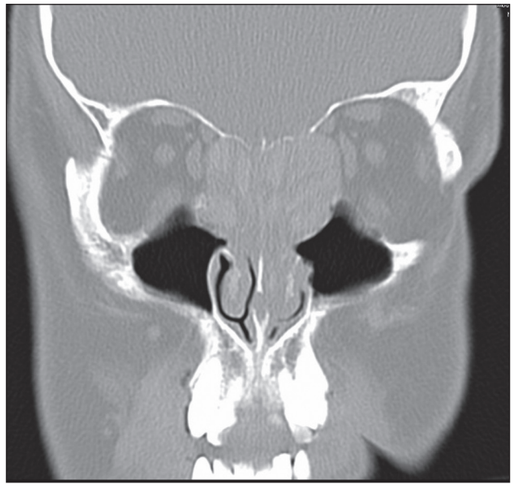


Figure 2: *Coronal CT sinus demonstrating erosion of lamina papyracea and skull base*

and a thick dark nasal discharge. There is often a history of recurrent symptoms following previous treatment or surgery and typically patients show an excellent response to oral corticosteroids, but not antibiotics. Patients may also present with signs and symptoms of bony erosion and involvement of the orbit, including proptosis and telecanthus.

On examination, there is usually gross nasal polyposis with thick, highly viscous mucin, classically described as the consistency of peanut butter (Figure 1).

Diagnosis

Many experts use Bent and Kuhn criteria[21] for diagnosis of AFRS (table 1). These criteria consist of both major and minor criteria, and all five major criteria must be met in order for a diagnosis to be made. The presence of minor criteria supports the diagnosis of AFR. The amount of fungal hyphae can be variable and sparse, therefore even in its absence, the presence of allergic mucin is virtually pathognomonic for AFRS.

Table 1. Bent and Kuhn Diagnostic Criteria

Major	Minor criteria
Type I hypersensitivity (history, skin test or in vitro testing)	Asthma
Nasal polyposis	Unilateral disease
Characteristic CT findings	Radiological bone erosion
Eosinophilic mucin without invasion	Fungal cultures
Positive fungal stain	Serum eosinophilia
	Charcot-Leyden crystals (eosinophil degradation products)

CT imaging typically shows characteristic pansinusitis, hyperattenuation of the intrasinus contents (representing thick allergic mucin) surrounded by lower attenuation hyperplastic mucosa. The 'double density' sign may be seen in affected sinuses i.e heterogeneous signal intensity due to the deposition of heavy metals within the mucin (Figure 2). Sinus walls are often expanded, remodelled or eroded due to the expansive nature of mucin and its propensity to incite a local inflammatory response (Figure 3). The MR imaging signal is variable, ranging

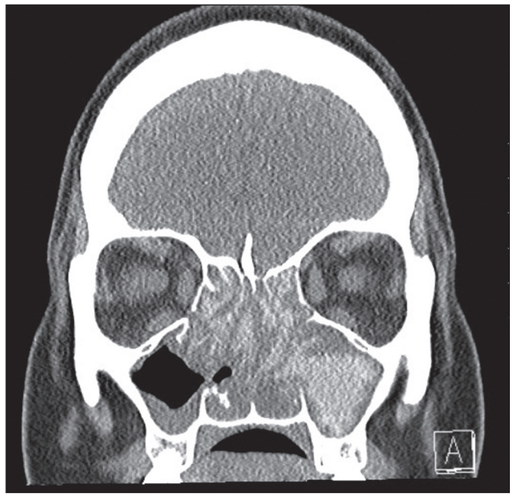


Figure 3: *Coronal CT sinus showing classic 'double density' sign seen in AFRS*

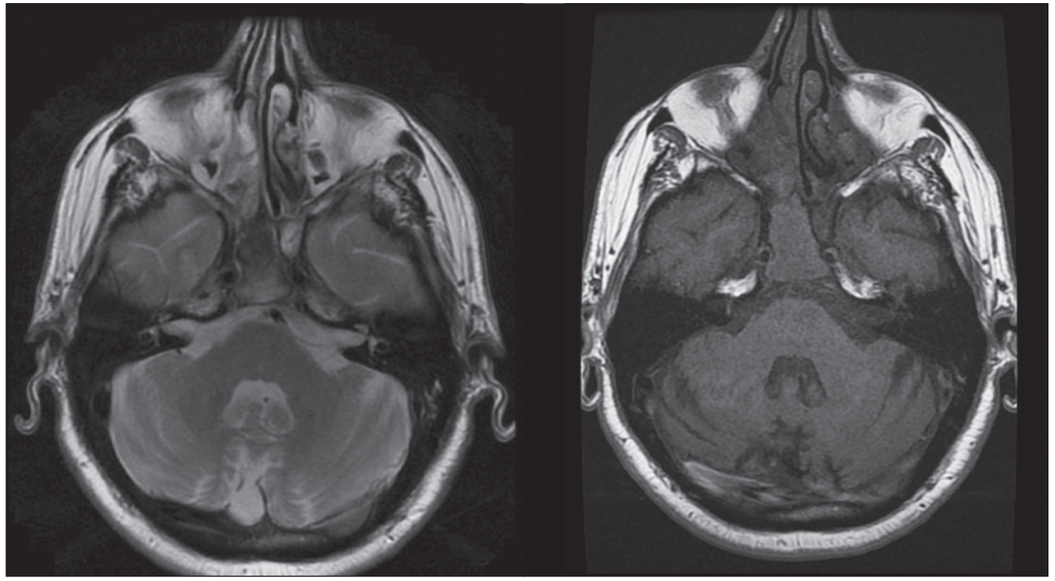


Figure 4: *Axial MRI sinus showing near signal void in sphenoid sinus on T2-weighted (left) compared to T1-weighted images (right)*

from isointense to hypointense signal to signal void on T1- and T2-weighted images, depending on the contents of the sinus. Therefore, MRI should always be interpreted in the presence of CT; on T2-weighted images, the high metal concentration within proteinaceous allergic fungal mucin may show up as a signal void (Figure 4), mimicking the appearance of a normally aerated sinus. Both T1 and T2 weighted images show peripheral enhancement.

Management

The mainstay of AFRS treatment remains surgery though adjunctive medical management is critical for optimal outcomes[22].

In 2014 Gan et al[23] published an evidence-based approach for the postoperative medical management of AFRS. The review concluded that poststoperative systemic and standard topical nasal steroids are recommended; oral antifungals, and immunotherapy[24] are options in cases of refractory AFRS; and did not provide recommendations for topical antifungals and leukotriene modulators due to lack of evidence. Recently, AFRS which is refractory to surgery and conventional medical treatment has been shown to be responsive to anti-IgE antibody, omalizumab[25].

Fungal Ball

A fungal ball consists of sequestered fungal hyphal elements within a sinus without allergic mucin, invasive or granulomatous changes[26]. It is distinct from saprophytic fungal infestation which corresponds to fungal spores found on crusts and mucus in the nose. Fungal balls are typically found in immunocompetent individuals. Aspergillus fumigatus is the most commonly implicated pathogen. Previous dental treatment[27] and radiotherapy are sometimes implicated in the development of fungal ball.

Clinical Features

Fungal balls commonly affect the the maxillary sinus followed by the sphenoid sinus. Patients may be completely asymptomatic with the diagnosis made incidentally on imaging. Other symptoms include headache or facial pain, post-nasal drip and cacosmia. Fungal balls affecting the sphenoid sinus may present with retro-orbital pain at the vertex.

Diagnosis

CT scanning is the imaging of choice for suspected fungal balls. Five CT features are commonly found, including a heterogenous soft tissue density in a single unilateral sinus, absence of an air-fluid level, erosion of the inner wall of the sinus, sclerosis of the lateral sinus wall and the presence of calcification. In particular, the presence of erosion of the inner wall of the sinus and the presence of calcification have a positive predictive value in the diagnosis of fungal balls of 94.6% and 93.2% respectively[28].

	Non-invasive		Invasive	
	Fungal ball (mycetoma)	**Allergic fungal sinusitis**	**Acute Invasive**	**Chronic invasive**
Pathogen	*Aspergillus species; Pseudallescheria boydii*	Primarily dematiaceous species: *Bipolaris, Alternaria, Curvularia*; also *Aspergillus* species and multiple other molds	Mucormycosis (Diabetics); Aspergillus Fumigatus (immunocompromised), Candida species, Fusarium	Aspergillus flavum, A fumigatus
Immune status of host	Immunocompetent	Atopic	Immunocompromised	Immunocompetent or mildly immunocompromised
Geographical distribution	Humid area	Humid area	Non-specific	Non-specific
Radiological findings	Hyperdense on CT, especially maxillary and sphenoid sinus, double density sign	CT- Heterogenous sinus opacification (double density), bony remodelling +/- erosion MRI – variable; hyper/ hypointense/ signal void on T2 depending on metal concentration within mucin	CT -sinus opacification, bony erosion and tissue infiltration MRI – 'black turbinate' sign, soft tissue, orbital and intracranial invasion	CT -sinus opacification, bony erosion and tissue infiltration MRI – 'black turbinate' sign, soft tissue, orbital and intracranial invasion
Treatment	Surgical	Surgical + medical	Reversal of underlying Immunocompromise, surgical + antifungal therapy	Surgical + medical

The presence of calcification is thought to be due to the deposition of calcium salts within the fungal ball.

MRI scanning is not usually necessary, but may be used as an adjunct to CT imaging to differentiate mucosal swelling or mucus retention from a fungal ball. On T2-weighted MR imaging fungal balls are often hypointense compared to mucous or mucosal swelling which is hyperintense.

Management

The treatment of fungal balls is surgical with no adjunctive medical treatment usually necessary. Functional endoscopic sinus surgery is employed to create a wide opening of the affecting sinus ostium. All fungal material should be removed and the sinus thoroughly irrigated with saline. Biopsies are taken from the underlying mucosa to rule out invasion. Any dental filling material present in the sinus should also be removed. In immunocompetent patients there is no role for the use of systemic antifungal agents.

Conclusion

Fungal sinusitis symptoms can overlap with bacterial or viral rhinosinusitis An important appreciation of the clinical presentation and radiological findings is vital for timely diagnosis, improving patient outcomes and limiting morbidity. A multidisciplinary team approach engaging various surgical and medical disciplines should be encouraged in the management of more complex cases of fungal sinusitis.

References

1. Chakrabarti, A. Denning, DW, Ferguson, BJ, et al. Fungal rhinosinusitis: a categorization and definitional schema addressing current controversies. The Laryngoscope 119, 1809–1818 (2009).
2. Gillespie, M. B., O'Malley, B. W. & Francis, H. W. An approach to fulminant invasive fungal rhinosinusitis in the immunocompromised host. Arch. Otolaryngol. Head Neck Surg. 124, 520–526 (1998).
3. Turner, J. H., Soudry, E., Nayak, J. V. & Hwang, P. H. Survival outcomes in acute invasive fungal sinusitis: a systematic review and quantitative synthesis of published evidence. The Laryngoscope 123, 1112–1118 (2013).
4. Thurtell, M. J. Chiu, S.L., Goold, L.A., et al. Neuro-ophthalmology of invasive fungal sinusitis: 14 consecutive patients and a review of the literature. Clin. Experiment. Ophthalmol. 41, 567–576 (2013).
5. Ghadiali, M. T., Deckard N.A., Farooq, U. et al. Frozen-section biopsy analysis for acute invasive fungal rhinosinusitis. Otolaryngol.--Head Neck Surg. Off. J. Am. Acad. Otolaryngol.-Head Neck Surg. 136, 714–719 (2007).
6. Safder, S., Carpenter, J. S., Roberts, T. D. & Bailey, N. The 'Black Turbinate' sign: An early MR imaging finding of nasal mucormycosis. AJNR Am. J. Neuroradiol. 31, 771–774 (2010).
7. Gorovoy, I. R., Vagefi, M.R.,Russell, M.S. et al. Loss of contrast enhancement of the inferior rectus muscle on magnetic resonance imaging in acute fulminant invasive fungal sinusitis. Clin. Experiment. Ophthalmol. 42, 885–887 (2014).
8. Aribandi, M., McCoy, V. A. & Bazan, C. Imaging features of invasive and noninvasive fungal sinusitis: a review. Radiogr. Rev. Publ. Radiol. Soc. N. Am. Inc 27, 1283–1296 (2007).
9. Carter, K. B., Loehrl, T. A. & Poetker, D. M. Granulocyte transfusions in fulminant invasive fungal sinusitis. Am. J. Otolaryngol. 33, 663–666 (2012).
10. Kajs-Wyllie, M. Hyperbaric oxygen therapy for rhinocerebral fungal infection. J. Neurosci. Nurs. J. Am. Assoc. Neurosci. Nurses 27, 174–181 (1995).
11. Tragiannidis, A. & Groll, A. H. Hyperbaric oxygen therapy and other adjunctive treatments for zygomycosis. Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis. 15 Suppl 5, 82–86 (2009).
12. Li, Y., Li, Y., Li, P. & Zhang, G. Diagnosis and endoscopic surgery of chronic invasive fungal rhinosinusitis. Am. J. Rhinol. Allergy 23, 622–625 (2009).
13. Yoon, J. H., Na., DG., et al. Calcification in chronic maxillary sinusitis: comparison of CT findings with histopathologic results. AJNR Am. J. Neuroradiol. 20, 571–574 (1999).
14. D'Anza, B. Stokken, J,.et al. Chronic invasive fungal sinusitis: characterization and shift in management of a rare disease. Int. Forum Allergy Rhinol. (2016). doi:10.1002/alr.21828
15. Mehta, R., Panda, N. K., Mohindra, S., Chakrabarti, A. & Singh, P. Comparison of efficacy of amphotericin B and itraconazole in chronic invasive fungal sinusitis. Indian J. Otolaryngol. Head Neck Surg. Off. Publ. Assoc. Otolaryngol. India 65, 288–294 (2013).
16. Rupa, V., Maheswaran, S., Ebenezer, J. & Mathews, S. S. Current therapeutic protocols for chronic granulomatous fungal sinusitis. Rhinology 53, 181–186 (2015).
17. Safirstein, B. H. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. Chest 70, 788–790 (1976).
18. Pant, H., Schembri, M. A., Wormald, P. J. & Macardle, P. J. IgE-mediated fungal allergy in allergic fungal sinusitis. The Laryngoscope 119, 1046–1052 (2009).
19. Loftus, P. A. & Wise, S. K. Allergic Fungal Rhinosinusitis: The Latest in Diagnosis and Management. Adv. Otorhinolaryngol. 79, 13–20 (2016).
20. Wise, S. K., Ghegan, M. D., Gorham, E. & Schlosser, R. J. Socioeconomic factors in the diagnosis of allergic fungal rhinosinusitis. Otolaryngol.--Head Neck Surg. Off. J. Am. Acad. Otolaryngol.-Head Neck Surg. 138, 38–42 (2008).
21. Bent, J. P. & Kuhn, F. A. Diagnosis of allergic fungal sinusitis. Otolaryngol.--Head Neck Surg. Off. J. Am. Acad. Otolaryngol.-Head Neck Surg. 111, 580–588 (1994).
22. Younis, R. T. & Ahmed, J. Predicting revision sinus surgery in allergic fungal and eosinophilic mucin chronic rhinosinusitis. The Laryngoscope (2016). doi:10.1002/lary.26248
23. Gan, E. C. Thamboo, A. Rudmik, L,. et al. Medical management of allergic fungal rhinosinusitis following endoscopic sinus surgery: an evidence-based review and recommendations. Int. Forum Allergy Rhinol. 4, 702–715 (2014).
24. Melzer, J. M., Driskill, B. R., Clenney, T. L. & Gessler, E. M. Sublingual Immunotherapy for Allergic Fungal Sinusitis. Ann. Otol. Rhinol. Laryngol. 124, 782–787 (2015).
25. Evans, M. O. & Coop, C. A. Novel treatment of allergic fungal sinusitis using omalizumab. Allergy Rhinol. Provid. RI 5, 172–174 (2014).
26. deShazo, R. D. et al. Criteria for the diagnosis of sinus mycetoma. J. Allergy Clin. Immunol. 99, 475–485 (1997).
27. Grosjean, P. & Weber, R. Fungus balls of the paranasal sinuses: a review. Eur. Arch. Oto-Rhino-Laryngol. Off. J. Eur. Fed. Oto-Rhino-Laryngol. Soc. EUFOS Affil. Ger. Soc. Oto-Rhino-Laryngol. - Head Neck Surg. 264, 461–470 (2007).
28. Chen, J.-C. & Ho, C.-Y. The significance of computed tomographic findings in the diagnosis of fungus ball in the paranasal sinuses. Am. J. Rhinol. Allergy 26, 117–119 (2012).

Odontogenic causes of maxillary sinusitis and their management

James Barraclough MMedSci FRCS(ORL-HNS)[1], **Andrew Birnie** BDS MFDS RCSEd MOralSurg[2] and **Zarina Shaikh** FRCS OMFS MFDS BDS[3]
[1]Consultant Rhinologist and Facial Plastic Surgeon, ENT Department, New Cross Hospital
[2]Specialist Oral Surgeon, Royal Cornwall Hospital, Truro, England, TR1 3LJ
[3]Consultant Oral and Maxillofacial surgeon, Royal Cornwall Hospital, Truro, England TR1 3LJ

Correspondence:
James Barraclough MMedSci FRCS(ORL-HNS)
Consultant Rhinologist and Facial Plastic Surgeon, ENT Department, New Cross Hospital
Royal Wolverhampton NHS Trust, West Midlands WV10 0QP
Email: mrjamesbarraclough@gmail.com

Abstract
Odontogenic maxillary sinusitis is an uncommon but important disease entity and is often recognised late. The increasing use of computed tomography (CT) in the assessment of unilateral sinus symptoms has improved the ability to recognise and manage this group of conditions. Here we discuss the details of a number of dental causes of maxillary sinus disease. A description of the journey of a tooth is used to demonstrate how certain pathologies occur and how they may lead to disease within this specific region. Management options are also discussed which often a require close collaboration with dental and oral/maxillofacial colleagues.

J ENT Masterclass 2016; 9 (1): 116 - 121.

Key words
Maxillary sinus, sinusitis, odontogenic

Introduction
Odontogenic sinusitis accounts for up to 10%-12% of all cases of maxillary sinusitis[1]. A simple look at the relevant anatomy explains the relationship, with the floor of the maxillary sinus formed by the alveolar process of the maxilla (Figure 1). The formation and continuing integrity of this alveolar bone is intimately linked to the development and maintenance of normal, healthy dentition.

A wide range of dental problems, both primary and iatrogenic, can compromise the normal functioning of the maxillary sinus. A disruption in the normal mucociliary pathway created by the ciliated pseudostratified columnar epithelium within the maxillary sinus can lead to mucus stasis, overgrowth of organisms and sinus mucosal inflammation[2]. There is a two-fold increase in maxillary sinus disease in patients with periodontal disease and this relates to the close proximity of teeth to the maxillary sinus[3]. All maxillary teeth have the potential for causing problems in the sinonasal cavities but the first and second permanent molars are those most commonly involved in maxillary sinusitis due to their root morphology and positioning. Less commonly, the maxillary second premolars and third molars can be involved[4] .

A dental cause for maxillary sinus disease should be considered in those patients with symptoms of unilateral maxillary sinusitis with a history of odontogenic infection, dento-alveolar surgery or in those patients resistant to conventional sinusitis therapy. The most common cause of odontogenic sinusitis is iatrogenic and this accounts for over half of cases reported in the literature[4].

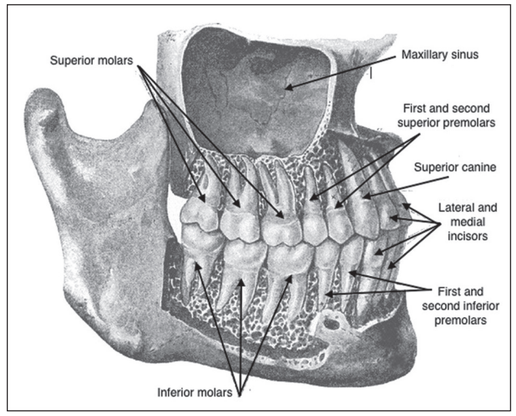


Figure 1: *Section showing the proximity of tooth roots to floor of maxillary antrum (adapted from Figure 1003 in 'Anatomy of the Human Body' - Henry Gray 1918*

The tooth journey
Knowing the basics of odontogenesis and the journey of a tooth from embryonic cells to an erupted, functional structure will give a greater understanding of the origin and behaviour of odontogenic pathology relevant to the maxillary sinus.

The *tooth germ* is essentially a collection of cells derived from the the first pharyngeal arch and neural crest. It is connected to the oral cavity via an in-growth of oral ectoderm – the *dental lamina* and is organised into three main parts:

- the *enamel organ* - gives rise to ameloblasts which produce enamel and also the Hertwig Epithelial Root Sheath which determines the shape of the tooth roots
- the *dental papilla* - produces odontoblasts which form dentine
- the *dental follicle* - produces cementoblasts, osteoblasts and fibroblasts which give rise to cementum, the periodontal ligament and alveolar bone which are the supporting structures of a tooth

Tooth development progresses through various cell production and organisation stages which include the bud, cap and bell stages, then the formation of the dental hard tissues and the formation of the tooth supporting structures. Each of the cell layers and stages of odontogenesis can give insight into the origin of future odontogenic pathology relevant to maxillary sinusitis. In addition to normal odontogenesis, teeth must follow particular eruption pathways to become functioning, healthy oral structures. Impacted teeth are common and can be associated with various pathological processes affecting underlying bone and adjacent structures.

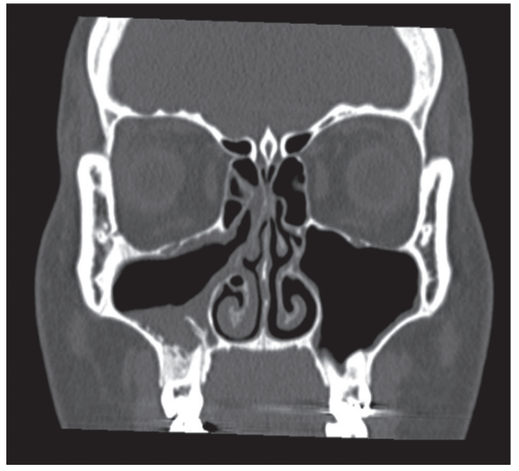


Figure 2: *Erupted radicular cyst of tooth right upper 1st molar causing maxillary sinus disease*

Even when teeth develop normally and erupt into anatomically correct positions, they enter a relatively hostile environment. A host of microorganisms exist in the oral cavity, deleterious to both the calcified tissues of the teeth themselves and the tooth supporting tissues. In addition, a variety of non-microbial threats such as mechanical abrasion/attrition/trauma and chemical agents also exist. The resultant pathology itself can impact upon the maxillary sinus, as can the treatment modalities used by dentists/surgeons to eliminate the pathology.

We discuss the common odontogenic causes of sinusitis below and their relationship to this journey. These can be categorised into three main categories; benign/malignant pathology, infective/inflammatory causes and iatrogenic causes.

A. Benign and malignant pathology

Ectopic teeth
Impacted teeth are relatively common occurrences, especially involving third molars, maxillary canines and maxillary second premolars[5]. Normal eruption is interrupted or impeded resulting in abnormal tooth positioning. This is especially true for late erupting teeth or those with long eruption pathways, such as the maxillary canine. Impacted teeth can remain dormant and cause no problems but any associated cystic change or surgical treatment to remove them can result in maxillary sinus disease.

Ectopic teeth/supernumeries/odontomes are only seen rarely in non-dentate areas such as the maxillary sinus. They are commonly only identified during imaging for investigation into the cause for any consequential maxillary sinusitis. When secondary pathology exists, early surgical intervention is recommended for removal of the tooth and any associated cyst which may require open or combined endonasal and oral approaches[6].

Odontogenic cysts
The lining of these cysts are all derived from the remnants of the tooth-forming organ and can be subdivided into developmental and inflammatory types. These lesions can cause significant bony destruction and the tissues surrounding them can become inflamed/infected and lead to secondary maxillary sinusitis.

Radicular cyst
- The most common odontogenic cyst, accounting for more than 65% of all such lesions[7]

- Always develop within granulomas in the periapical tissues of non-vital teeth (but not all periapical granulomas progress to cysts).
- Lining is derived from the rests of Malassez which are groups of cells left over from Hertwig's epithelial root sheath and is supported by a chronically inflamed fibrous capsule.
- Enlarge slowly and generally do not grow to very large dimensions (Figures 2 and 3).
- Treatment involves either endodontic therapy or removal of the non-vital tooth and enucleation of the cyst lining.

Dentigerous cyst
- Originate in the follicular tissues overlying the crown of unerupted teeth
- Lining is supported by a fibrous capsule free from inflammatory cell infiltration.
- True dentigerous cysts are attached to the amelocemental junction of the tooth.
- Most commonly associated with late erupting teeth, such as third molars, second premolars and upper canines.
- Can become very large, causing significant bony resorption.
- Reports of mucoepidermoid carcinoma are associated with dentigerous cysts but this is extremely rare[8]
- Simple enucleation of the cyst lining along with removal of the impacted tooth is usually curative in the case of dentigerous cysts, although studies have shown good success rates with surgical decompression techniques[9]

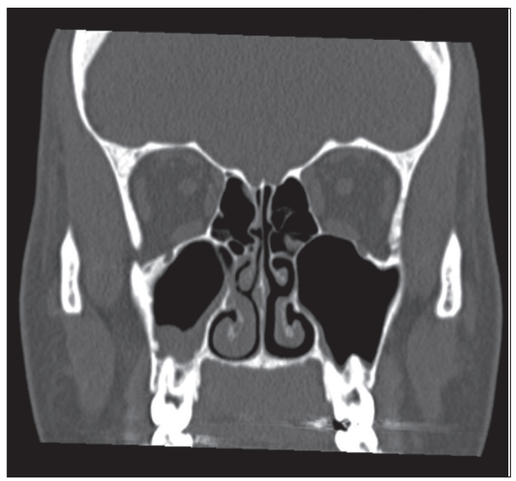


Figure 3: *Note how left contralateral tooth does not cause significant sinus disease despite root penetration into maxillary sinus*

Keratocystic odontogenic tumour (KCOT):
- Arise from the remnants of the dental lamina
- Locally aggressive growth pattern (hence the terminology of tumour)
- Tendency to recur due to friable nature of the cyst wall and tendency to advance with finger-like projections into surrounding bone, therefore surgical curettage alone is often inadequate
- Can reach large sizes with few symptoms and less bony deformity than other cysts due to antero-posterior expansion
- Radiologically can have a multi-loculated appearance with resorption of associated teeth roots
- Multiple keratocysts can be associated with Gorlin syndrome (Basal Cell Nevus Syndrome)
- KCOT's require a more aggressive surgical approach to ensure clearance.

Invasive odontogenic lesions
These are rare lesions, the most common of which is the ameloblastoma.

Ameloblastoma
- Benign but locally invasive tumour of odontogenic epithelium.
- Majority occur in the mandible but those which do arise in the maxilla can often involve the maxillary sinus.
- Generally slow growing and asymptomatic in the early stages.
- Can cause significant bony expansion, tooth resorption and increasing facial deformity.
- Radiographically they are multi-loculated in appearance, although a separate unicystic ameloblastoma exists that is more amenable to conservative surgical treatment.
- Normal ameloblastomas have a high recurrence rate following simple curettage. Due to islands of tumour infiltrating cancellous marrow spaces.

Most other benign odontogenic tumours, except perhaps the odontogenic myxoma, follow a less aggressive pattern than the ameloblastoma.

Malignant odontogenic tumours, according to the WHO classification, consist of:

a. Malignant Ameloblastoma

b. Primary Intraosseous Carcinoma

c. Other carcinoma arising from odontogenic epithelium, including from odontogenic cysts

These are rare lesions but again have potential to impact on the maxillary sinus.

B. Infective and inflammatory causes

Oral infective/inflammatory causes of maxillary sinusitis include dental periapical pathology, advanced periodontal disease, secondary infection of (non-inflammatory) odontogenic cysts and rarely Actinomycosis, a subacute/chronic bacterial infection usually caused by Actinomyces israelii.

Periapical pathology
In a non-vital tooth, either as a result of dental caries or trauma, the necrotic pulp tissue loses its ability to counter invasion by micro-organisms from the oral cavity. As a result the root canal space becomes colonised by microbial communities which initiate and sustain inflammatory processes in the tissues surrounding the tooth roots. This can lead to tissue necrosis and abscess formation.

Periodontal disease
In periodontal disease the initial site of bacterial colonisation is the gingival sulcus (the space between the tooth and gingiva) rather than within the root canal system. The inflammatory process begins as gingivitis which is not associated with alveolar bone loss but depending on a number of complex factors, this can progress to periodontal disease which causes bony resorption and apical migration of the disease process.

The thickness of the maxillary floor may influence the chance of inflammatory tooth disease leading to ascending sinus inflammation. Direct communication between the odontogenic (or otherwise) inflammatory process and the sinus lining influences the mucociliary pathways within the maxillary antrum, leading to mucus stasis, bacterial colonisation and a proliferating inflammatory process. Most infective cases involve a polymicrobial aerobic-anaerobic infection with gram negative anaerobes particularly prominent. Other cases involve anaerobic streptococci, gram-negative bacilli, and Enterobacteriaceae[10].

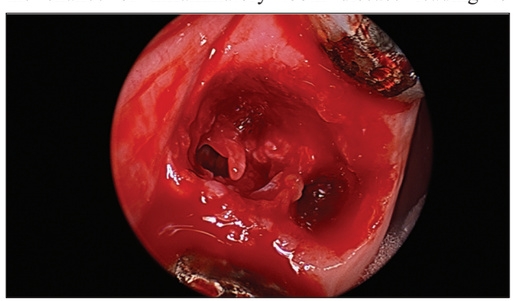


Figure 4: *View into socket of upper right 1st molar of previous patient with radicular cyst post dental extraction. Granulations and an oro-antral communication can be seen*

C. Iatrogenic causes

The other main causes of sinus pathology are those related to dental procedures and their associated complications, accounting for more than 60% of cases in the literature[4]. Any change in the normal anatomy of the teeth and the surrounding structures can lead to a greater propensity for consequential sinus disease.

Extractions
These can sometimes lead to an oro-antral communication (OAC), allowing material and organisms from the oral cavity to enter the maxillary sinus. The close proximity of the roots to the sinus and the morphology of certain multi-rooted teeth can mean that very little or no bone remains after a tooth is extracted. Sometimes an OAC is inevitable (Figure 4) and unavoidable but there are surgical techniques to help minimise the risk.

Small OACs may close spontaneously but any communication can develop into an oro-antral fistula (a pathological epithelial-lined communication between the sinus and oral cavity) especially in the presence of underlying sinus pathology. It is important the surgeon takes note of any communication and initiates appropriate management. This can consist of conservative management of small defects (antibiotics, decongestants, avoidance of sharp air pressure changes within the sinus) and a variety of surgical techniques to primarily close larger communications. It is important to excise the epithelial lining of established fistula tracts prior to surgical closure. Techniques commonly involve local soft tissue flaps (buccal advancement/palatal rotation flaps) sometimes in conjunction with the buccal fat pad (Figure 5-7). A variety of bone grafts, pedicled tongue flaps, resorbable and non-resorbable membranes, bone substitutes and different combinations of these have all been used with varying degrees of success to close such defects[11]. Treatment by the endoscopic approach has also been described[12].

In addition to OACs, the roots of teeth can be displaced into the antrum during oral surgical procedures. In some instances this may result in no associated sinus pathology

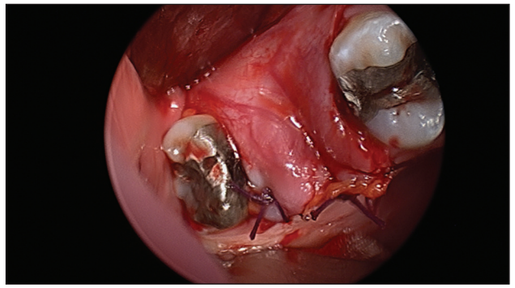


Figure 5: *Buccal mucosal advancement flap with buccal fat pad to obliterate the oro-antral communication*

but the majority require surgical removal. Simple radiographs can be helpful in locating these displaced fragments but often CT or cone beam CT imaging is required. Surgical approaches to retrieve displaced roots can be trans-alveolar or via a Caldwell-Luc approach intra-orally or via an endonasal approach which requires a wide antrostomy to gain access (Figures 8 and 9).

Implants

Dental implants require osseo-integration within sufficient healthy bone to be successful. Insufficient planning and poor surgical technique can lead to protrusion of a dental implant into the maxillary sinus and this in turn can act as a nidus of infection. The placement of dental implants is increasingly being facilitated by sinus-lift procedures. These involve different approaches to access and lift the Schneiderian membrane lining of the sinus and to encourage the growth of new alveolar bone, allowing placement of the implant. The use of osseo-conductive

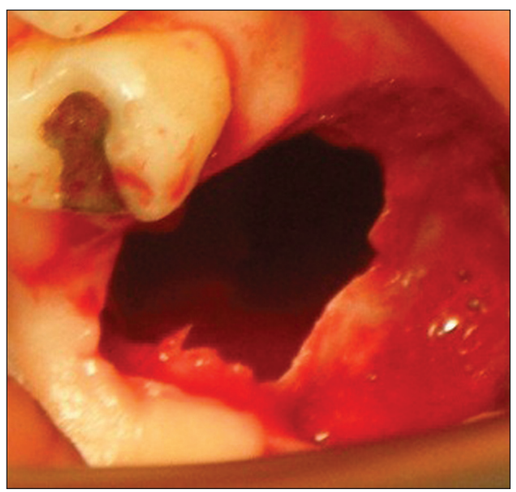


Figure 6: *Large oro-antral fistula*

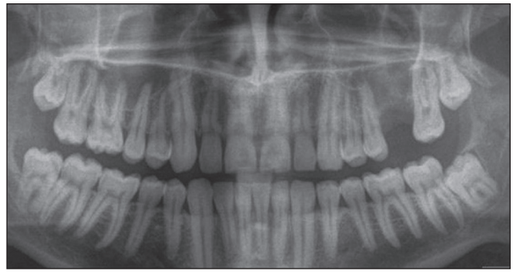


Figure 7: *Dental panoramic radiograph of an oro-antral fistula*

bone substitutes and (usually) resorbable collagen membranes often form part of this surgical procedure. Such surgical techniques in themselves carry the risk of initiating and establishing inflammatory sinus pathology, especially if the Schneiderian membrane is perforated and they do not completely prevent the potential for secondary sinusitis[13].

There is evidence however, that penetration of a dental implant into the maxillary sinus with membrane perforation does not have long term clinical or radiological sequellae especially if penetration is less than 3mm[14]. There is on-going discussion regarding the use of prophylactic antibiotics for surgical dental implant procedures and currently their use is recommended[15].

Root canal therapy

Conventional root canal therapy involves the chemico-mechanical preparation of the root canal system of a tooth to remove necrotic pulpal debris and reduce the microbial load within. This is followed by three dimensional obturation and sealing of the canals to prevent residual bacteria releasing products into the surrounding periapical tissues. The root filling material gutta-percha is commonly used to obturate the resultant open canal following

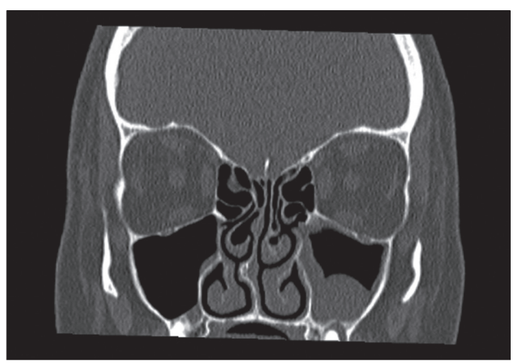


Figure 8: *Left periapical cyst of left upper 2nd molar pre-operatively*

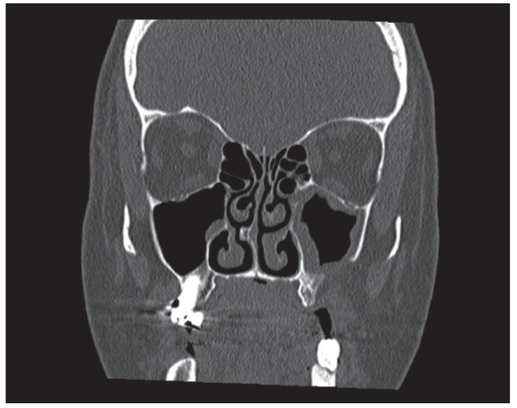


Figure 9: *Post-operative findings after Caldwell Luc approach for cyst removal and tooth extraction. Mucosal flap repair of defect. Residual sinus disease present*

preparation. Extrusion of materials/chemicals/instruments used during root canal therapy beyond apex of tooth into sinus is possible. Whilst the obturating material itself is inert and unlikely to cause much inflammation, irrigants such as sodium hypochlorite which are used in root canal therapy before application of the gutta percha could be forced into the maxillary sinus. This can lead to localised necrosis, pain and infection.

Foreign bodies

A variety of foreign bodies/materials can enter the maxillary sinus via the oral cavity. These include the aforementioned root filling materials, irrigant solutions, fractured instruments, dental implants/components and socket-packing materials. They can facilitate the passage of oral microbes into the sinus and the foreign body can impede the normal mucociliary clearance pathways, cause a localised inflammatory reaction and lead to acute or chronic maxillary sinusitis. If the object is confined to the sinus itself then a wide antrostomy and retrieval may be possible but sometimes these require an oral, combined and rarely an open approach.

Conclusions

The majority of causes for odontogenic maxillary sinusitis are secondary to dentally related procedures. Occasionally a primary lesion of the teeth may lead to a source of maxillary sinusitis. Radiological investigations are increasingly identifying the causes of this disease entity and aid with the planning for surgical management, particularly for the approach required. A broad awareness of local anatomy and pathology with a mulidisciplinary team approach to treatment is the best way to successfully manage this potentially refractory type of sinusitis.

References

1. Mehra P, Murad H. Maxillary sinus disease of odontogenic origin. Otolaryngol Clin North Am. 2004; 37:347-64
2. Al-Rawi MM, Edelstein DR, Erlandson RA. Changes in nasal epithelium in patients with severe chronic sinusitis: a clinicopathologic and electron microscopic study. Laryngoscope.1998; 108:1816–1823
3. Abrahams JJ, Glassberg RM. Dental disease: a frequently unrecognized cause of maxillary sinus abnormalities. Am J Roentgenol. 1996; 166: 1219-23
4. Lechien JR, Filleul O, Costa de Araujo P. Chronic maxillary rhinosinusitis of dental origin: a systematic review of 674 patient cases. Int J Otolaryngol. 2014; 2014:465173. Published online Apr 8, 2014
5. Kramer RM, Williams AC. The incidence of impacted teeth: A survey at Harlem Hospital. Oral Surg Oral Med Oral Pathol. 1970; 29(2):237-241
6. Ramanojam S1, Halli R, Hebbale M. Ectopic tooth in maxillary sinus: Case series. Ann Maxillofac Surg. 2013 Jan; 3:89-92
7. Daley TD, Wysocki GP, Pringle GA. Relative incidence of odontogenic tumours and oral and jaw cysts in a Canadian population. Oral Surg Oral Med Oral Pathol. 1994; 77 (3):276-80
8. Aggarwal P, Saxena S. Aggressive growth and neoplastic potential of dentigerous cysts with particular reference to central mucoepidermoid carcinoma. Br J Oral Maxillofac Surg. 2011; 49:e36-9
9. Sammut S, Morrison A, Lopes V, Malden N. Decompression of large cystic lesions of the jaw: a case series. Oral Surg. 2012; 5(1):13-17
10. Brook I. Microbiology of acute and chronic maxillary sinusitis associated with an odontogenic origin. Laryngoscope. 2005; 115:823–825.
11. Visscher S, Baucke van Minnen D, Bos R. Closure of oroantral communications: a review of the literature. Oral Maxillofac Surg. 2010; 68:1384-1391
12. Hajiioannou J, Koudounarakis E, Alexopoulos K, et al. Maxillary sinusitis of dental origin due to oroantral fistula, treated by endoscopic sinus surgery and primary fistula closure. J Laryngol Otol. 2010; 124:986–989
13. Doud Galli SK, Lebowitz RA, Giacchi RJ, et al. Chronic sinusitis complicating sinus lift surgery. Am J Rhinol. 2001; 15:181–186
14. Najm SA, Malis D, Hage ME et al. Potential adverse events of endosseous dental implants penetrating the maxillary sinus: Long-term clinical evaluation. Laryngoscope. 2013; 123(12):2958-61
15. Testori T, Drago L, Wallace SS et al. Prevention and treatment of postoperative infections after sinus elevation surgery: clinical consensus and recommendations. Int J Dent. 2012;2012:365809. Epub 2012 Aug 9

Body dysmorphic disorder and aesthetic treatment

Max Malik[1] and **Ayman Zaghloul**[2]
[1]Aesthetic Doctor and Hair Restoration Surgeon, Harley Street, London and Edgbaston, Birmingham
[2]Consultant Psychiatrist, Coventry and Warwickshire Partnership Trust and
Hon. Associate Clinical Professor Warwick University

Correspondence
Dr Ayman Zaghloul FRCPsych Consultant Psychiatrist
Hon. Associate Clinical Professor Warwick University Clifford Bridge Road
Walsgrave Coventry CV2 2TE
Email: ayman.zaghloul@outlook.com

J ENT Masterclass 2016; 9 (1): 122 - 125.

Body Dysmorphic Disorder, BDD, is a distressing and potentially disabling condition characterised by a preoccupation with imagined or slight physical defects in appearance, this results in time consuming rituals causing significant psychological distress or impairment in personal, social and occupational functioning.

Common areas of concern are skin, face, hair, body build and breasts. Patients most common negative beliefs are that their skin is discoloured or a body part is deformed or flawed or that the size and shape of their body parts are not correct or there is an asymmetry present, for example in the eyes or nose. As a result, to improve or disguise these perceived flaws most patients engage in ritualised behaviours such as staring in the mirror, skin picking, hair pulling, excessive make up, intricate or elaborate rituals such as grooming routines, feeling the body part to test for smoothness, size and flaws, constant mirror checking, seeking reassurance from friends and family and shopping extensively for doctors for aesthetic or surgical treatments. However, avoiding mirrors and bright lights and public places may also be a feature of Body Dysmorphic Disorder.

The main questions seem to be where does this normal concern with looking as good as possible and becoming preoccupied with looks change into becoming pathological? What are the implications for aesthetic practitioners and surgeons? Should such patients be treated by performing aesthetic and surgical procedures to rectify perceived cosmetic imperfections? This is a relevant question not only for those routinely performing cosmetic procedures, such as rhinoplasty, but for all doctors since these patients will present to varying degrees in many clinical settings.

Human beings have always been concerned with their appearance, and being content helps develop self-esteem, confidence and a place in family and society. Not having this emotional peace with one's own body and appearance may lead to significant psychological and social problems. Historically, Thersites was said to be the ugliest Greek in the Trojan War and from an ancient Greek point of view an ugly soul must inhabit an ugly body. Dysmorphia is a term was derived from the Greek word 'dysmorfia,' meaning misshapen or ugly. Excessive concerns with physical deformity has been known in the past as 'Quasimodo Complex'.

Sigmund Freud's Wolfman became famous and he was later described by Brunswick[1]:

"He neglected his daily life and work because he was engrossed, to the exclusion of all else, in the state of his nose. On the street he looked at himself in every shop window; he carried a pocket mirror, which he took out every few minutes. First he would powder his nose; a moment later he would inspect it and remove the powder. He would then examine the pores, to see if they were enlarging, to catch the hole, as it were, in its moment of growth and development. Then he would again powder his nose, put away the mirror, and a moment later begin the process anew. His life was centered on the little mirror in his pocket, and his fate depended on what it revealed or was about to reveal."

The prevalence of BDD varies, for example, a German population study[2] gave a prevalence of 1.7%. However, the prevalence of Body Dysmorphic Disorder in cosmetic surgery settings and dermatology clinics suggest that the disorder is much more common in these populations, with a prevalence of between 3 and 10%, it affects men and women equally, however women seek treatment for BDD more frequently than men[3], cultural factors may also play a part. In one study involving aesthetic rhinoplasty candidates 24.5% fulfilled the DSM IV criteria for BDD[4].

Unfortunately, Body Dysmorphic Disorder is poorly diagnosed in psychiatric settings, so it follows that it is less frequently diagnosed in aesthetic clinics and surgical settings. Although the diagnosis is often missed, it is easy to make.

The picture may be complicated, however, by co-existing conditions, for example depression is present in 80 – 90%[5] of patients with BDD and over one third suffer from social phobia[6] amongst other psychiatric diagnoses. However, it seems that the social phobia onset was typically before that of Body Dysmorphic Disorder and not caused by concerns about appearance[7]. Although BDD is considered to be in the spectrum of Obsessive Compulsive Disorders is interesting to note that patients with BDD do not get relief from their anxiety when they perform checking rituals, such as mirror checking, in fact these may increase the sense of despair, unlike in Obsessive Compulsive Disorders. Despair may be accompanied by feelings of self-loathing, guilt, shame, embarrassment and fear of being judged.

Frequency of perceived defects:

- Skin (73%)
- Hair (56%)
- Nose (37%)
- Weight (22%)
- Abdomen (22%)
- Breasts/chest/nipples (21%)
- Eyes (20%)
- Thighs (20%)
- Teeth (20%)
- Face size/shape (12%)
- Lips (12%)
- Buttocks (12%)
- Chin (11%)
- Eyebrows (11%)
- Hips (11%)
- Ears (9%)
- Arms/wrists (9%)
- Waist (9%)
- Genitals (8%)
- Cheeks/cheekbones (8%)
- Calves (8%)
- Height (7%)
- Head size(6%)[8] .

Most doctors have experienced patients expressing concerns about their appearance at some stage. Hence such concerns are very common and cultural factors may play a significant part, as well as sex, demographics and social subcultures. However, as in much of psychiatry, where there is significant impact on personal, social and occupational functioning or the degree of preoccupation, often proposed as one hour a day, despite the perceived defects or flaws being very slight or not observable to others then the concern and preoccupation reaches significant proportions in terms of psychological morbidity.

The relevance of Body Dysmorphic Disorder in aesthetic or surgical settings is important. Perhaps the most important thing to bear in mind is that most patients will not reveal their symptoms[9]. Very few reported these symptoms voluntarily to their psychiatrist although these were a significant factor towards their suicidality, perhaps due to embarrassment or fear of being judged. Many may even believe that they are fundamentally unacceptable and therefore unlovable. This often leads to high levels of social isolation and poor social support for sufferers of BDD and this must be a contributing factor to the fact that up to 80% of patients with BDD have experienced suicidal thoughts.

If the diagnosis is missed the consequences can be significant. It is unlikely that a person suffering from Body Dysmorphic Disorder will be satisfied with any aesthetic intervention or any number of cosmetic surgical procedures. Insight can vary in patients with BDD from excellent, which are fewer in number to poor or absent insight to delusional, which are the majority, about three quarters of all patients.

There is, of course, a continuum of preoccupations and there are many patients who are concerned about their appearance and do not suffer from BDD because they are not preoccupied or distressed or dysfunctional; when these patients seek aesthetic treatment and cosmetic surgical intervention to improve their looks, confidence and self-esteem, and these interventions appropriately performed can change someone's quality of life.

In other patients with BDD, however, this can lead to multiple surgery and even attempts at self-body modifications, some attempts may include self-mutilation. All of these attempts usually fail and the patient's flaws and defects in their perception are not improved and very rarely is quality of life improved.

The nature of the illness in BDD may fluctuate and there may be periods of fairly normal functioning. Many people with BDD have particular difficulties with photographs and may even avoid family events and photographs, which only seem to confirm their beliefs. It is commonly believed that media influences affect illnesses such as eating disorders it may also be the case that by emphasising the necessity of aesthetic beauty, these influences may also contribute to Body Dysmorphic Disorder in a similar way[10].

It is possible to screen with screening tests, however sometimes a few simple questions may be sufficient to alert the physician that further inquiry, screening or referral may be appropriate. Many patients (and some doctors) do not realise that BDD is treatable and in fact research has shown that patients want their clinician to ask them about BDD symptoms, so if done in a sensitive manner, this should not be any more difficult than other routine questions a clinician asks in practice.

For example: 'Some people worry a lot about their appearance. Do you worry a lot about the way you look and wish that you could think about it less?' If this receives a positive answer, then follow up questions to clarify the extent and nature of bodily concerns can be asked. 'Are you worried about the way you look?' For example, questions may be asked about skin, acne, scars, hair, shape and size of your nose, mouth, jaw, lips, stomach, hips, or any other body part. 'How has this problem affected your life? On an average day, how much time do you usually spend thinking about how you look?' (Add up all the time in total in a day)[11].

The COPS Questionnaire contains 9 pertinent questions to which graded responses are possible:

1. How often do you deliberately check your features? Not accidently catch sight of them. Please include looking at your features in a mirror or other reflective surface like a shop window or looking at them directly or feeling them with your fingers.
2. To what extent do you feel your features are currently ugly, unattractive or 'not right'?
3. To what extent do your features cause you a lot of distress?
4. How often do your features currently lead you to avoid situations or activities?
5. To what extent do your features currently preoccupy you? That is, you think about it a lot and it is hard to stop thinking about it?
6. If you have a partner, to what extent do your features currently have an effect on your relationship with an existing partner? (e.g. affectionate feelings, number of arguments, enjoying activities together). If you do not have a partner, to what extent do your features currently have an effect on dating or developing a relationship?
7. To what extent do your features currently interfere with your ability to work or study, or your role as a homemaker?
8. To what extent do your features currently interfere with your social life? (with other people, e.g. parties, pubs, clubs, outings, visits, home entertainment).
9. To what extent, do you feel that your appearance is the most important aspect of who you are[12]?

Although therapeutic interventions in terms of medications and psychological therapies are possible, BDD is often a chronic illness and even with specialist intervention and treatment many relapses may occur and the prognosis for complete recovery is poor[13].

In terms of treatment of BDD, Cognitive Behaviour Therapy, CBT, is considered to be the treatment of choice[14], pharmacological therapy has been based around antidepressants mainly Selective Serotonin Reuptake Inhibitors, SSRI, which are needed in higher doses and for longer durations than usual. However, on discontinuation relapse rates are high.

The UK NICE guidelines for OCD and Body Dysmorphic Disorder (National Collaborating Centre for Mental Health 2005) make use of a graduated approach to treatment. For mild cases self-help books with guidance are recommended[15]. Some evidence from a meta-analysis exists for both psychological and SSRI treatment[16]. Moderate cases therefore should be offered CBT or a SSRI and a combination of both should be offered to severe cases.

In terms of patients with BDD seeking treatment from doctors, the most commonly visited doctors were dermatologists, followed by patients seeking surgical rhinoplasty[17], and treatment for acne and surgical intervention did not improve the BDD. Surgical or cosmetic intervention can result in the patient transferring concern to another flaw or further increasing focus on the surgically altered one, which may never be seen as 'beautiful', with requests for further surgery that can become a vicious cycle, causing significant problems for the patient and doctor.

The relevance of BDD in aesthetic treatments and cosmetic surgery is clear. These patients present commonly and are on a spectrum, men are just as likely as women to have sought cosmetic surgery[18] and suicidality may increase when cosmetic surgery is denied and 25–30% of patients with Body Dysmorphic Disorder in a psychiatric clinic have had a history of attempted suicide[19]. Many patients with poor insight seek cosmetic treatments as an alternative to psychiatric or psychological treatment. Insight is not a significant factor in terms of aesthetic treatment; the outcome is likely to be poor even in those patients with relatively good insight since they may continue to see their defect or flaw as still ugly after treatment or surgery.

It is possible, with judicious selection, to greatly improve the quality of life of patients requesting aesthetic or surgical interventions since, of course, most people who attend aesthetic clinics or request surgical intervention are not suffering from BDD. However, it is important to realise that BDD is common in such settings, has significant implications in terms of dissatisfaction and it is not in the patients' best interest that aesthetic interventions are offered to them.

In conclusion, in view of the prevalence of BDD, a case can be made for a screening questionnaire to be carried out on all patients requesting aesthetic interventions. It is interesting to note that BDD occurs on a spectrum and the milder end of the spectrum may be more difficult to detect in aesthetic or surgical clinics. However, by asking a few simple screening questions, which should be part of routine consultation prior to agreeing to undertake any aesthetic procedure it is relatively easy to screen for BDD. If positive answers are forthcoming from the patient, then advice can be given in a sensitive and empathetic manner and referral should be offered to appropriate psychiatric services.

This simple and easy process, which takes a few minutes during initial consultation may prevent significant heart ache in the future and would probably be in the best interest of the doctor and certainly be in the best interest of the patient who may be suffering from Body Dysmorphic Disorder.

References

1 Brunswick RM (1928) A supplement to Freud's 'History of an Infantile Neurosis'. International Journal of Psychoanalysis 9: 439–76.
2 Rief W, Buhlmann U, Wilhelm S, et al (2006) The prevalence of body dysmorphic disorder: a population-based survey. Psychological Medicine 36: 877–85.
3 Phillips KA (2005a) The Broken Mirror: Understanding and Treating Body Dysmorphic Disorder (2nd edn). Oxford University Press.
4 Alavi M, Kalafi Y, Dehbozorgi GR et al Body Dysmorphic Disorder and other psychiatric morbidity in aesthetic rhinoplasty candidates Journal Plastic Reconstructive Aesthetic Surgery.
5 Phillips KA, Pinto A, Menard W, et al (2007) Obsessive–compulsive disorder versus body dysmorphic disorder: a comparison study of two possibly related disorders. Depression and Anxiety 24: 399–409.
6 Coles ME, Phillips KA, Menard W, et al (2006) Body dysmorphic disorder and social phobia: cross-sectional and prospective data. Depression and Anxiety 23: 26–33.
7 Coles ME, Phillips KA, Menard W, et al (2006) Body dysmorphic disorder and social phobia: cross-sectional and prospective data. Depression and Anxiety 23: 26–33.
8 Phillips KA (2005a) The Broken Mirror: Understanding and Treating Body Dysmorphic Disorder (2nd edn). Oxford University Press.
9 Conroy M, Menard W, Fleming-Ives K, et al (2008) Prevalence and clinical characteristics of body dysmorphic disorder in an adult inpatient setting. General Hospital Psychiatry 30: 67–72.
10 Neziroglu F, Khemlani-Patel S, Veale D (2008) Social learning theory and cognitive behavioral models of body dysmorphic disorder. Body Image 5: 28–38.
11 Picavet V, Gabriels L, Jorissen et al (2011) Screening Tools for Body Dysmorphic Disorder in a cosmetic surgery setting Laryngoscope 2011 Dec, 1 21 (12) 2535
12 Veale D, Ellison N, Werner T et al, Development of a Cosmetic Procedure Screening Questionnaire (COPS) for Body Dysmorphic Disorder Journal of Plastic, Reconstructive and Aesthetic Surgery April 2012 Volume 65, Issue 4, Pages 530-532
13 Ross J, Gowers S, Body Dysmorphic Disorder, Advances in Psychiatric Treatment (2011) vol 17, 142-149
14 Veale D, Neziroglu F (2010) Body Dysmorphic Disorder: A Treatment Manual. Wiley-Blackwell.
15 Veale D, Wilson R, Clark A (2009) Overcoming Body Image Problems Including Body Dysmorphic Disorder: A Self-Help Guide Using Cognitive Behavioral Techniques. Robinson.
16 Williams J, Hadjistavropoulos T, Sharpe D (2006) A meta-analysis of psychological and pharmacological treatments for Body Dysmorphic Disorder. Behavior Research and Therapy 44: 99–111.
17 Crerand C, Franklin M, Sarwer D (2006) Body dysmorphic disorder and cosmetic surgery. Plastic and Reconstructive Surgery 118: 167-80
18 Phillips KA, Diaz SF (1997) Gender differences in body dysmorphic disorder. Journal of Nervous Mental Disorders 185: 570–7.
19 Veale D, Gournay K, Dryden W, et al (1996) Body dysmorphic disorder: a cognitive behavioral model and pilot randomized controlled trial. Behavior Research and Therapy 34: 717–29.

Haemorrhagic hereditary telangiectasia in ENT

Suzanne Jervis[1], **Tom Beech**[1] and **Derek Skinner**[2]
[1]University Hospitals Birmingham, NHS Trust – Queen Elizabeth – ENT dept
[2]Ent Dept, Shrewsbury and Telford NHS Trust, Princess Royal Hospital, Telford.

Correspondence:
Mrs Suzanne Jervis, FRCS (ORL HNS)
Queen Elizabeth Hospital, Mindelsohn Way, Birmingham B15 2TH.
Email: suziejervis@hotmail.com

Abstract
Hereditary haemorrhagic telangiectasia (HHT) or Osler-Weber-Rendu disease is a rare autosomal dominant condition characterised by arterio-venous malformations (AVM). These can affect the mucous membranes, but also the lungs, brain and liver. Epistaxis is a common symptom, so ENT often sees these patients and there are recommendations as to which of these AVMs to screen for. The management consists of trying to reduce the frequency, intensity and/or duration of epistaxis so as to improve the patient's quality of life and their need for transfusions, as no cure exists. Systemic medications such as bevacizumab, tranexamic acid and tamoxifen have a role. Surgery in the form of coagulating vessels and reducing the number of telangiectasia also helps, but these will usually need to be repeated. Young's procedure still remains the definitive operation for problematic symptomatic patients.

J ENT Masterclass 2016; 9 (1): 126 - 130.

Key words
Epistaxis, Screening, Hereditary
Haemorrhagic Telangiectasia

Introduction
Hereditary haemorrhagic telangiectasia (HHT) or Osler-Weber-Rendu disease is an autosomal dominant condition with high penetrance and variable phenotype. A recent population based UK study demonstrated prevalence as 1 in 9400 individuals, with women more predominantly affected[1]. It is characterised by arteriovenous malformations (AVMs) – both at the capillary level forming telangiectasias on mucous membranes of the nose, mouth (Figure 1), fingers and face, but also within larger vessels causing arteriovenous shunting within the malformation. These larger malformations, or AVMs are observed in the lungs, brain, gastro-intestinal tract, liver and rarely the spine. Point mutations occur in 1 of 3 known genes[2-4] in the majority (88%5) of patients – all are involved in the TGF-β superfamily signalling pathway. These mutations result in loss of the intervening capillary bed due to weakness of the peri-vascular connective tissue causing post-capillary venule enlargement and union with dilated arterioles[6]. Clinically, this results in the mucosal malformations bleeding easily on minimal contact, but additional prolonged bleeding due to lack of the contractile vascular elements.

Diagnosis of patients with HHT is made using the Curaçao criteria[7] with the core symptoms and signs being epistaxis, telangiectasias at characteristic sites, diagnosis of visceral AVMs and 1st degree relative with the condition (see Figure 1.) The involvement of the ENT clinician in these patients is related to their epistaxis, which in some patients can be difficult to manage. A recent study demonstrated ENT involvement in 79% of patients with HHT but instigation of screening from ENT departments is very low[8]. Awareness of the systemic manifestations of the disease by the clinician is paramount, as targeted screening is necessary to identify systemic AVMs early to avoid significant morbidity or even mortality.

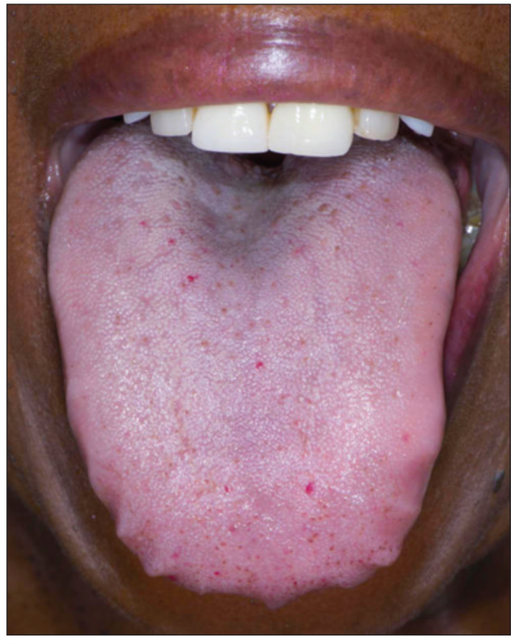


Figure 1: *Characteristic tongue telangiectases in a person with hereditary hemorrhagic telangiectasia*

This review will explore the current evidence for the management of epistaxis in these patients in addition to the screening issues that face them with respect to the systemic aspect of the condition.

Diagnosis and screening
In 2009, the International HHT Foundation published guidelines on the diagnosis and management of the condition on best available evidence, in addition to consensus from international HHT experts[9]. The subsequent publication of new data in the field regarding management of systemic AVMS has resulted in re-evaluation of these guidelines, especially within the context of a UK healthcare system. Taking each AVM in turn we have evaluated the literature to provide current appropriate guideline for patients with HHT:

Pulmonary AVM
The need to identify a pulmonary AVM early is paramount because if untreated, these can result in cerebrovascular accidents, cerebral abscesses and even worse, death[10]. The International Guidelines had already determined that outcomes following embolization of pulmonary AVMs were highly successful with a good safety profile[9]. Since the publication further evidence of the use of the AMPLATZER plug into larger malformation has added further weight to the argument for embolisation in these patients and thus screening in all HHT patients for the detection of such an AVM[11]. In terms of the screening tool of choice, the guidelines recommend a transthoracic bubble echo, which has limited availability in the UK due it being operator dependent. Given that high resolution CT is much more accessible and correctly identifies pulmonary AVMs when they are at treatable size[12], this would be the recommended screening investigation of choice if transthoracic bubble echo is unavailable.

Cerebral AVM
The guidelines published in 2009 stated that cerebral AVMs should be screened for using MRI. The recommendation was on the basis that approximately 23% of HHT patients harboured an AVM and awareness of one would enable treatment to prevent a potential cerebral bleed[13]. HHT patients under 45 years old have a 1.4-3% per annum per patient lifetime risk of a haemorrhagic stroke[14] but further data may suggest that this risk is lower for HHT patients than those without HHT[15,16]. More recent data has suggested that the prevalence of a cerebral AVM in the HHT population is lower than originally demonstrated; 7.7% for AVM and cerebral aneurysms in 2.4%[17]. They were largely supratentorial (85%) and all were less than 3cm. The Brain Vascular Malformation Consortium HHT Investigator Group has also demonstrated no statistically significant differences in the types of cerebral AVMs and the genotype of the patient[18]. They identified 3 major types; capillary vascular malformations (commonest – 61%), arterio-venous malformations and arterio-venous fistulae. Multiplicity of lesions was common, as was the largely superficial nature of the lesions. Previous studies have also shown that haemorrhages from the commonest type (capillary) have not been observed[19]. Despite this, a large multicentre blinded RCT trial examined treatment options for cerebral AVMs – medical versus surgical[20]. The trial was stopped early due to inordinately high morbidity and mortality in the surgical arm of the trial. This therefore poses the question of should patients be screened for something when there is debate over the treatment, or lack of, for it? Granted, the likelihood of a detected AVM is small and supratentorial and therefore more amenable and accessible to treatments with higher success rates. But the converse argument of the low risk of these small AVMs bleeding in the first instance vs the risk of surgical intervention is also to be considered. This is a dilemma and one which should be discussed open and honestly with patients. At the Hammersmith in London, one of two National HHT centres, it is now their practice not to routinely screen patients for cerebral AVM.

Gastrointestinal telangiectasia
Patients with symptomatic gastrointestinal AVMs present with melaena and anaemia, which may be out of context from their usual epistaxis. The standard investigation for these patients is with upper gastrointestinal endoscopy however, emerging evidence suggests that the endoscope, in HHT patients can actually trigger significant bleeding[21]. Capsule endoscopy appears to be a safer alternative, resulting in fewer bleeds, if the option is available[22]. Recent data has offered argon plasma coagulation (APC) as an effective treatment for treating the gastrointestinal vascular malformations[23] in addition to emerging case reports on the efficacy of Bevacizumab in severe gastrointestinal bleeding[24-26].

In patients who are asymptomatic with respect to gastro-intestinal AVMs, the International Guidelines screening advice of yearly haemoglobin checks in patients above 35

years would still be recommended9and onward referral for a oesophagogastroduodenoscopy/capsule endoscopy if found to be anaemic.

Hepatic AVM

Current recommendations are that patients with HHT and abnormal liver enzymes and /or symptoms of hepatic AVMs (high output cardiac failure; oedema, exertional dyspnoea, orthopnoea, portal hypertension; variceal bleed, ascites) should undergo Doppler ultrasound imaging to detect them[9]. More recent studies have shown however, that routine liver function testing does not appear to be an accurate predictor of the presence of symptomatic hepatic AVM and therefore enzyme testing should be discontinued as a marker of AVM[27,28]. Effective treatments for hepatic AVMs are limited – the morbidity and mortality of embolising them is high[29] such that the only real considered treatment until recently was a liver transplant. Again, the advent of Bevacizumab however, has raised possibilities as a potential treatment in these patients, although this is early data[30,31]. Therefore it is our recommendation that Doppler ultrasound should be utilised in patients with symptoms suggestive of hepatic AVMS and routine enzyme testing should be discontinued.

Genetic screening

This is an area that is somewhat more difficult to navigate. The International Guidelines state that everyone with possible or definite HHT on Curaçao criteria and their families should undergo genetic screening for the causative gene[9]. Although there are recognised genes that cause the disease, up to 20% of HHT families do not have the causative gene identified[32-34]. Equally, and conversely, detection of an affected gene does not always translate into specific phenotypes, potentially affecting a patient's medical history (and associated impact eg. insurance) but not the patient themselves. Therefore, genetic testing is not helpful in patients with 'definite' HHT by the Curaçao criteria. It may offer an advantage in determining 'possible' patients with HHT but appropriate genetic counselling should always be given prior to any testing.

Management of Epistaxis

As there is no cure at present for this condition, treatments aim to improve the patient's quality of life by reducing the frequency and/or severity of their episodes of epistaxis. This will in part be down to education of patients on how to self manage their nosebleeds, but also how we can manage the patients in the acute setting at times and more importantly electively to prevent the acute admission. The acute management is best managed with as little trauma to the lining of the nose as is possible, i.e. soft dressings that encourage haemostasis rather than more rigid nasal packing, but ultimately may end up the same as for managing common epistaxis.

For the elective patient the treatments revolve around either protecting the fragile telangiectasia, helping to prevent bleeding in general or removing/reducing the telangiectasia. There is generally a step wise fashion on how to treat this condition, starting with simple medical treatments and moving onto the less invasive surgical techniques (coagulation) and then to the more invasive, having nasal closure (Young's procedure) as a last resort.

Medical management

This can either be topical or systemic treatment.

Topical treatments

A wide variety of topical treatments have been tried for HHT. Emollients to protect the telangiectasias are a simple treatment and appear effective, with one study in particular finding 33 out of 49 of their HHT patients were controlled with emollients alone[35].A recent randomised controlled study using topical bevacizumab (anti-vascular endothelial growth factor monoclonal antibody), estriol (induces squamous metaplasia of mucosa, hence protecting telangiectasia), tranexamic acid (stabilises blood clot) or placebo found no difference between the treatments[36]. This is disappointing as there were some case reports suggesting bevacizumab would have a role here. Timolol (a beta blocker) has also been tried with minimal success but runs the risk of causing bradycardia.

Systemic medications

Contrary to their topical format bevacizumab, anti-androgrens (tamoxifen) and tranexamic acid have all been found to improve frequency of epistaxis when given systemically, although usually in very small trials[37,38,39]. Thalidomide, working as an anti-angiogenesis agent, has also been shown to reduce the frequency, intensity and duration of epistaxis episodes[40]. However, another study looking at patients use of the medication, found that not many patients continued with the treatment due to side effects[41]. Therefore it seems systemic medication can have a role to play in less severe patients, but as usual larger trials are needed.

Surgical management

Reducing the number of telangiectasia

There are many different ways of doing this and they are all time limited as the telangiectasia will reoccur. Simple silver nitrate cautery is possible for small telangiectasia. Other well recognised techniques are bipolar cautery, LASER (using either KTP or Nd:YAG) and more recently coblation. All of these techniques appear to improve symptoms, but as mentioned will need to be repeated at various points in time.

Another technique rather than coagulating the telangiectasia is to remove the lining of the septum down to the perichondrium and replace this with a split skin graft (septodermoplasty, first described by Saunders in 1964)[42]. Whilst this is not a long-term solution and there is risk of septal perforation and donor site morbidity, it appears to result in improvement in symptoms for patients.

A free flap reconstruction of the entire nasal lining and cavity has been described in the literature for a severe case, but there are other treatments mentioned below that may be more suitable[43].

Protecting the telangiectasia

This has always traditionally been via a Young's procedure, which involves closing one or both nostrils at the front of the nose. It has been reported as having a high degree of success, with one study showing bleeding cessation in 30 out of 36 patients[44]. It is generally reserved for the patients with more severe symptoms, as it is not without its problems. Patients obviously cannot breathe through the nostril treated, which can be distressing with resultant impairment of smell and taste. Occasionally there can be difficulty if patients do develop epistaxis and the Young's procedure may need reversing in order to successfully pack the nose.

More recently nasal obturators have been trialled to mimic the benefits of the Young's procedure, whilst minimising the problems[45]. Other options that have been tried are silastic splints insertion and closing the nostril by taping[46]. However, these need more evidence to support their use.

Reducing bleeding in general

Embolisation and arterial ligation can loosely be classed in this section as they aim to reduce the blood supply to the offending telangiectasia. These techniques are really reserved for the acute setting. There are a few articles about radiological embolization, and the consensus is that it rarely completely stops the bleeding, but does reduce the symptoms for a while. There is nothing in the literature about elective vessel ligation alone for this condition.

Conclusion

HHT is rare but problematic condition and patients can be difficult to manage. Screening for related AVMs and genetic testing of family members should be considered and discussed with patients, as there are implications of the potential findings. Simple emollients work well for most patients, then coagulation is the next step in the management along with considering systemic medications. Young's procedure still appears to be the most definitive treatment but less restrictive alternative innovations are available.

References

1. Donaldson J, McKeever T, Hall I, et al. The UK prevalence of hereditary haemorrhagic telangiectasia and its association with sex, socioeconomic status and region of residence: a population-based study. Thorax 2014;69(2):161-167.
2. Gallione C, Repetto G, Legius E, et al. A combined syndrome of juvenile polyposis and hereditary haemorrhagic telangiectasia associated with mutations in MADH4 (SMAD4). Lancet 2004;363:852-859.
3. Johnson D, Berg J, Baldwin M, et al. Mutations in the activin receptor-like kinase 1 gene in hereditary haemorrhagic telangiectasia type 2. Nat Genet 1996;13:189-195.
4. McAllister K, Grogg K, Johnson D, et al. Endoglin, a TGF-beta binding protein of endothelial cells, is the gene for hereditary haemorrhagic telangiectasia type 1. Nat Genet 1994;8:345-351.
5. Letteboer T, Mager J, Snijder R, et al. Genotype-phenotype relationship in hereditary haemorrhagic telangiectasia. J Med Genet 2006;43:371-377.
6. Braverman I, Keh A, Jacobson B. Ultrastructure and three-dimensional organization of the telangiectases of hereditary heamorrhagic telangiectasia. J Invest Dermatol 1990;95:422-7.
7. Shovlin C, Guttmacher A, Buscarini E, et al. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). Am J Med Genet 2000;91:66-67.
8. Jervis S, Skinner D. Screening for arteriovenous malformations in hereditary haemorrhagic telangiectasia. J.Laryngol.Otol. 2016;130(8):734-742.
9. Faughnan M, Palda V, Garcia-Tsao G, et al. International Guidelines for the Diagnosis and Management of Hereditary Haemorrhagic Telangiectasia. J Med Genet 2011;48:73-87.
10. Shovlin C, Jackson J, Bamford K, et al. Primary determinants of ischaemic stroke/brain abscess risks are independent of severity of pulmonary arteriovenous malformations in hereditary haemorrhagic telangiectasia. Thorax 2008;63:259-266.
11. Kucukay F, Ozdemir M, Senol E, et al. Large pulmonary arteriovenous malformations: long-term results of embolization with AMPLATZER vascular plugs. Journal of Vascular and Interventional Radiology 2014;25:1327-32.
12. van Gent M, Post M, Snijder R, et al. Real prevalence of pulmonary right-to-left shunt according to genotype in patients with hereditary hemorrhagic telangiectasia: a transthoracic contrast echocardiography study. Chest 2010;138:833-839.
13. Fulbright R, Chaloupka J, Putman C, et al. MR of hereditary Haemorrhagic telangiectasia: prevalence and spectrum of cerebrovascular malformations. Am J Neuroradiol 1998;19:477-484.
14. Easey A, Wallace G, Hughes J, et al. Should asymptomatic patients with hereditary haemorrhagic telangiectasia (HHT) be screened for cerebral vascular malformations? Data from 22 061 years of HHT patient life. J Neurol Neurosurg Psychiatry 2003;74:743-748.
15. Maher C, Piepgras D, Brown R, et al. Cerebrovascular manifestations in 321 cases of hereditary hemorrhagic telangiectasia. Stroke 2001;32:877-882.
16. Willemse R, Mager J, Westermann C, et al. Bleeding risk of cerebrovascular malformations in hereditary hemorrhagic telangiectasia. J Neurosurg 2000;92:779-784.
17. Woodall M, McGettigan M, Figueroa R, et al. Cerebral vascular malformations in hereditary hemorrhagic telangiectasia. J Neurosurg 2014;120:87-92.
18. Krings T, Kim H, Power S, et al. Neurovascular Manifestations in Hereditary Hemorrhagic Telangiectasia: Imaging Features and Genotype-Phenotype Correlations. American Journal of Neuroradiology 2015;36:863-870.

19. Krings T, Ozanne A, Chng S, et al. Hereditary hemorrhagic telangiectasia. Neurovascular phenotypes and endovascular treatment. Clin Neuroradiol 2006;16:76-90.
20. Mohr J, Parides M, Stapf C, et al. Medical management with or without interventional therapy for unrupturedbrainarteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet 2014;383:614-621.
21. Rozenberg D, Faughnan M. Bronchoscopy and gastrointestinal (GI) endoscopy in patients with hereditary hemorrhagic telangiectasia (HHT). Chest 2011;140:868A.
22. Greve E, Moussata D, Gaudin J, et al. High diagnostic and clinical impact of small-bowel capsule endoscopy in patients with hereditary hemorrhagic telangiectasia with overt digestive bleeding and/or severe anemia. Gastrointest End 2010;71:760-767.
23. Manfredi G, Crino S, De Grazia F, et al. Long-term results of extensive endoscopic treatment of GI teleangiectases in patients with hereditary hemorrhagic telangiectasia (HHT) and gastrointestinal bleeding. Digestive and Liver Disease 2014;46(S45).
24. Lupu A, Stefanescu C, Treton X, et al. Bevacizumab as rescue treatment for severe recurrent gastrointestinal bleeding in hereditary hemorrhagic telangiectasia. J Clin Gastroenterol 2013;47:256-257.
25. Epperla N, Hocking W. Blessing for the bleeder: bevacizumab in hereditary hemorrhagic telangiectasia. Clin Med Res 2015;13:32-35.
26. Kochanowski J, Sobieszcza-ska M, Tubek S, et al. Successful therapy with bevacizumab in a case of hereditary hemorrhagic telangiectasia. Hum Vaccin Immunother 2015;11:680-681.
27. Singh S, Swanson K, Kamath P. Clinically significant hepatic involvement in hereditary hemorrhagic telangiectasia (HHT). Gastroenterology 2012;142:S947.
28. Singh S, Swanson K, Kamath P. Liver enzyme abnormalities in predicting presence and progression of hepatic vascular malformations in hereditary hemorrhagic telangiectasia (HHT). Gastroenterology 2012;142:S947-S948.
29. Chavan A, Luthe L, Gebel M, et al. Complications and clinical outcome of hepatic artery embolisation in patients with hereditary haemorrhagic telangiectasia. Eur Radiol 2013;23:951-957.
30. Dupuis-Girod S, Ginon I, Saurin J, Marion D, Guillot E, Decullier E, et al. Follow-up of HHT patients treated with bevacizumab for severe hepatic vascular malformations and high cardiac output (metafore clinical trial). Haematology Reports 2013;5:2038-8322.
31. Young L, Henderson K, White R, Garcia-Tsao G. Bevacizumab: Finding its niche in the treatment of heart failure secondary to liver vascular malformations in hereditary hemorrhagic telangiectasia. Hepatology 2013;58:442-445.
32. Bossler A, Richards J, George C, et al. Novel mutations in ENG and ACVRL1 identified in a series of 200 individuals undergoing clinical genetic testing for hereditary hemorrhagic telangiectasia (HHT): correlation of genotype with phenotype. Hum Mutat 2006;27:667-675.
33. Letteboer T, Zewald R, Kamping E, et al. Hereditary hemorrhagic telangiectasia: ENG and ALK-1 mutations in Dutch patients. Hum Genet 2005;116:8-16.
34. Prigoda N, Savas S, Abdalla S, et al. Hereditary haemorrhagic telangiectasia: mutation detection, test sensitivity and novel mutations. J Med Genet 2006;43:722-728.
35. Folz BJ,Tennie J, Lippert BM,Werner JA. Natural history and control of epistaxis in a group of German patients with Rendu-Osler- Weber disease. Rhinology. 2005;43:40-6.
36. Whitehead KJ, Sautter NB, McWilliams JP, et al. Effect of Topical Intranasal Therapy on Epistaxis Frequency in Patients With Hereditary Hemorrhagic Telangiectasia: A Randomized Clinical Trial. JAMA. 2016;316:943-51.
37. Arizmendez NP, Rudmik L, Poetker DM. Intravenous bevacizumab for complications of hereditary hemorrhagic telangiectasia: a review of the literature. Int Forum Allergy Rhinol. 2015;5:1042-7.
38. Yaniv E, Preis M, Hadar T, et al. Antiestrogen therapy for hereditary hemorrhagic telangiectasia. Laryngoscope. 2009;119:284-288.
39. Geisthoff UW, Seyfert UT, Kübler M, et al. Treatment of epistaxis in hereditary hemorrhagic telangiectasia with tranexamic acid - a double-blind placebo-controlled cross-over phase IIIB study. Thromb Res. 2014;134:565-71.
40. Invernizzi R, Quaglia F, Klersy C, et al. Efficacy and safety of thalidomide for the treatment of severe recurrent epistaxis in hereditary haemorrhagic telangiectasia: results of a non-randomised, single-centre, phase 2 study. Lancet Haematol. 2015;2:e465-73.
41. Hosman A, Westermann CJ, Snijder R, et al. Follow-up of Thalidomide treatment in patients with Hereditary Haemorrhagic Telangiectasia. Rhinology. 2015;53:340-4.
42. Saunders W. Hereditary hemorrhagic telangiectasia: effective treatment of epistaxis by septal dermoplasty. Acta Otolaryngol 1964;58:497–502.
43. Choi JW, Joo YH, Jeong WS, Jang YJ. Free-flap reconstruction for the management of life-threatening hereditary hemorrhagic telangiectasia. Auris Nasus Larynx. 2016 Sep 8. (epub ahead of print)
44. Richer SL, Geisthoff UW, Livada N, et al. The Young's procedure for severe epistaxis from hereditary hemorrhagic telangiectasia. Am J Rhinol Allergy. 2012;26:401–4.
45. Woolford TJ, Loke D, Bateman ND (2002) The use of a nasal obturator in hereditary haemorrhagic telangiectasia: an alternative to Young's procedure. J Laryngol Otol 116: 455-456.
46. Wirsching KEC, Kuhnel TS. Update on Clinical Strategies in Hereditary Hemorrhagic Telangiectasia from an ENT Point of View. Clinical and Experimental Otorhinolaryngology 2016 July 21(epub ahead of print)

Endoscopic vidian neurectomy for intractable vasomotor rhinitis

Bhaskar Ram and Vamsidhar Vallamkondu
Department of Otolaryngology,
Aberdeen Royal Infirmary
Aberdeen, Scotland UK

Correspondence:
Bhaskar Ram, Department of Otolaryngology,
Aberdeen Royal Infirmary
Aberdeen, Scotland UK
Email: b.ram@nhs.net

Abstract
Vasomotor rhinitis (VMR) is the most common form of non-allergic rhinitis. Vidian neurectomy was described five decades ago for intractable vasomotor rhinitis, however, in the pre endoscopic era it was not popular due to limited access and significant complications. The advent of endoscopic sinus surgery has allowed surgeons to revisit the technique. This article provides a brief overview on the management of VMR and discusses the various endoscopic surgical approaches to vidian neurectomy.

J ENT Masterclass 2016; 9 (1): 131 - 134.

Key words
vasomotor rhinitis, vidan neurectomy

Introduction
VMR is a form of non-allergic, non-infectious rhinitis. Studies have estimated that 14 million people in the United States are affected by VMR and that this disease costs $2–3 billion annually.[1,2] VMR is an upper respiratory hyper-responsiveness to non- specific triggers like exposure to strong smells, changes in air temperature, humidity, alcohol ingestion or tobacco smoke. It is difficult to differentiate non-allergic rhinitis from allergic rhinitis and post infectious rhinitis as in all three forms nasal mucosa has hypersensitivity to non-specific triggers. Therefore, its diagnosis is based on rhinitis features with exclusion of allergy, infection, structural lesions, drug abuse, or systemic disease.

Several pathologic mechanisms have been described in the literature including parasympathetic hyper stimulation, sympathetic hypostimulation or an imbalance between sympathetic and parasympathetic innervation to nasal mucosa.

The mainstay of treatment is conservative management like any form of rhinitis focussing on symptom control and improving quality of life. This includes avoidance of stimulants, use of nasal anticholinergic nasal sprays along with topical nasal steroids. Surgery is indicated only in patients with severe symptoms who fail to respond to medical therapy.

Vidian neurectomy is advocated for the management of intractable VMR. This procedure was first described by Golding-Wood in the 1960s. It became unpopular because of difficulty in accessing the vidian nerve and the associated surgical morbidity, mainly from the approach, including bleeding, poor visualisation, difficulty in accessing and identifying the vidian nerve, damage to maxillary nerve, maxillary vessels, and infraorbital hypoaesthesia.

However, recently endoscopic vidian neurectomy has gained polularity. The advances in endoscopic techniques have overcome the inherent risks of conventional vidian neurectomy, which has revolutionised the technique, improved access with better visualisation and risk of complications.

In this article we describe the anatomy of the vidian nerve, current surgical approaches for vasomotor rhinitis and discuss the associated complications with each of these procedures.

Surgical anatomy of vidian nerve
The vidian nerve is formed by the fusion of the greater superficial petrosal nerve and deep petrosal nerve which runs in the pterygoid (vidian) canal to enter into the pterygo palatine fossa (PPF). The deep petrosal nerve carries sympathetic fibres which originate from the internal carotid artery whereas the greater superficial

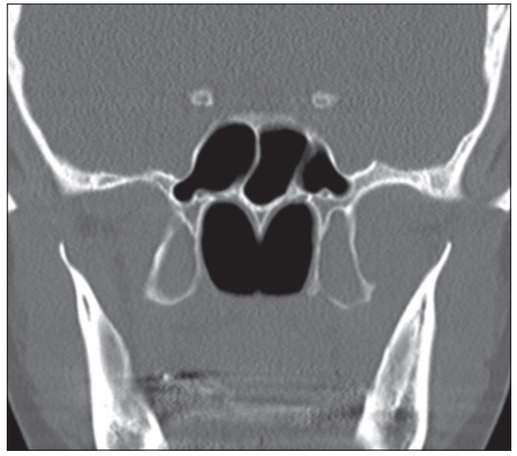


Figure 1: *type 1 (vidian nerve is protruding in sphenoid sinus cavity)*

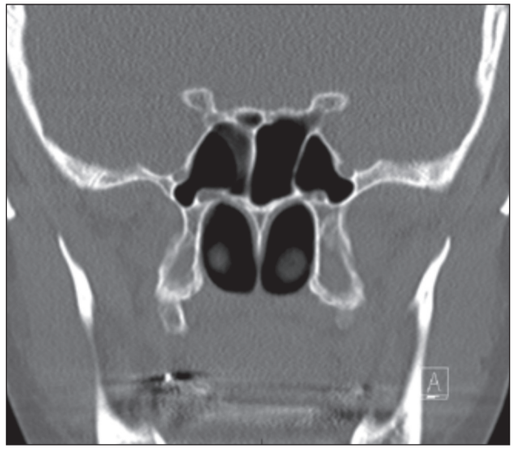


Figure 2: *type 2 (vidian nerve on the floor of sinus)*

petrosal nerve carries pre ganglionic secretomotor fibres for the lacrimal, palatine and nasal glands. On passing through PPF the vidian nerve emerges to join the sphenopalatine ganglion.

Parasympathetic fibres synapse with cell bodies of the ganglion, and the sympathetic component of the vidian nerve passes through the ganglion.

The pterygoid (vidian) canal transmits the vidian nerve and vessels. The anterior opening of the pterygoid (vidian) canal is located inferomedial to foramen rotundum on the upper medial part of the anterior surface of the pterygoid process of the sphenoid bone. The pterygoid (vidian) canal (PC) then courses in the floor of sphenoid sinus.

Lee et al,.[3] classified the PC into three types based on CT findings. The pterygoid canal protruding completely within sphenoid sinus - type 1 (Fig 1); the pterygoid canal is on the floor of the sinus or partially protruding into the sphenoid sinus -type 2 (Fig 2); The PC is completely embedded in the sphenoid corpus - type 3 (Fig 3). Yazer et al[4] reported that type 2 PC is found most commonly (54%), followed by type 3 VC (36%) and type 1 (10%).

There are huge anatomical variations of PC from person to person and from one side to the other therefore it is very important to evaluate and analyse the anatomic variations on CT pre operatively.

Surgical approaches to vidian neurectomy:

Golding–Wood first described vidian neurectomy (VN; performed through a transantral approach) for VMR in 1961[5]. Later, a transseptal approach to the pterygopalatine fossa (PPF) and VN was described by El-Guindy[6]. Due to difficult access and significant complications, these procedures were abandoned.

The recent advances in endoscopic sinus surgery has revitalized an interest in delineating the anatomy of the vidian nerve and PPF and new endonasal approaches to this area began to surface

Endoscopic vidian neurectomy (EVN)

There are various approaches described in literature.

1. Pterygopalatine fossa (PPF) approach

Robinson and Wormald[7] described a technique of EVN where a U-shaped incision is made over the sphenopalatine foramen (SPF) and a mucosal flap is raised up and over the anterior sphenoid face. The bone from SPF to the anterior face of sphenoid is drilled down up to periosteum. The periosteum is incised to open into PPF and the vidian nerve is identified in the PPF and is cut. The sphenopalatine artery is cauterized early on to prevent bleeding.

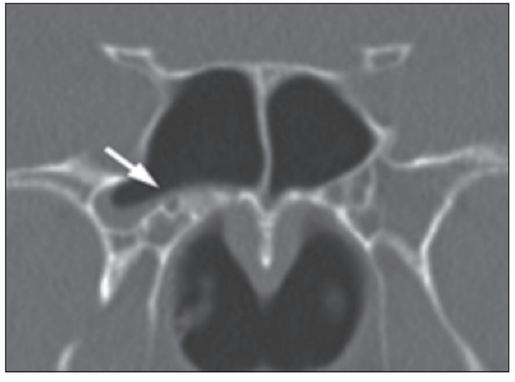


Figure 3: *Type 3 (vidian nerve in the corpus of sphenoid sinus)*

2. Transsphenoidal/Intrasphenoidal Approach

Su et al.[8] introduced an antegrade transsphenoidal approach with two subtypes. The subtypes depend on how much (or how little) the pterygoid (vidian) canal protrudes into the sphenoid cavity above the sinus floor. A generous sphenoidotomy at the sphenoid ostium is performed in both types. The first subtype is intrasphenoidal approach which consists of de-roofing the superior aspect of the bony vidian canal in the floor of the sphenoid sinus followed by isolating a length of the nerve to then divide it (Fig 4). This approach can only be used for those well-pneumatized sphenoid sinuses in which the pterygoid (vidian) canal is thin and well isolated from the surrounding bone of the sinus floor and walls. This anatomic variation is uncommon.

Second subtype is transsphenoidal approach, where the bone of the anterior wall of the sphenoid is taken down, and this bony removal is carried out laterally to the sphenoid process of the palatine bone. The sphenoid process is resected until the pterygoid (vidian) canal can be identified. A curved probe can be used to “hook” the vidian nerve, and once isolated, the nerve is then divided.

Endoscopic posterior nasal neurectomy

This procedure involves transection of the posterior nasal nerve (PNN) for the treatment of intractable VMR. PNN is a nerve ramus from the pterygopalatine ganglion innervating the nasal mucosa. This nerve supplies only nasal mucosa therefore transection of PNN avoids the postoperative complication of dry eyes, Palatal numbness may also be avoided, because the posterior nasal nerve is not located as close to the maxillary nerve as is the vidian nerve. Two separate techniques for PNN transection have been described. The first, referred to as the trans turbinate approach, is typically performed in combination with submucosal resection (SMR) of the inferior turbinate. From the incision in the turbinate, the mucosa of the middle meatus/lateral nasal wall is elevated and the periosteum cut and elevated until the sphenopalatine foramen (SPF) is visualized. The nerve bundle identified as the posterior nasal nerve courses from the SPF toward the inferior turbinate. This is isolated and cut, or when it cannot be isolated from the sphenopalatine artery, the structures are taken altogether.[9] A second technique uses a transnasal approach similar to that described for transnasal endoscopic sphenopalatine artery ligation and begins with a vertical incision made in the middle meatus roughly 5 mm anterior to the lateral attachment of the middle turbinate. A mucoperiosteal flap is elevated posteriorly to the crista ethmoidalis and then above and below this point until the SPF is identified.[10] The posterior nasal nerve is identified along with the sphenopalatine artery (SPA) and divided.

Complications of vidian neurectomy

The most common complication after VN is postoperative xerophthalmia (dry eyes). This occurs in 23–100% of the patients.[11-13] Some authors considered xerophthalmia as confirmatory sign for vidian neurectomy. These effects are

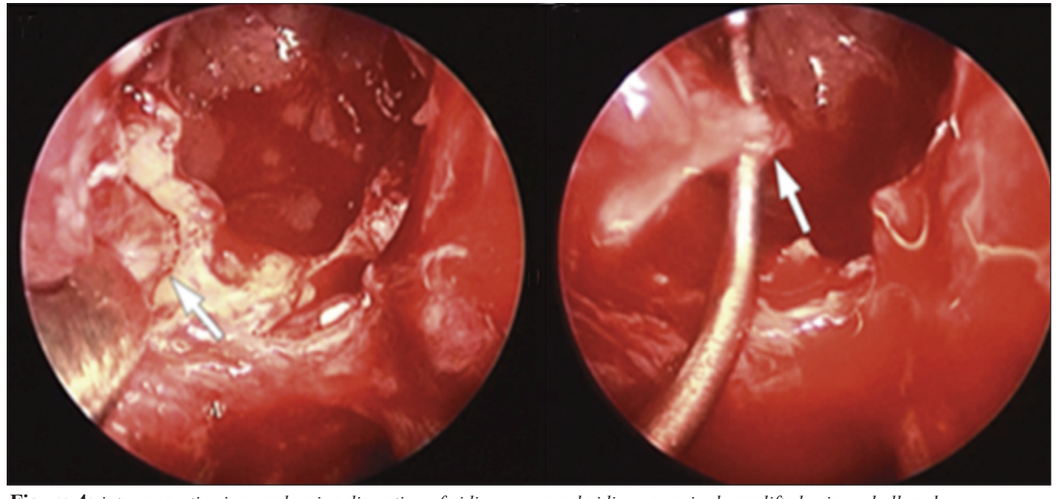


Figure 4: *intra operative image showing dissection of vidian nerve and vidian nerve is shown lifted using a ball probe*

temporary and most reported resolution of dry eyes within 1–5 months without the need for ongoing treatment.[11-13] No long-term complications from xerophthalmia were reported. Nasal crusting or dryness occurred in 15–28% of patients.[7,8]

Cheek, palate and/or gingival numbness was reported to occur in 3 - 22% of patients.[7,8,11,12] All of the numbness resolved within 1 week to 12 months and no cases of permanent numbness were reported.[11-13]

From recent systematic reviews on surgical management of VMR, it is evident that EVN is effective in controlling symptoms of retractable VMR in most patients and its effects are maintained over a period of 2-5 yrs. EVN is associated with less morbidity than traditional transantral approach and they are transient.[14,15]

Discussion

First line-treatment of VMR is medical and in the form of topical therapies including intranasal corticosteroids, intranasal antihistamines, and intranasal ipratropium bromide. Surgical intervention should only be considered in the event that aggressive medical therapy has failed to control a patient's symptoms. A variety of surgical options for medically refractory VMR have been described. Postoperative xerophthalmia is significantly more likely to occur when using the intrasphenoidal or transsphenoidal approach compared with the PPF approach. Alternatively, cheek/palatal numbness is significantly more likely to occur after the PPF approach than the intra- or transsphenoidal approach. Fortunately, any complications experienced after EVN are self-limiting and will most likely resolve on their own. The choice of approach should be based on the patient's anatomy and the surgeon's experience. If the patient's anatomy is favorable for intrasphenoidal identification and resection of the vidian nerve, this approach should be used above others because it is considerably less invasive. This anatomic configuration is not common, however; thus, the second consideration should be the surgeon's experience. It is reasonable to counsel patients with medically refractive VMR that surgical options are more likely than not to provide them with some benefit. EVN is a safe procedure and it is unlikely that patients will suffer permanent negative sequelae from it. Finally, successful outcomes from surgery for VMR are generally experienced immediately postoperatively. If the surgery does result in an improvement, it is likely that this benefit will persist.

References

1. Pattanaik D, and Lieberman P. Vasomotor rhinitis. Curr Allergy Asthma Rep 10:84–91, 2010.
2. Scarupa MD, and Kaliner MA. Nonallergic rhinitis, with a focus on vasomotor rhinitis: Clinical importance, differential diagnosis, and effective treatment recommendations. World Allergy Organ J 2:20–25, 2009.
3. Lee JC, Kao CH, Hsu CH, and Lin YS. Endoscopic transsphenoidal vidian neurectomy. Eur Arch Otorhinolaryngol. 268:851–856, 2011.
4. Yazar F, Cankal F, Haholu A, et al,. CT evaluation of the vidian canal localization. Clin Anat. 2007 Oct;20(7):751-4.
5. Golding-Wood PH. Observations on petrosal and vidian neurectomy in chronic vasomotor rhinitis. J Laryngol Otol 75:232–247, 1961.
6. El-Guindy A. Endoscopic transseptal vidian neurectomy. Arch Otolaryngol Head Neck Surg 120:1347–1351, 1994.
7. Robinson SR, and Wormald PJ. Endoscopic vidian neurectomy. Am J Rhinol 20:197–202, 2006.
8. Su WF, Liu SC, Chiu FS, and Lee CH. Antegrade transsphenoidal vidian neurectomy: Short-term surgical outcome analysis. Am J Rhinol Allergy 25:e217–e220, 2011.
9. Kobayashi T, Hyodo M, Nakamura K, et al. Resection of peripheral branches of the posterior nasal nerve compared to conventional posterior neurectomy in severe allergic rhinitis. Auris Nasus Larynx 39:593–596, 2012.
10. Ikeda K, Yokoi H, Saito T, et al. Effect of resection of the posterior nasal nerve on functional and morphological changes in the inferior turbinate mucosa. Acta Otolaryngol 128:1337–1341, 2008.
11. Tan G, Ma Y, Li H, et al. Long-term results of bilateral endoscopic vidian neurectomy in the management of moderate to severe persistent allergic rhinitis. Arch Otolaryngol Head Neck Surg 138:492–497, 2012.
12. Ma Y, Tan G, Zhao Z, et al. Therapeutic effectiveness of endoscopic vidian neurectomy for the treatment of vasomotor rhinitis. Acta Otolaryngol 134:260–267, 2014.
13. Jang TY, Kim YH, and Shin SH. Long-term effectiveness and safety of endoscopic vidian neurectomy for the treatment of intractable rhinitis. Clin Exp Otorhinolaryngol 3:212–216, 2010.
14. Halderman A1, Sindwani R. Surgical management of vasomotor rhinitis: a systematic review. Am J Rhinol Allergy. 2015 Mar-Apr;29(2):128-34.
15. Marshak T, Yun WK, Hazout C, et al. A systematic review of the evidence base for vidian neurectomy in managing rhinitis. J Laryngol Otol. 2016 Jul;130 Suppl 4:S7-S28.

Abstracts: ENT Masterclass Trainees' Gold Medal 2016

2 cases of lemierre's syndrome: the return of the forgotten disease!

Mrs H Kanona[1], Mr A Koukkoullis[1], Mr P Stimpson[1]
[1]ENT Department, Whipps Cross University Hospital, London, UK

Background:

Lemierre's Syndrome (a.k.a 'the forgotten disease') became extremely rare since the discovery of antibiotics. It is characterised by a history of recent oropharyngeal infection associated with clinical or radiological evidence of deep neck vein thrombosis and the isolation of Fusobacterium Necrophorum. Complications are often a result of septic emboli, which can lead to serious morbidity and mortality if the patient is not diagnosed early. Both cases had sore throat prior to admission which was missed.

Case 1: A 23 year old female presented to the A&E with a 2 week history of odynophagia and otalgia. Initially, she was diagnosed with otitis external and discharged, but later represented with sepsis and was admitted. An ultrasound scan of the neck revealed a partially thrombosed right IJV. This was later complicated by multiple septic pulmonary emboli. She was treated long term with cefuroxime and rivaroxaban, and following 6 months, made a full recovery

Case 2: A 37 year old male, was admitted with 2 day history of abdominal pain, diarrhoea and pyrexia. An initial diagnosis of gastroenteritis and renal colic was made and the patient underwent Computer Tomography of the Kidney, ureter and bladder. This showed evidence of a myocotic aneurysm of the aorta and multiple septic emboli. Further investigation with cardiac angiography revealed a thrombus within the left ventricle and a large aneurysm of the left anterior descending artery. The patient was underwent Endovascular Repair of Aneurysm, a Coronary Artery bypass graft and eventually self-discharged on oral clindamycin and warfarin.

A 1 year audit of thyroid nodule FNAs followed by a 1 year re-audit after recommendation to actively report and investigate every radiologically detected incidentaloma. Cytological, operative, histological and patient focused outcomes.

Mr Joseph D. Sinnott, Dr Sarah Hancox, Professor David Howlett, Mr Paul Kirkland.

Introduction:

Ultrasound guided thyroid nodule FNA is a common procedure throughout the United Kingdom and is part of the assessment of a thyroid nodule. Incidental findings from radiological investigations are an increasingly common phenomenon.

Aim:

To determine the number of FNAs performed each year, before and after recommendations. Determine the number incidentalomas and the type of scan where they were detected. Determine whether there was a significant increase in the number of worrying lesions found, whether more operations were performed and whether there was any benefit for patients. Also, to study the relationship between the Thy3 lesions and number of follicular carcinomas.

Methods:

A 1 year audit and a 1 year re-audit of thyroid nodule FNAs. 121 FNAs in the first year and 173 the second year. Referral source, number of FNAs, success of FANs, core biopsy and cytology results were determined. The number of operations (total thyroidectomy or lobectomy) was then

determined and the results of histological analysis were compared to the cytology results.

Results:
A significant increase in the number of referral for thyroid nodule investigation following recommendations. Significant increase in the number of thyroid FNAs performed. No increase in the number of thyroid lobectomies or total thyroidectomies. No increase in the cancer detection rate. No perceived patient benefit.

Discussion:
Incidental findings of thyroid nodules is a controversial topic. Core biopsies are becoming more popular. Small nodules are a common finding within the thyroid gland and to perform FNAs or core biopsies in every lesion may be causing more harm than good.

Conclusions:
No significant increase in cancers or thyroidectomise following significantly increased reporting of reporting of incidental findings from radiology.

Setting up a Parathyroid Multi-disciplinary Team (MDT) Meeting. Experience from the first year of implementation. Structure, Function, Perceived Benefits and Outcomes.

Mr J.D. Sinnott, Dr S. Hancox, Professor D. Howlett, Mr P. Kirkland.

Introduction:
A Parathyroid MDM was set up East Sussex Health Care Trust (ESHT) to provide the best possible care for patients with suspected parathyroid pathology. It was felt that a MDM would maximize the chances of achieving the correct management decision. All new hyperparathyroidism cases were discussed. In attendance, there was a consultant ENT surgeon, radiologist and endocrinologist.

Methods:
We looked at the current literature on parathyroid MDT meetings and the perceived benefits of the meeting. Data was collected on the number of referrals in our trust, number of operations and management outcomes from the first year of implementation.

Results:
In the first year of implementation, 132 new patients were discussed in the parathyroid MDT meeting. Over 70% of patients were recommended for a minimally invasive parathyroidectomy. There was a high yield of localized lesion following recommendations by the consultant radiologist and a variety of investigations including nuclear medicine, ultrasound, CT and MRI. Many of the patients managed conservatively or medically were discussed a second time following initial trial of treatment. A pathway for radiological investigation has been established. Subjectively the consultant members of the meeting feel it has be benefits such as better communication and more appropriate pathways for patients.

Conclusions:
The MDT meetings have been successful so far with perceived benefits for patients and increased efficiency of the referral pathways and more appropriate management of patients.

Giant Parathyroid Adenomas: A Minimal Invasive Parathyroidectomy Approach to 15 cases

Sidhartha Nagala, Mahmoud Daoud, Selene Chew, Muhamad Quraishi
Presenting Author:
Selene Chew
Email: Selene.chew@doctors.org.uk
Address: ENT Department, Doncaster Royal Infirmary, Thorne Road, Doncaster DN2 5LT

Abstract Introduction
We present a case series of 15 giant adenomas and discuss the challenges of a minimally invasive surgical approach. The entity of "giant parathyroid adenomas" is defined as those with a pathological weight > 3.5g.–They have a greater pre-operative calcium and parathyroid hormone level.

Methods:
A case note review of 15 giant adenomas operated on at a single institution by the senior author was performed (2006-2015). There were 7 males and 8 females, with a median age of 60.8 years. Data was collected on patient demographics, symptoms, biochemistry, ultrasound and sestamibi results, operation outcomes, complications and histopathology.

Results:
All giant adenomas were treated successfully with a single minimally invasive operation. The location of the glands in the pre-operative imaging was 100% concordant with the intra- operative location. The weight of the adenomas ranged from 3.5g – 20g with a mean of 6.33g. Histology confirmed all the glands to be benign. All patients had a complication-free postoperative period.

Discussion:
Our case series of 15 demonstrates that adenomatous glands up to 20g in weight and 60mm in the largest dimension can be excised using a lateral skin crease incision via a minimal invasive approach. The key to success and our zero rate conversion to the traditional bilateral neck exploration is the pre-operative work done by a dedicated multidisciplinary parathyroid team, which include our endocrinology colleagues and our dedicated parathyroid radiologists.

Hybrid Tracheostomy: a safe, effective technique with elimination of waiting times for emergency theatre?

Mr Navin Mani, Dr Greg Cook and **Mr Sean Loughran**
Corresponding Author:
Miss Pooja Bijoor
Manchester Royal Infirmary, Oxford Road, M13 9WL
Email: pooja.bijoor@gmail.com

Introduction:
Percutaneous tracheostomy gained popularity as it can be performed by intensivists, on the unit without transfer to an operating theatre.

Surgical tracheostomy is reserved for patients in whom a percutaneous tracheostomy is deemed unsuitable.

From our experience, patients have prolonged delays due to lack of a suitable emergency theatre slot and availability of ENT personnel.

In order to streamline the surgical tracheostomy provision, we developed a hybrid tracheostomy technique.

This paper describes the technique, its advantages and reviews the outcomes of our small pilot study.

Methods:
A minimally invasive technique of hybrid tracheostomy combines the open approach of a surgical tracheostomy, to allow direct visualisation of the trachea and deal with any bleeding or anatomical difficulties, followed by

percutaneous tracheostomy technique for insertion of the tracheostomy tube.

Results:

A total of 9 patients have undergone the hybrid tracheostomy as part of our pilot study.

It avoids transfer of the critically ill patient from the ICU to the operating theatre

It is a shorter procedure than a percutaneous tracheostomy (Range 5 – 10 minutes).

The time between referral to tracheostomy being performed was reduced as the waiting period for an emergency theatre slot was eliminated. (Waiting period range was 8 – 96 hours).

There were no reported intra-operative or post-operative complications.

Conclusion:

This is a safe technique performed under direct vision, and allows effective insertion of a tracheostomy tube. It reduced waiting times and can be scheduled for a convenient time.

We would recommend that other departments consider the implementation of this technique.

References:

1. Durbin CG. Techniques for performing tracheostomy. Respir Care 2005; 50 (4): 488 – 496
2. Susanto I. Comparing percutaneous tracheostomy with open tracheostomy. BMJ Editorials 2002; 324: 3 – 4.
3. Makowski RL & Moe KS. Hybrid Tracheostomy: A Safe, Effective Compromise. (2011 August) J Otolaryngology – Head and Neck Surgery. 145 (2 suppl), P168.

Head & Neck Surgery
ENT

NHS

Free Intensive Courses for StRs, Consultants, SAS grades & trainees

Increased seats for specialist registrars & exam candidates

CALENDER OF FREE RESOURCES 2017

ENT Masterclass® Africa

International Academic Travelling Club

Cape Town, S Africa. 29th April to 1st May 2017

2nd ENT Masterclass® China

Beijing, China, 20-21st May 2017

• 4th Consultants' ENT Masterclass®	4th March 2017
• 3rd Audiology & Balance ENT Masterclass®	10-11th March 2017
• 6th ENT Emergencies' Masterclass®	23rd June 2017
• 10th Thyroid & Salivary Gland Masterclass®	24th June 2017
• 8th ENT Radiology Masterclass®	25th June 2017

- o Limited places, on first come basis. Early applications advised.
- o Masterclass lectures, Panel discussions, Clinical Grand Rounds
- o Oncology, Plastics, Pathology, Radiology, Audiology, Medico-legal

Visit our website: www.entmasterclass.com
for FREE CYBER TEXTBOOK
on operative surgery (400 videos)
Journal of ENT Masterclass®, Trainees' Gold Medal,
Application forms

Course director: **Mr. M. Shahed Quraishi,** FRCS, FRCS (ORL, H&N)
Consultant Otolaryngologist, Thyroid & Parathyroid surgeon
Visiting Professor Capital Medical University, Beijing,
Hon Clinical Senior Lecturer in Surgical Oncology
Doncaster & Bassetlaw NHS Foundation Trust
Tel: 01302 642418 **E-mail: secretary@entmasterclass.com**

ENT Masterclass®

These courses are sponsored by the Faculty Members with Institutional support

Head & Neck Surgery
ENT

ENT MASTERCLASS® REVISION TEXT BOOK

ENT Masterclass launches the
"ENT Masterclass Revision Textbook"
125 chapters, 712 colour pages in hard cover binding.
A book from International experts to cover the curriculum.

Very popular with senior trainees and clinicians who wish to update and prepare for postgraduate exams. We have compiled this by binding together in hardcover five editions (2011-2015) of the yearbook into one easy unit.

Limited Edition. Order your copy now.
Details on Bulletin page:
http://www.entmasterclass.com/bulletinboard.htm

www.entmasterclass.com