XII MANUAL

ARGENTINE ASSOCIATION OF ENT & PEDIATRIC PHONOAUDIOLOGY

SPECIAL EDITION
WORLD CONGRESS OF PEDIATRIC ENT
BUENOS AIRES, APRIL 2019

PUBLISHER
DR. HUGO RODRÍGUEZ

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Asociación Argentina de Otorrinolaringología y Fonoaudiología Pediátrica

Asociación Argentina de Otorrinolaringología y Fonoaudiología Pediátrica

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PROLOGUE

It seems distant, that June 2017, when I was in Paris with the proposal to organize a World Congress of ENT, an idea that we had had for a long time. We decided to launch it, thinking at that time (and we were not wrong) that all large regional societies of pediatric otolaryngology were mature enough to celebrate an event that united them all. Some of these societies already exist for years with extensive experience and recognition and others are younger, but together they cover the world in our subspecialty: IAPO - Interamerican Association of Pediatric Otorhinolaryngology, ASPO - American Society of Pediatric Otolaryngology, ESPO - European Society of Pediatric Otorhinolaryngology, APOG - Asia Pacific Paediatric Otolaryngology Group, ANZSPO - Australian and New Zealand Society of Paediatric Otorhinolaryngology, PENTAFRICA - African Society of Otolaryngology. That was the point at which Dr. Tania Sih instantly joined us. Dr. Sih is undoubtedly one of the greatest disseminators of education in our specialty, working tirelessly on permanent travels around the world. Together we managed to set up a committed and enthusiastic team.

Then came 2019, the year in which the 1st World Congress of Pediatric ENT was held from April 7 to 10 in the City of Buenos Aires.

The countries represented at the congress were Argentina, Brazil, the United States, Peru, Chile, Portugal, Uruguay, Colombia, Bolivia, Paraguay, Mexico, Italy, Romania, Spain, Venezuela, the United Kingdom, Russia, Poland, Denmark, Canada, Costa Rica, Germany, China, Israel, Panama, Japan, Taiwan, Turkey, the Netherlands, Ecuador, Australia, El Salvador, Greece, Ukraine, Vietnam, Yugoslavia (ex), Nicaragua, Sweden, Switzerland, Malaysia, New Zealand, Honduras, Hungary, the Philippines, Slovakia, Austria, Saudi Arabia, Afghanistan, Croatia, Cuba, South Korea, Slovenia, France, United Arab Emirates, India, Iraq, Guatemala, Nigeria, Montserrat, Mozambique and Puerto Rico.

The Congress was sponsored by BA Tourism, National Tourism, the Garrahan Foundation, the Government of the City of Buenos Aires, FASO – Argentine Federation of Otolaryngology Societies, AAOFP – Argentine Association of Pediatric Otolaryngology and Speech Therapy, the SAP – Argentine Society of Pediatrics, the CIOA - Center for Otoaudiological Research, the Directorate of Intermediate Organizations and Public Diplomacy (DINTE), the Undersecretariat for Institutional Relations and Public Diplomacy (SUINS), and the Ministry of Foreign Affairs. The congress was declared of special interest by the Argentine Senate.

The high scientific level of all participants and the possibility to see how the five continents worked together, in addition to the traditional camaraderie, gave the meeting extra shine and excellence.

This Handbook reflects a part of the presentations held at that World Congress by selected teachers who, making one more effort, generously collaborated with its contents.

For me it has been a pleasure and an honor to be part of this dream: to unite pediatric ENT.

Acknowledgments

Thanks:

To Dr. Tania Sih, a pillar of the ENT community and the best president you can have.

To our dear friend, founder of IAPO and AAOFP, and our Honorary President Dr. Alberto Chinski.

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To Ms. Luciana González, Mr. Jorge Merino and Matías Merino for their ongoing support and collaboration.

And a special thanks to Ms. Romina Merino who was the "alma mater" of the congress with her ideas, her unconditional support, her responsibility, and her flawless work.

To my workmates at the hospital who replaced me in the care for the patients.

To my whole family that always supported me, even if it meant less time for them.

And to all our pediatric patients who show us every day that we made the right choice, that this is what we want to do, and that we want to get better and better, for them.

Hugo Rodríguez

In April 2019, there was a fantastic opportunity for the pediatric ENT community from around the world when the First World Congress of our subspecialty was organized in Buenos Aires. All major ENT Societies from the different continents were present: ASPO (US and Canada), ESPO (East and West Europe), Asia Pacific (Asia and the Middle East), Pentafrica (Africa), IAPO (Latin America), and Australasia (Oceania). This first-time magnificent event, conceived by Dr. Hugo Rodriguez and led by a group of enthusiastic collaborators, made a dream come true: to join hands among all of us who are interested in updates on clinical and surgical topics, to strengthen the network of colleagues from different countries, and to exchange not only knowledge but also friendships. More than 2000 colleagues from around 60 countries came to Buenos Aires for this unforgettable event.

This Handbook is the concrete result of the great effort of colleagues on the Congress Scientific Commission providing access to the best talks and workshops presented at the congress. The possibility of "participating" in the event a posteriori by reading the update lectures is a generous sign that valuable information should not be restricted. On the contrary, it is the seed of knowledge the World Congress has sown so that all of us, whether present or not, can continue to grow through the ongoing medical education that this book provides us.

Those of us who were able to witness this great scientific achievement were lucky. Our Argentine colleagues who made this dream come true with an enormous effort in situations of economic upheaval deserve our greatest admiration and respect.

Tania Sih

In 1997 we started thinking about organizing a World Congress of Pediatric ENT in Argentina. However, it was only in 2018 that the necessary conditions were there for us to join our efforts to make this event come true in the City of Buenos Aires.

The initial condition was for the congress to have a solid base, chaired by Dr. Tania Sih from Brazil, as a leader in the field, together with Dr. Hugo Rodríguez, who has extensive experience in the organization of meetings, as the general secretary, in addition to the relevant support from the national societies of otolaryngology.

International support was achieved through international partnerships with different societies, such as ASPO, ESPO, IAPO, APOG, ANZSPO, and PENTAFRICA, while national dissemination was in the hands of Argentine associations, including FASO and AAOFP. Furthermore, the ENT specialists who collaborated ad honorem to make the event a success should be especially acknowledged. On the other hand, I cannot fail to mention my personal pride for having been appointed Honorary President of the congress.

Attendance was large, consisting of 2153 physicians, of whom 1102 were Argentinian and 1051 from other countries from the five continents. First-level speakers participated in the different modalities provided: round tables, lectures, workshops, up-to-dates on relevant topics, live surgeries, discussion of scientific papers, inspiring debates, and exchange of ideas.

This handbook is a synthesis of the event with a compilation of selected lectures, written in the original language used in the presentation.

The aim of this joint effort is to continue on this path of teaching and learning, trying to reach a wider audience than those who actually attended the Congress, paving the way for ongoing discussion in another format.

Professor Alberto Chinski
Honorary President of the First World Congress of Pediatric ENT of this millennium

GENERALITIES

Patient safety: Are humans the problem or the solution?

Ellen S. Deutsch, MD, MS, FACS, FAAP, FSSH, CPPS.

Introduction

Pennsylvania hospitals and ambulatory surgical facilities reported that 28 surgical fires occurred on the operating field or in the patient's airway from July 1, 2011 through June 30, 2016 [(1)].

Pennsylvania hospitals and ambulatory surgical facilities reported that 49 wrong site surgery events occurred during 2018 [(2)].

Patient care events that cause patient harm are distressing for patients, their families, and their healthcare providers. Concern about patient harm has appropriately stimulated efforts to improve patient safety, and focused efforts to reduce discrete harms have been successful [(3)]. However, patient harm continues to occur, and the impact of patient safety efforts has been "disappointingly small"[(3,4)]. The overall rate of harm may not be improving despite widespread interest and investments in patient safety [(3-5)]. We may be able to improve outcomes by re-thinking our approach to patient safety interventions.

The response to events which cause patient harm is often to look for the human – or humans – who are assumed to have made the mistakes which contributed to an adverse outcome. In this chapter, we will explore whether humans are really the problem underlying undesirable events, or whether humans are valuable resources that usually prevent harm, solve problems, invent, create, and improve healthcare delivery. Instead of looking for the human's failure, perhaps we can take advantage of the extraordinary capabilities of healthcare workers and healthcare delivery systems.

"People working in health care are among the most educated and dedicated work force in any industry. The problem is not bad people, the problem is that the system needs to be made safer" [(6)].

Healthcare delivery systems are created by humans

Healthcare delivery is a human-modified system, a system created by humans and integrated into a natural system as a subsystem [(7)]. Healthcare providers must continually adjust how they work in circumstances that are only partly knowable because of incompletely understood or underspecified work conditions [(8-10)]. "Work-as-imagined," the conceptualization of how work should occur, is useful for planning and regulatory purposes but does not always align exactly with "work-as-done," which includes the realities faced by healthcare workers at the front line. Healthcare delivery is not a static process because healthcare delivery occurs within continuously changing relationships and environmental conditions. Healthcare workers must continually manage goal conflicts, such as considering the optimal resource allocation for an individual patient while conserving resources for future patients. Healthcare workers must provide care while responding to unanticipated events such as individual patient care emergencies, unexpected surges in patient volume, unforeseen technology

malfunctions, and even pandemics, all of which occur within settings of constrained resources. It is not possible to anticipate all the consequences of process or resource decisions [8-11].

Because healthcare delivery is a human-made system, "*the search for a human*

in the path of a failure is bound to succeed. If not directly at the sharp end – as a 'human error' or unsafe act – one can usually be found a few steps back.

The assumption that humans have failed therefore always vindicates itself" [12].

Healthcare delivery systems are complex adaptive systems

Healthcare delivery systems are more than complicated, they are complex adaptive systems [11]. Healthcare delivery involves networks of many agents each of whom constantly acts in ways that are not always totally predictable, and constantly reacts to other agents. Conditions are in constant evolution with fluid, dynamic changes. Although some components of healthcare delivery may be mechanical or linear, and potentially decomposable into constituent parts, the interactions between the myriad components of healthcare delivery systems are complex and incompletely predictable. These systems then further influence, and are influenced by, the environments in which they operate. Small events can produce large results; and large efforts may have limited impact [11,13,14].

As a modest example, let's explore the process of driving to work. We know our starting point and our intended destination, we know the expectation that we will stay in our lane, and we may have a regular route that we use. But perhaps today there is a detour because of construction – we will need to adapt to this environmental change. Perhaps there is an even more abrupt and unplanned event – a car heading toward us from the other direction swerves into our lane to avoid a pothole or because the driver is texting and inattentive. Or we swerve because there is a new pothole in our lane. We must respond to these unpredicted deviations to avoid harm. Had we continued to drive forward as we had initially intended, without adjusting to the unanticipated threats, we may have ended up in a crash. In fact, our trip to work may involve many adaptations that enable us to arrive safely. Although this example is more simplistic than providing healthcare, the point is that established protocols are important but we also need to adapt when necessitated by environmental conditions or the actions of other agents.

Because circumstances are constantly evolving and healthcare providers continually adjust their work to changing resource constraints and environmental conditions, effective responses may include implementing workarounds. While a specific workaround may be either problematic or pragmatic, the workaround itself demonstrates the presence of competing objectives, such as the need to follow established protocols conflicting with a lack of resources or the development of a more efficient or effective process [15].

Safety is not inherent in systems

Work by Cook and Rasmussen demonstrates that healthcare delivery systems contain contradictions between multiple goals that people must pursue simultaneously [16]. There are multiple pressures pushing providers toward less safe patient care. Organizations drive efficiency to avoid economic failure and healthcare workers seek

the least reasonable effort to avoid work overload. In correct proportion these are reasonable goals, but they must be counter-balanced with attention to patient safety. Patient safety may be supported by campaigns, regulations and resources. One very important contribution to safety that is often under-appreciated is the professionalism and judgment of HCW. As described by Cook and Rasmussen, these balances between competing pressures are dynamic and the marginal boundaries, the thresholds of safe actions and the limits of the capacity to adapt are often not clearly visible or understood. Within these complex adaptive systems, HCW create conditions that support safety [16,17].

There's rules to riding a horse
But the horse won't necessarily know 'em
-Texas Bix Bender

Does blaming humans contribute to burnout?

In addition to limiting our understanding of factors that might improve patient safety, the constant focus on what humans have done wrong may be contributing to clinician burnout. The constant drumbeat of searching for and eradicating what healthcare providers are doing wrong has consequences for the people who come to work trying to do things right, and consequences for their patients. Clinician burnout is prevalent across health care settings [18,19] and may impair clinicians' ability to maintain safe practices and detect emerging safety threats [20,21]. Patient care units with high emotional exhaustion among healthcare providers had higher standardized mortality ratios [22]. A meta-analysis of the relationship between professional burnout and quality and safety demonstrated that "greater burnout among healthcare providers was associated with poorer-quality healthcare and reduced safety for patients" [23].

How can we learn to provide safer care?

The traditional safety focus on learning from failure misses opportunities to also learn from success. In a different domain that none-the-less has lessons for healthcare, the performance of soldiers doing successive navigation exercises improved significantly when they were debriefed on their successes as well as their failures, compared with others who reviewed their failed events only after each training day. Examining success helps to clarify outcomes that result from ability versus luck, and this insight may be most important when the cost of errors is high, as in healthcare delivery [24].

Contemporary simulation has emerged as another effective way to enhance the learning of individuals and teams. When healthcare workers participate in patient care scenarios, whether in simulation centers or "in situ" (in actual patient care locations) they can practice and reflect on their decisions and actions in settings without direct risks to patients [25,26].

Simulation provides unique opportunities to surface successful strategies and adaptations as well as actions that could be improved. During simulations, we often observe workarounds and during debriefings we often hear participants express concerns about patient safety. Some workarounds are identified by simulation participants and some have become so routine that they are not even be recognized by participants. During the debriefing following the simulation we have the opportunity to explore actions, adaptations and system function.

The Safety-II approach

This perspective that humans are valuable, and that it is people who create the conditions that support safety, aligns with the theories behind "Safety-II" [27]. Our earlier discussion about looking for the human's mistake is characterized as "Safety-I," with attention paid to the relatively small proportion of healthcare delivery interactions which result in undesirable, or even disastrous, results. The Safety-I perspective seeks to understand what has gone wrong, while Safety-II seeks to learn from what has gone right, and to learn from both extraordinary and ordinary patient care events. Safety-II complements, rather than replacing, Safety-I. Undesired outcomes need our attention; we can also seek deeper understanding of processes resulting in good outcomes (Table 1).

Safety-I	Safety-II
What goes wrong	What goes right
Defined by failure	Defined by success
Achieved by constraints	Achieved by adaptation
Inquiry tone is critical	Inquiry tone is appreciative

Table 1. Contrasting approaches to patient safety, based on From Safety I to Safety II White Paper [27].

Safety II is a paradigm shift, a change in our perspective. One of the major challenges in implementing a Safety-II perspective is that it is hard to find time to prioritize debriefing successful activities; it's easier to just complacently accept them. It's hard to replace complacency with appreciation and inquiry. Solutions may involve integrating the Safety-II perspective into the fabric of hospital systems and taking advantage of existing event analysis structures [28].

Humans have limitations

As we explore ways to improve patient safety, we do need to understand the limitations of humans; not to assign blame but so we can take advantage of tools, technologies and other resources to augment our capabilities. For example individual humans may be strong but there are simple machines that have more strength and endurance than any human. There are machines that can perform technical skills with greater precision. Computers can store more data than human brains and perform complex calculations more quickly. There are limits to our knowledge, understanding, energy, attention and vigilance [29,30]. We are reminded that "to err is human" (6) and even "To err is human--and let's not forget it" [31].

Humans also have amazing capabilities

To better is human [32]

To blame is human. The fix is to engineer [17]

To care is human [33]

Humans also have strengths that can be leveraged. Humans have situation awareness, they perceive what is happening, comprehend events and can even project future actions and outcomes [34]. Humans understand and sense-make in complex contexts[35,36]. They can focus in dynamic, chaotic environments; they recognize patterns and classify information [29,35]. They make decisions and set goals. Perhaps most importantly, they think and they care.

The irony of rigid dependence on protocols, equipment and technology is that when they fail, we expect humans to compensate and overcome…[12].

In conclusion

Humans are awesome! Humans are essential assets and sources of creativity and solutions. We learn, and we improve ourselves, our teams and the complex systems we work with. We invent and create; we develop healthcare advances and solutions. And we offer empathy and compassion as we provide ever-improving healthcare [37].

Be kind to your fellow humans, and make the best use of their capabilities.

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Training implications of the WHO 2009 initiative on patient safety

Denise Cafarelli Dees, AuD, and **Diane Irvine.**

Over the past decade, the W.H.O. patient safety initiatives proposed since 2009 have raised awareness and led to numerous patient safety and human factors training programmes within healthcare systems, across the world. Two of the key elements of this initiative are the development of good communication within the clinical team and the essential effective communication with patients and their families to ensure that they are closely involved in all aspects of their care and promote good patient outcomes.

This manual addresses:
1) **Why** communication skills training is important to patient safety:
– Review of communication failure as a root cause in sentinel events pre and post the WHO initiative: Human Factors in Patient Safety, 2009.
– Impact of communication skills on patient complaints/malpractice cases
2) **What** are the barriers to effective communication?
3) **How** to implement communication skills into best practice:
– Within clinical teams (including trainees).
– With patients and their families.

1. Why communication skills training is important

In their review of sentinel events from 1995-2005, The Joint Commission on Accreditation of Organizations in Healthcare (JACOH) found that ineffective communication was the root cause for nearly 66% of all sentinel events. As shown in Figure 1 of this same review, communication errors was found to be the root cause in almost 80% of 455 wrong site surgery events.

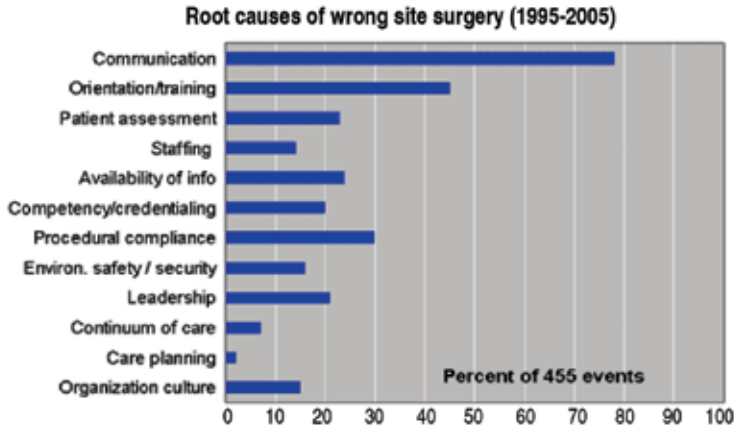

Figure 1. JCAOH review: Root Causes of Wrong Site Surgery January 1995 - December 2005.

The risk to patient safety from communication error is supported by Lingard et.al (2004) in their observational study of over 90 hours of 48 surgical procedures. 129 communication failures were found out of 421 communication events. They concluded: "Communication failures in the Operating Room exhibited a common set of problems. They occurred in approximately 30% of team exchanges and a third of these resulted in effects which jeopardized patient safety by increasing cognitive load, interrupting routine and increasing tension in the Operating Room". Lingard and colleagues categorized communication failures as:

– Content- Insufficiency or inaccuracy of information transferred.
– Audience – Gaps in composition of group involved in communication.
– Purpose - Purpose of communication unclear, not achieved or inappropriate.
– Occasion – Problems in situation or context of information transfer.

Following the 2009 WHO initiative, awareness was raised, new processes and checklist put in place following best safety practices of the aviation industry. However, a JCAOH review, in years following implementation of the WHO initiatives; revealed that human factors including communication remain among the most frequently identified root causes of sentinel events even 3, 4 and 5 years later (as shown in Figure 2).

Most frequently identified root causes of sentinel events reviewed by the joint commission by year

The majority of events have multiple root causes (Please refer to subcategories listed on slides 5-7)

2012 (N=901)		2013 (N=887)		2014 (N=764)	
Human Factors	614	Human Factors	635	Human Factors	547
Leadership	557	Communication	563	Leadership	517
Communication	532	Leadership	547	Communication	489
Assessment	482	Assessment	505	Assessment	392
Information Management	203	Information Management	155	Physical Environment	115
Physical Environment	150	Physical Environment	138	Information Management	72
Continuum of Care	95	Care Planning	103	Care Planning	72
Operative Care	93	Continuum of Care	97	Health information technology-related	59
Medication Use	91	Medication Use	77	Operative Care	58
Care Planning	81	Operative Care	76	Continuum of Care	57

Figure 2. Most Frequently Identified Root Causes of Sentinel Events Reviewed by the Joint Commission by Year 2012-2014.

Safety checklists and procedures do help especially in addressing shift change and handover of care communications however, they are not enough. These safety measures need to be underpinned by effective training in the key elements of human factors - leadership, situational awareness, decision making and communication. Such training also needs to be delivered with a structured educational approach that can easily transfer knowledge and skills into practice.

It is beyond the scope of this manual to include the 4 key human factors: Situational awareness, decision making, leadership and communication and reference to established training programs is made in the reference list. This manual focuses on communication skills alone because:

- Communication failure is a root cause in many sentinel events and is identified as a key factor in -the 2017 WHO initiative: Medication without Harm
- Studies found that:
  - "physicians rated in the bottom third of patient satisfaction surveys had a 110% increased risk of incurring patient complaint or risk management episode compared to physicians rated in the top third of patient satisfaction surveys."
  - physicians who never had a medical malpractice claim filed against them:
    - Laughed and used more humour.
    - Asked patients their opinions.
    - Encouraged patients to talk and interact.
    - Educated patients regarding expectations.
    - Spent on average over 3 minutes more with patients during routine visits.

Summary

Since the WHO initiative on Patient Safety was implemented some progress has been made, however, evidence of consistent effective communication remains to be seen, and communication failures are still found in many sentinel events.

Q: In what percentage (%) of all sentinel events reviewed by JCAOH from 1995-2005, was communication (error) found to be the root cause?

Q: What are the 4 human factors highlighted in the WHO report by Flin et.al April 2009?

Q: Why does this manual focus only on developing effective communication skills?

2. What are the key elements of good communication?

Good communication requires active participation of both parties, each taking turns as speaker and listener. Figure 3 is the commonly used illustration of 'The Speech Chain´.

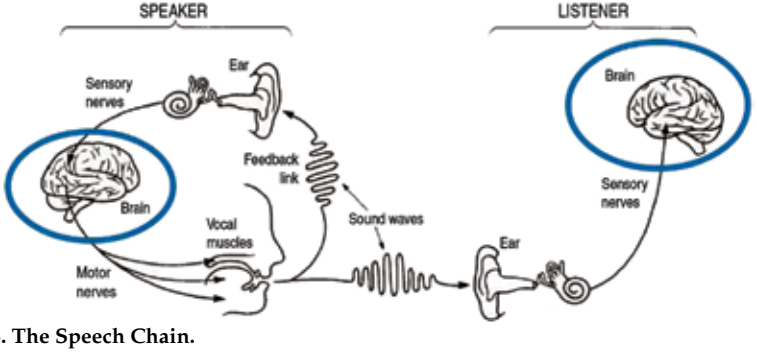

Figure 3. The Speech Chain.

Using the categories from Lingard et al. 2004iii: The Speaker has some information (Content). to share or gather from the Listener (Audience). The Speaker formulates the content into speech sounds via motor nerves and vocal muscles (articulators) to produce sound waves that are received by auditory systems (ear-sensory system-auditory cortex of the brain) of both the listener and the speaker, themselves (as feedback). Meaning is conveyed by voice (intonation and vocal level) facial expression and body language as well as the actual words. This involves the active focus of the brains of both the Listener and the Speaker.

For example, Mother, when her daughter's profound bilateral sensorineural hearing loss was confirmed…. Recalls: "When they first told me she was deaf; all I could think was… Will she be laughed at in school? …… Will she have a boyfriend?"

This mother stopped listening after the word, "hearing loss" –in fact she heard "deaf"…. Thus, like many other parents, she missed much of the rest of the information that was said to her.

It is important to remember effective communication is a two-way process:

– Just because something is said, doesn't mean that it has been understood, and just because you left a voicemail doesn't mean it has been received-

"Tell me and I will forget
Show me and I may remember
Involve me and I will understand"
Chinese Proverb, Confucius

– In the field of pediatric otolaryngology, parents are likely to experience grief from any diagnosis of an impairment such as hearing loss, or disease. While they are in bereavement and experiencing emotional overload the capacity of the brain to receive and process new information is compromised, and effective communication can be very difficult to achieve.

– There are many other factors that can impede good communication between physicians and patients and between staff members. These 'barriers' may be external or internal:

• Noise.

E.g. Some surgical teams like to have background music in the operating room (OR); but if the music is too loud or in addition to the OR equipment noise, it can interfere with essential communication

• Soft voice.
• Deafness.
• Separation in space and time (telephone).

Visual cues of facial expressions and body language are not available in a voice call.

• Lack of visual cues (i.e. surgical masks).
• Shift change.
• Language difference.
• Culture.
• Hierarchy.
• Motivation.
• Expectations.
• Past experience.
• Emotions/Moods.

Strategies to overcome these barriers and to foster good communication include:

– **Environment:**

Where possible, avoid or reduce noise interference and improve access to visual cues.

Try to hold conversations away from interfering noise, e.g. off the ward, away from the waiting room, or in an office. This also helps keep private conversations private.

Sit where there is good lighting to allow a clear view of visual cues (facial expressions and body language) this is especially true when speaking with someone who has a hearing impairment, so that they can use lip-reading as well.

– **For people with a hearing impairment or if your natural speaking volume is soft:**

Use hearing aid or assistive listening device to amplify the speech to an audible yet comfortable volume.

Add visual cues by facing them so they can see your facial expression. Facial expressions and body language should be consistent with the meaning you want to convey.

Ensure appropriate lighting on your face.

Speak louder but without shouting.

Use a slower but natural pace of speaking.

– **When you are not able to talk face to face e.g. telephone:**

Speak clearly and at a slow but natural pace.

Ask clarifying questions to ensure that information is understood.

– L**ack of visual cues** (e.g. wearing surgical masks):

Speak slightly louder, slowly and clearly.

Try to include any visual cues such as gestures or an agreed system of hand signals. Gestures or hand signals can be a challenge within the sterile field, so it is best to agree any hand signals before the surgical procedure.

– **Shift change:**

Use a transfer of care communication process/checklist to ensure all relevant information is provided for the next clinical team member(s) taking over the patient's care. Many hospitals already have their own checklist and hand-over process. Find it and use it. If there isn't a checklist/process in place, write one. There are several examples available through the numerous medical organisations and publications including WHO.

– **Language difference:**

The most obvious language difference is between 'medical jargon' and 'layman's terms'. Where possible try to avoid jargon or medical abbreviations when speaking with people who are not known medical staff.

While it seems obvious that an interpreter is required for someone who uses a foreign language or sign language, it is important to know how to facilitate the use of an interpreter.

– It is important to face the individual not the interpreter, ask the interpreter to take a position next to you, so that you are both facing the listener.
– Speak clearly and not too quickly with much longer pauses at the end of a sentence; to give time for the interpreter to take in what you have said, convey in the language of the patient and to receive a reply or question for further clarification.

– **Culture:**

It may not be possible, to find out about any potential cultural differences e.g. hand gestures that may influence meaning, especially those hand gestures that may be innocent in local culture but cause offence to the other person (e.g. patient or their family). Nevertheless, it is important to be aware of this possibility and although hand gestures can be a useful visual cue, when speaking with someone from a different culture it may be preferable to avoid colloquial hand gestures.

– Hierarchy:

Authority gradients are a known barrier to effective communication, and it is the responsibility of Leaders to welcome and encourage input or feedback from team members at all levels, including the patient and their family.

– **Motivation, Past Experience, Expectations, Moods/Emotions:**

Remember that in any verbal exchange both brains (of the speaker and the listener) have to be actively engaged for real communication to take place. Put aside your own critical thoughts and try to 'actively listen' rather than 'wait to reply'.

Listen without interruption and aim to understand, rather than just wait for your turn to speak.

Try to rephrase what has been said in summary- using some of the same terms that were used. If you are unsure of what was meant by a term, ask with genuine interest, "what did you mean when you said… "

Use a modulating voice – avoid using a monotone, even if having to convey bad news.

When having to convey bad news, speak with empathy (in this case defined as a similar level of concern).

SOF(T)EN your body language:

- **S**mile.
- **O**pen posture.
- **F**orward lean.
- (**T**ouch) their forearm as a sign of empathy- touch in a clinical setting may not be appropriate and is also subject to cultural differences.
- **E**ye contact – try to maintain eye contact without staring.
- **N**od.

Clearly describe any expectations and avoid long sentences to keep what you say short. This leaves more time for the other person to talk, and to clarify their own understanding and any expectations they may have.

In follow-up or review sessions, describe in detail what went well (descriptive praise), ask the other person what they think went well; before discussing how things could have been improved. Even if everything went well and there is nothing to improve, it is still important to describe what went well in specific terms. In this way, good performance is reinforced and more likely to continue. These last two strategies to addressing hierarchy, motivation, expectations etc are addressed in more detail within the next section on implementation of communication skills.

In summary

True communication requires the active involvement and engagement of both parties. In order to ensure involvement, it is important to address the internal and external barriers to effective communication.

Q: What are the barriers to communication?

There are a number of communication skills and strategies that will help overcome these barriers. In general, these strategies may be summarised as:

- ACTIVELY LISTEN without interruption.
- INVOLVE to achieve engagement by asking open and closed questions. Avoid medical jargon or abbreviations.
- Be consistent across all mediums of communication, in your WORDS, BODY LANGUAGE, FACIAL EXPRESSIONS and VOICE.
- What you say should be LOUD ENOUGH to be audible without strain, spoken CLEARLY and SLOWLY.
- Use LISTENING AIDS for people with a hearing impairment.
- Use DESCRIPTIVE PRAISE.
- SUMMARIZE, Confirm (and AGREE NEXT STEPS/EXPECTATIONS).

4. How to implement good communication skills into best practice

Communication skills training should be part of the curriculum of all specialists in communicative disorders. The audiology and speech language pathology specialists within the same department may be able to deliver direct face to face communication skills training for new members or trainees of established clinical teams and a refresher for existing Pediatric Otolaryngology team members. There are also a range of public courses available that focus on human factors including communication in healthcare, if there is no option for in-house training.

Once training has been completed, these new communication skills need to be 1put into practice on a regular basis. To measure success, it may be useful to complete an in-house audit of communication failures and sentinel events prior to the training and the to repeat the audit at 3 months and 12 months post training. To help assist the transfer of this knowledge and skills into professional practice, it is important to start applying them in all professional interactions. In the section that follows, the implementation of key communication strategies and skillsets are described for two situations: with clinical staff and with patients and their families.

- **Within clinical team (clinical staff including trainees):**
- All team members are experts of their own individual team role. Even the most
- junior member of the team may have observed something about a particular case that may help achieve a good clinical outcome and should be listened to.
- Clinical leaders need to invite input and/or feedback from all members of the
- team using open questions to obtain and encourage them to be confident of their role and involvement.
- Describe in detail any expectations including time frame if appropriate. The
- less clear the expectations; the less likely the team will be able to meet them.
- When mistakes have been made, they need to be addressed promptly, clearly and politely. After the mistake has been addressed, there is/ there should be a review of what happened and what can be done to avoid mistakes, in the future. During this review it is important to ask what went well, however small, using descriptive praise when summarizing the incident as well as any lessons that may be learned from the error. Then again, agree the expectations for next time.

e.g. "Thank you for bringing this ('your error') to my attention so promptly; in this review of what happened so we can learn from it and avoid future errors. Let's start with what went well." (pause may be quite long, if the team member still can't think of

anything positive, the leader should step in with something positive – however small) … "you noticed your own mistake. That's real attention to detail".
"On this case, I see such an improvement on your…skills".
"You noticed that I made a mistake. That shows you're really paying attention and you let me know in a helpful manner."

This last statement is not used very often, possibly because team members are still hesitant to be seen criticizing the 'boss'. In this situation, the leader may wish to actively invite feedback, as one of their expectations for their team, and reward their constructive criticism.

Those team members who are not leaders should equally convey any constructive feedback respectfully and probably in a one to one conversation.

– When planning and delivering training, the structure should employ the 4-step method of teaching a clinical skill. This approach is successful as it accommodates the natural learning style of the trainee; requiring the trainer to design training that is delivered with equal focus on each of the main learning styles - visual, auditory and kinaesthetic.

– **With patients and their families:**

In patient interactions, the Pediatric Otolaryngologist is the expert in Otolaryngology and the child together with their parents are the experts in the child's life. Therefore, it is essential to encourage parents and the child to talk and ask questions. In this way, they are actively involved and more likely to support and comply with their child's treatment plan. Parent and child involvement is achieved by:
– Asking their opinions.
– Educating them about expectations.
– Avoiding medical jargon or abbreviations where possible and if it isn't possible defining the medical term in clear and simple words and then checking that this is understood by all.

Use visual aids models, audiograms, drawings to help educate patients and their families. This is because most patients and their families don't understand the medical prescription labelling and medical instructions. A quick verbal prescription is easily forgotten or may not have been fully understood. This means that they may be at risk to appropriately comply with treatment plans.
– Actively listening without interruption then summarising what they have said to
– check for your understanding and then say…. "is there anything else?"
– Typically, the most important information is left to last as they are walking out of
– the door…
– By asking if there is anything else, patients and their families are more likely to provide all necessary information in full and be actively involved in their child's treatment plan.

In summary

For many Pediatric Otolaryngology teams, communication skills training may be led by local staff, specializing in Audiology and/or Speech Language Pathology.

Implementation of good communication skills into professional practice, requires regular use with colleagues as well as patients and their families.

Q. What is descriptive praise and why is it useful in reviewing errors?

Q. Why is it important to avoid medical jargon when speaking with patients or their families?

Q. Why is it important to ask patients/their families if there is anything else?

Conclusion

This manual provides a review of the key elements of effective communication, why it is important to patient safety, and how improved communication skills may be implemented as part of routine professional practice. Good communication is an essential component of patient care.

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Autism spectrum disorder

Berenice Dias Ramos, MD.

Introduction

The main contemporary challenges for professionals working with children with language delay are related to diseases that do not have laboratory tests available to establish the diagnosis and also do not have surgical or clinical treatment to change their evolution [(1)]. The prognosis depends on establishing the diagnosis as soon as possible and on the right specific therapy [(1)]. In this scenario, the two most significant diseases are autism spectrum disorder (ASD) and specific language disorder [(1)].

Definition

ASD is a common neurodevelopmental disorder that can cause significant social, communication and behavioral challenges [(2-5)]. Core deficits are identified in two domains: social communication/interaction and restrictive, repetitive patterns of behavior [(2,3)]. Children and youth with ASD have service needs in behavioral, educational, health, leisure, family support, and other areas [(2)]. A diagnosis of ASD now includes several conditions that used to be diagnosed separately: autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger syndrome [(2-5)].

Prevalence

About 1 in 59 children (approximately 1.7%) has been identified with ASD according to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network [2,4]. ASD is reported to occur in all racial, ethnic, and socioeconomic groups and is about 4 times more common among boys than among girls [2-5].

Higher rates may reflect more widespread awareness of the symptoms among parents, schools, and health care providers and improved rates of screening in health supervision care [5]. Other possibilities are expansion of the **diagnostic and statistical manual of mental disorders** (DSM)-IV criteria, differences in the methodology of the studies or real increase in frequency of the disorder [5].

Etiology and risk factors

ASD does not have a single cause. It is a disorder with many causes, where several of the factors associated with the disorder are still unknown. Currently we know that there are genetic factors, which explain a greater incidence in certain families and a high matching between identical twins. Studies have shown that among identical twins, if one child has ASD, then the other will be affected about 36-95% of the time. In non-identical twins, if one child has ASD, then the other is affected about 0-31% of the time [6,7]. Parents who have a child with ASD have a 2%–18% chance of having a second child who is also affected [8,9].

There are also environmental factors, which act as risk factors, leading to the emergence of the disorder. Children born to older parents are at a higher risk for having ASD [10]. A small percentage of children who are born prematurely or with low birth weight are at greater risk for having ASD [11].

Signs and symptoms

People with ASD often have problems with social, emotional, and communication skills [5]. They might repeat certain behaviors and might not want change in their daily activities [5]. Many people with ASD also have different ways of learning, paying attention, or reacting to things [5]. Signs of ASD begin during early childhood and typically last throughout a person's life [5].

Children or adults with ASD might:

– not point at objects to show interest (for example, not point at an airplane flying over);
– not look at objects when another person points at them;
– have trouble relating to others or not have an interest in other people at all;
– avoid eye contact and want to be alone;
– have trouble understanding other people's feelings or talking about their own feelings;
– prefer not to be held or cuddled, or might cuddle only when they want to;
– appear to be unaware when people talk to them, but respond to other sounds;
– be very interested in people, but not know how to talk, play, or relate to them;
– repeat or echo words or phrases said to them, or repeat words or phrases in place of normal language;
– have trouble expressing their needs using typical words or motions;
– not play "pretend" games (for example, not pretend to "feed" a doll);
– repeat actions over and over again;
– have trouble adapting when a routine changes;
– have unusual reactions to the way things smell, taste, look, feel, or sound;
– lose skills they once had (for example, stop saying words they were using) [5].

Diagnostic criteria

Research has shown that a diagnosis of autism at age 2 can be reliable, valid, and stable [12]. Even though ASD can be diagnosed as early as age 2 years, most children are not diagnosed with ASD until after age 4 years [5].

In the absence of a biological marker, its diagnosis remains clinical, based on the criteria of the American Psychiatric Association – DSM V [3]. Core deficits are identified in two domains [3]:

A) Persistent deficits in social communication and social interaction across multiple contexts, as manifested by all the following, currently or by history (examples are illustrative, not exhaustive; see text) [3,13].

1) Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.

2) Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.

3) Deficits in developing, maintaining, and understand relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends;

The 2018 update clarifies that all three of the criterion A items are required to establish the diagnosis [13].

B) **Restricted, repetitive patterns of behavior, interests, or activities**, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text) [3]:

1) Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases).

2) Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).

3) Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).

4) Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g. apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

Severity is based on social communication impairments and restricted, repetitive patterns of behavior [3].

Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life) [3].

Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning [3].

These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level [3].

One of the paradigmatic features of ASD is its genotypic and phenotypic heterogeneity. On the phenotypic level, heterogeneity is expressed with regard to symptom severity and associated impairment in other domains of development, such as cognitive ability, language skills and adaptive behavior [14]. Such heterogeneity hinders attempts to predict clinical outcomes, develop individualized treatment targets and strategies, and identify etiological factors associated with ASD [14].

The diagnostic and statistical manual represents an attempt to capture such heterogeneity in a dimensional manner, and to organize it in clinically relevant ways by unifying the prior diagnoses of autism, Asperger disorder and pervasive developmental disorder-NOS (PDD-NOS) under the term ASD [3,14]. Associated clinical specifiers are then used to describe co-morbid developmental and psychiatric challenges such as language impairment, intellectual disability, and attentional or anxiety problems [3]. Intervention planning typically occurs at the time of ASD diagnosis and any diagnosis should, as much as possible, capture important symptoms or co-morbidities that increase the predictive validity of the classification (i.e., relevance for later outcomes) [3,14].

Approximately one-quarter of children with ASD will be reported to have a regression in language or social skills, most typically between 18 and 24 months of age [2]. The reason for this loss of previously acquired milestones is not yet known [2].

Co-occurring symptoms and conditions

Clinicians need to keep in mind the high prevalence of associated diagnoses with an ASD diagnosis, and the possibility that in younger children other symptoms or disorders may be masking or obscuring core symptoms of ASD, which would lead to a diagnosis [15].

ASD commonly co-occurs with other developmental, psychiatric, neurologic, chromosomal, and genetic diagnoses [15]. The co-occurrence of one or more non-ASD developmental diagnoses is 83%, one or more psychiatric diagnoses is 10%, one or more neurologic diagnoses is 16%, and at least one possibly causative genetic or neurologic diagnosis is 4% [15]. Children with a previous ASD classification and co-occurring psychiatric or neurologic conditions were more likely to be diagnosed or classified at a later age [15]. ASD among children with Down syndrome is 17 to 20 times higher than the estimated ASD prevalence in the general population [16].

Co-occurring conditions may have great effects on child and family functioning and clinical management [2]. Examples include medical conditions such as sleep disorders and seizures; other developmental or behavioral diagnoses, such as attention-deficit/ hyperactivity disorder (ADHD), anxiety, and mood disorders; and behavioral disorders, such as food refusal, self-injury, and aggression [2]. Approximately 30% of children with a diagnosis of ASD will also have intellectual disability [4], and 30% are minimally verbal [2].

There are certain diseases in which a higher incidence of ASD occurs, such as fragile X syndrome (90%), Rett syndrome, Angelman syndrome (42%), tuberous sclerosis (20 to 50%), Prader-Willi syndrome, hypomelanosis of Ito, Down syndrome (10%), congenital rubella syndrome, neonatal hypoxic-ischemic encephalopathy, fetal alcohol spectrum disorders, valproic acid embryopathy, etc [17].

Screening and diagnosis of ASD

Recent randomized controlled trials have added new evidence that for many children aged 3 years, early intervention can improve outcomes, including core deficits of ASD (i.e., social attention), intelligence quotient, language, and symptom severity [5,6], thus increasing the potential benefits of early diagnosis facilitated by early screening [18].

Studies have shown that parents of children with ASD notice a developmental problem before their child's first birthday [5]. Concerns about vision and hearing were more often reported in the first year, and differences in social, communication, and fine motor skills were evident from 6 months of age [5].

Given that parents of children with ASD generally report initial concerns before the child is aged 18 to 24 months, considerable opportunity exists to shorten the stressful "diagnostic odyssey" that many families experience [18,19], maximize opportunities for children with ASD to benefit from early intensive interventions, and further develop evidence-based interventions for this age group [18,20].

In most cases, patients with language delay or learning disability are initially seen by an otorhinolaryngologist for suspected hearing loss [1]. What should be the role of the otorhinolaryngologist in these cases? Every time we see a child with language delay and normal hearing, we should think that, simply stating that the exam is normal, that everything is fine and that the child should speak soon, we may be delaying the correct diagnosis and losing a few months or even years of great neuroplasticity [1]. A more thorough assessment, followed by appropriate guidance, can dramatically change a child's future [1]. A standardized screening specifically for ASD should be performed when parents raise concerns between well-child visits or when concerns are raised upon general developmental surveillance or screening during scheduled visits [18].

Modified Checklist for Autism in Toddlers (M-CHAT), Revised with Follow-Up (M-CHAT- R/F) [21,22]

Robins et al. reported validation data for a new version of the original M-CHAT screening tool, the M-CHAT-R/F, in 16 115 toddlers [21]. The questionnaire was reduced to 20 items, removing 3 items that had performed poorly ("peek-a-boo," "playing with toys," and "wandering without purpose"); wording on other items was simplified and/or examples provided for further clarity. A scoring algorithm with 3 risk ranges was developed. Children in the low-risk range (i.e., 3 items endorsed) did not require the follow-up interview or any other additional evaluation (93% of all cases). Children in the medium-risk range (i.e., 3-7 items endorsed [6% of all cases]) required the follow-up interview to clarify their risk for ASD; if at least 2 items remained positive, then referral for diagnostic evaluation was indicated[21,22]. Children in the high-risk range (i.e., $\geq$8 items endorsed [1% of all cases]) were at sufficiently high risk to be referred directly for diagnostic assessment without the follow-up interview [21,22]. This revised scoring and referral algorithm reduced the initial screen-positive rate (from 9.2% to 7.2%) and increased the overall rate of ASD detection (67 vs 45 per 10 000) compared with the original follow-up M-CHAT [21,22]. Children who screened positive on M-CHAT - R/F were 114 times more likely to receive an ASD diagnosis than children who screened negative [21,22].

Additional information at: https://mchatscreen.com/wp-content/uploads/2015/09/M-CHAT-R_F_Rev_Aug2018.pdf [Consulted on: January 31st, 2020] [22].

Developmental screening

Developmental screening is a short test to tell if children are learning basic skills when they should, or if they might have delays. During developmental screening the doctor might ask the parent some questions or talk and play with the child during an exam to see how she learns, speaks, behaves, and moves. A delay in any of these areas could be a sign of a problem [5].

The American Academy of Pediatrics (AAP) recommends that all children be screened for developmental delays and disabilities during regular well-child doctor visits at [2,5]:

- 9 months
- 18 months
- 24 or 30 months
- Additional screening might be needed if a child is at high risk for developmental problems due to preterm birth, low birth weight or other reasons.

In addition, all children should be screened specifically for ASD during regular well-child doctor visits at [2,5]:

- 18 months
- 24 months
- Additional screening might be needed if a child is at high risk for ASD (e.g., having a sister, brother or other family member with an ASD) or if behaviors sometimes associated with ASD are present.

It is important for doctors to screen all children for developmental delays, but especially to monitor those who are at a higher risk for developmental problems due to preterm birth, low birth weight, or having a brother or sister with an ASD [2,5].

If there are any signs of a problem, a comprehensive diagnostic evaluation is needed [5].

Comprehensive diagnostic evaluation

The second step of diagnosis is a comprehensive evaluation. This thorough review may include looking at the child's behavior and development and interviewing the parents. It may also include a hearing and vision screening, genetic testing, neurological testing, and other medical testing [5,23].

In some cases, the primary care doctor might choose to refer the child and family to a specialist for further assessment and diagnosis. Specialists who can do this type of evaluation include [5]:

- Pediatric Neurologists (doctors who work on the brain, spine, and nerves) [5].
- Pediatric Psychologists or Psychiatrists (doctors who know about the human mind) [5].
- Developmental Pediatricians (doctors who have special training in child development and children with special needs) [5].
- Phoniatricians (doctors who work with communication: hearing, voice, speech, language, and swallowing disorders) [1].

Diagnostic tools

There are many tools to assess ASD in young children, but no single tool should be used as the basis for diagnosis. Diagnostic tools usually rely on two main sources of information-parents' or caregivers' descriptions of their child's development and a professional's observation of the child's behavior [5].

In some cases, the primary care provider might choose to refer the child and family to a specialist for further assessment and diagnosis. Such specialists include neurodevelopmental pediatricians, developmental-behavioral pediatricians, child neurologists, geneticists, phoniatricians, and early intervention programs that provide assessment services [5].

Selected examples of diagnostic tools [5]:

– **ADI-R** - Autism Diagnosis Interview – Revised [24].

A clinical diagnostic instrument for assessing autism in children and adults. The instrument focuses on behavior in three main areas: reciprocal social interaction; communication and language; and restricted and repetitive, stereotyped interests and behaviors. The ADI-R is appropriate for children and adults with mental ages about 18 months and above.

– **ADOS-G** - Autism Diagnostic Observation Schedule – Generic [25].

A semi-structured, standardized assessment of social interaction, communication, play, and imaginative use of materials for individuals suspected of having ASD. The observational schedule consists of four 30-minute modules, each designed to be administered to different individuals according to their level of expressive language.

– **CARS** - Childhood Autism Rating Scale [26].

Brief assessment suitable for use with any child over 2 years of age. CARS includes items drawn from five prominent systems for diagnosing autism; each item covers a particular characteristic, ability, or behavior.

– **GARS-2** - Gilliam Autism Rating Scale – Second Edition [27].

Assists teachers, parents, and clinicians in identifying and diagnosing autism in individuals ages 3 through 22. It also helps estimate the severity of the child's disorder.

In addition to the tools above, the American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5) provides standardized criteria to help diagnose ASD [3].

Early intervention services

Research shows that early intervention treatment services can greatly improve a child's development [5]. Early intervention services help children from birth to 3 years old (36 months) learn important skills [5]. Services include therapy to help the child talk, walk, and interact with others [5]. Monitoring healthy development means not only paying attention to symptoms related to ASD, but also to the child's physical and mental health, as well [5].

Therapies

A. Behavior and Communication Approaches - provide structure, direction, and organization for the child in addition to family participation [5].

1) **ABA** (Applied Behavioral Analysis) - encourages positive behaviors and discourages negative behaviors in order to improve a variety of skills. The child's progress is tracked and measured [5].
2) **DIR** (Developmental, Individual Differences, Relationship-Based Approach; also called "Floortime") - focuses on emotional and relational development (feelings, relationships with caregivers). It also focuses on how the child deals with sights, sounds, and smells [5].
3) **PLAY** Project (Play & Language for Autistic Youngsters) - is an evidence-based developmental intervention for families of young children with ASD. The PLAY Pro-

ject is the pragmatic application of the theory of DIR (Developmental Individual Differences & Relationship-Based)/Floortime and emphasizes the importance of helping parents become their child's best PLAY partner [28].

4) **ESDM** (Early Start Denver Model) - a comprehensive developmental behavioral intervention, for improving the outcomes of toddlers with ASD [29,30]. Children receiving the ESDM intervention demonstrated significant improvements in IQ, language, adaptive behavior, and autism diagnosis [29,39].
5) **TEACCH** (Treatment and Education of Autistic and related Communication-handicapped Children) - uses visual cues to teach skills. For example, picture cards can help teach a child how to get dressed by breaking information down into small steps [5].
6) **Occupational Therapy** - teaches skills that help the person live as independently as possible. Skills might include dressing, eating, bathing, and relating to people [5].
7) **Sensory Integration Therapy** - helps the person deal with sensory information, like sights, sounds, and smells. Sensory integration therapy could help a child who is bothered by certain sounds or does not like to be touched [5].
8) **Speech Therapy** - helps to improve the person's communication skills. Some people are able to learn verbal communication skills. For others, using gestures or picture boards is more realistic [5].
9) **PECS** (The Picture Exchange Communication System) - uses picture symbols to teach communication skills. The person is taught to use picture symbols to ask and answer questions and have a conversation [5].

B) Medication

There are no medications that can cure ASD or treat the core symptoms. There are medications that can help some people with ASD function better. For example, medication might help manage high energy levels, inability to focus, depression, or seizures [5].

It is also important to remember that children with ASD can get sick or injured just like children without ASD [5].

C) ASD and Otitis Media with Effusion (OME)

OME is the most common cause of hearing impairment in children [31]. Otitis media may be related to difficulties in speech and reading, delayed response to auditory input, limited vocabulary, and disturbances in attention [31,32]. It may also be associated with being less task oriented and less capable of independent classroom work [33]. According to a prospectively measured parental report, 76% of children with OME suffer from otalgia, 64% from sleep disruption, 49% from behavioral problems, 33% to 62% from speech and hearing concerns, and 15% from balance symptoms [33,34]. Although definitive studies are lacking, children who are at risk for developmental difficulties would likely be more affected by hearing problems from OME [31].

At-risk children with OME require more frequent hearing assessment and prompt management to prevent additional impact on developmental outcomes [31,35,36]. This category includes children with speech-language or academic delay and children with developmental disability of any cause, especially ASD, Down syndrome and other craniofacial anomalies in which OME is very common and persistent [31]. Children in these categories should receive otologic and hearing screening or assessment when the speech-language delay is identified to allow prompt treatment for OME [31]. Children with ASD should be monitored and treated as soon as possible with ventilation tubes [31]. Hearing should be reassessed following medical or surgical treatment, at ongoing intervals, or as recommended in relevant clinical practice guidelines [31].

D. Dietary Approaches

Some dietary treatments have been developed by reliable therapists. But many of these treatments do not have the scientific support needed for widespread recommendation. An unproven treatment might help one child, but may not help another [5].

E. Complementary and Alternative Treatments

These types of treatments are very controversial [5].

Prognosis

The prognosis and trajectory of development for a young child diagnosed with ASD typically cannot be predicted at the time of diagnosis [2]. However, most children (≥80%) who are diagnosed with ASD after a comprehensive evaluation at less than 3 years have retained their diagnosis [37,38]. It may be more difficult to recognize mild symptoms of ASD in children younger than 3 years of age, especially if they have average or above-average cognitive abilities [39]. Across early childhood development, communication skills and social affective symptoms may improve, whereas repetitive behaviors may change, possibly reflecting maturation and/or intervention [40].

In general, young children with ASD with language impairment appear to have more social difficulty than do children with ASD without language impairment. Children with ASD and intellectual disability have the most difficulty developing social competence [41].

Approximately 9% of children who are diagnosed with ASD in early childhood may not meet diagnostic criteria for ASD by young adulthood. Youth who no longer meet criteria for ASD are more likely to have a history of higher cognitive skills at 2 years of age, to have participated in earlier intervention services, and to have demonstrated a decrease in their repetitive behaviors over time [42]. A change in clinical diagnosis (e.g., to ADHD or obsessive-compulsive disorder [OCD]) is more likely in children who were diagnosed with ASD before 30 months of age or had a diagnosis of PDD-NOS per the DSMIV [43,44].

Measured intelligence (e.g., intelligence quotient) and language ability in childhood tend to predict outcome in adulthood [45,46,47]. However, reported quality of life in high-functioning adults with ASD was associated more with the presence of family and community supports than their symptoms related to ASD [48].

ASD and parental stress

ASD can have a profound impact on family life, including the roles and responsibilities that parents assume. Parents of children with ASD experience strong feelings of grief. Reception of the diagnosis is associated with loss of the child that they had up to this time. The parents must make a major effort to come to terms with feelings of loss. Emotional work with these parents is necessary to deal with these feelings [49,50].

Parents with ASD children are exposed to stress in the areas of obtaining a diagnosis for the child's condition, of family support, of information, of appropriate short-term services, and of finding group homes for their young adults [49,50]. The chronic nature of ASD can affect parents negatively and there is a danger of becoming exhausted and pessimistic with a risk for burnout [50]. Mothers of ASD children report significantly greater stress, greater depression, greater social isolation, and a lower level of marital intimacy when compared to mothers of normal children and mothers of Down's Syndrome children [49,50].

Beyond every doubt, families with a child with an autism spectrum disorder do not get the support for their daily life situation needed [49,50]. On the contrary, they need much more functional support focused on the whole [49,50]. Interventional steps to enhance parental coping skills and resiliency are more important for parental mental health and the family-centered care of children with ASD than merely reducing parental stress [49]. Parental training is known to improve a mother´s mental health [50]. A variety of services are needed from social habilitation units in the municipalities, better adjustment of special pedagogy on all levels of school training, and an adapted social policy for autism as a communication disability legalized by the government [49].

The importance of discipline and structure

If there is one thing that children (with or without autism) absolutely need to thrive, it's structure and discipline [51]. If there is one thing that frightens and overwhelms a child, it is a lack of adult involvement in creating a safe, structured, and orderly world [51].

A child who is raised or educated without the benefit of structure and discipline is almost certain to suffer the consequences as he or she grows up and finds it impossible to integrate into the community or the workplace [51]. Every child deserves the respect and support represented by clear structure, consistent rules, and discipline [51]. These tools, along with some flexibility, patience, and imagination, can help a child with autism to understand his world and feel safe and confident as he grows up [51].

In the vast majority of cases, autistic children are capable of understanding and complying with basic rules of conduct [51]. Those rules may need to be modified or bent, depending upon the circumstances. Even a child with no words may be quite capable of understanding and complying with behavioral expectations, assuming that child can communicate via sign, communication board, PECS cards, or other means [51].

Children (with or without autism) should:

1) Sleep early and at least 10 hours [52]. Adequate sleep duration for age on a regular basis leads to improved attention, behavior, learning, memory, emotional regulation, quality of life, and mental and physical health [52]. Not getting enough sleep each night is associated with an increase in injuries, hypertension, obesity and depression, especially for teens who may experience increased risk of self-harm or suicidal thoughts [52].

Research shows that an early bedtime (between 7:00 p.m. and 8:00 p.m. works best for babies and kids through school age) and a consistent, soothing, wind-down routine with no screen time, such as TVs, tablets, and the like, will lead to better sleep [52]. Infants 4 months to 12 months should sleep 12 to 16 hours per 24 hours (including naps) on a regular basis to promote optimal health [52].

- Children 1 to 2 years of age should sleep 11 to 14 hours per 24 hours (including naps) on a regular basis to promote optimal health [52].
- Children 3 to 5 years of age should sleep 10 to 13 hours per 24 hours (including naps) on a regular basis to promote optimal health [52].
- Children 6 to 12 years of age should sleep 9 to 12 hours per 24 hours on a regular basis to promote optimal health [52].
- Teenagers 13 to 18 years of age should sleep 8 to 10 hours per 24 hours on a regular basis to promote optimal health [52].

2) Avoid digital media use (except video-chatting) in children younger than 18 to 24 months [53]. Children younger than 2 years need hands-on exploration and social interaction with trusted caregivers to develop their cognitive, language, motor, and social-emotional skills [53]. Because of their immature symbolic, memory, and attentional skills, infants and toddlers cannot learn from traditional digital media as they do from interactions with caregivers, and they have difficulty transferring that knowledge to their 3-dimensional experience [53].

3) For children 2 to 5 years of age, limit screen use to 1 hour per day of high-quality programming [53]. No screens 1 hour before bedtime, and remove devices from bedrooms before bed [53]. Increased duration of media exposure and the presence of a television, computer, or mobile device in the bedroom in early childhood have been associated with fewer minutes of sleep per night [53]. Even infants exposed to screen media in the evening hours show significantly shorter night-time sleep duration than those with no evening screen exposure [53]. Mechanisms underlying this association include arousing content and suppression of endogenous melatonin by blue light emitted from screens [53].

Conclusions

1) The incidence of ASD is increasing and is currently around 1.7%.
2) The diagnosis should be made as soon as possible, to take advantage of the period of greatest brain neuroplasticity. A standardized screening specifically for ASD should be performed when parents raise concerns between well-child visits or when concerns are raised upon general developmental surveillance or screening during scheduled visits.
3) Pediatricians should be able to screen children at 18 and 24 months to identify those with suspected ASD and refer them to a comprehensive diagnostic assessment, but especially to monitor those who are at a higher risk for developmental problems due to preterm birth, low birth weight, or having a brother or sister with an ASD. A more thorough assessment, followed by appropriate guidance, can dramatically change a child's future.
4) It is necessary to have knowledge about the best therapies for ASD, as well as empathy and compassion with parents, advising and referring them for training.
5) Otitis media is highly prevalent in childhood, and children with ASD should be monitored and treated as soon as possible with ventilation tubes.
6) ASD child, as any other child, deserves the respect and support represented by clear structure, consistent rules, and discipline.

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Robin sequence

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Introduction

Robin Sequence (RS) is a congenital craniofacial anomaly defined by micrognathia as a primary characteristic, in addition to other mandatory diagnostic findings such as glossoptosis and airway obstruction [1]. Cleft palate may also be considered an additional feature. Pierre Robin originally defined glossoptosis as a backward and downward fall of the tongue base [2], while the posterior pharyngeal wall remains in a stationary position (different from pharyngomalacia). More recently Donnelly et al. defined it as a posterior movement of the tongue during sleep, reinforcing the dynamic nature of such hallmark and its main manifestations during sleep [3].

Clinical manifestations of RS are heterogeneous and therefore treatment has to be individualized, aiming for adequate breathing and optimized growth and development. That the care of these patients should be multidisciplinary is unequivocal, but there is no consensus on the diagnostic work-up and treatment.

Clinical manifestations

RS patients can present varying degrees of respiratory and swallowing dysfunction, ranging from mildly affected children who require no support, to severely affected ones who present with disabling airway obstruction and are unable to feed. The presence of other malformations, aside from the possibility of cleft palate, contributes for the variations in clinical manifestations in these patients. Also, abnormal maxillary morphology causing midface hypoplasia has also been described in RS children and may contribute to airway obstruction.

Airway obstruction symptoms can occur spontaneously or with feeding, and during daytime or sleep.

Obstructive sleep apnea (OSA), associated with failure to thrive, behavioral deficits and sudden infant death, has a high prevalence in patients with RS, not always accompanied by snoring. Accordingly, snoring did not appear to correlate with OSA severity [4]. The obstruction may be present at birth, may become progressively worse in the first weeks of life or may even develop much later in life. Premature infants tend not to develop obstruction until nearly term gestational age ([5]. It is important to emphasize that upper airway obstruction may not be clinically apparent at birth and OSA in these patients may manifest as failure to thrive instead of obvious obstruction. The children with RS expend a great deal of energy to breathe against an obstructed airway. OSA in combination with known feeding difficulties can further exacerbate growth failure. Airway disorders can also be triggered by incidental surgical procedures [6].

Swallowing disorders are frequent in patients with RS and are characterized by low oral intake, feeding times greater than 30 minutes, fatigue, and coughing, gagging, and vomiting. These feeding difficulties are thought to be secondary to airway obstruction, inasmuch as impaired breathing can lead to incoordination of sucking and swallowing, and glossoptosis prevents forward positioning of the tongue required for suction. Besides airway obstruction, the swallowing disorder can be further compounded by additional neurologic disorders, through diffuse hypotonia and an uncoordinated swallowing mechanism. In addition, if cleft palate is present, it becomes increasingly

difficult to generate the negative intraoral pressure necessary to sucking. In isolated RS children with feeding difficulties, early airway intervention can dramatically reduce the need for feeding intervention. Chronic feeding difficulties and eventual gastrostomy tube placement incidences are higher in glossoptosis when associated with concomitant syndromes, other malformations and neurologic abnormalities, despite the timing of airway intervention [7].

Gastroesophageal reflux is also prevalent in RS patients and can complicate airway obstruction, since it causes airway inflammation and edema, increasing secretion production. The evaluation of gastroesophageal reflux is particularly important if there is a persistence of some degree of airway obstruction despite optimal medical management.

There are several attempts to classify patients with RS, based on symptomatology, presence of concomitant syndrome or malformation or regarding endoscopic findings. Although there is no consensus on what the best approach for these patients should be, those classifications are useful, especially when comparing treatment results. Based on the severity of symptoms and signs, Cole et al. devised a classification for RS: **grade 1**: no respiratory distress when nursed supine, inconsistent glossoptosis, feeding assessment satisfactory; **grade 2**: intermittent evidence of mild respiratory obstruction when nursed supine, none nursed on side, consistent glossoptosis, feeding precipitates some respiratory distress; **grade 3**: moderate to severe respiratory distress when nursed supine, evidence of airway obstruction remains when nursed on side, consistent glossoptosis, unable to feed orally [8].

Medical comorbidities

RS patients can be divided according to their presentation in isolated RS, RS plus – associated with additional congenital malformations without a known specific diagnosis - and syndromic RS [9]. More than 40 syndromes associated with RS have been described and the most common associated syndromes are Stickler, Velocardiofacial, Treacher-Collins, and facial and hemifacial microsomia. The proportion of syndromic diagnosis in RS patients varies between 14.6% and 46% [10-12].

Because of this frequent association with syndromes, a geneticist should be involved in the multidisciplinary assessment of the RS patients, to aid in the identification of a specific syndromic diagnosis and to provide recommendations for genetic testing. Furthermore, the high frequency of associated anomalies, with or without a diagnosed syndrome, warrants an active investigation with an echocardiogram, neonatal hearing screening, ophthalmological evaluation and ancillary specific investigations based on clinical suspicion.

Evaluation

1. Anatomical airway evaluation

There is uniform agreement on the need for a careful evaluation of the upper airway with flexible fiberoptic laryngoscopy (FFL) in all infants with RS, since a multitude of airway abnormalities may be present [13]. Aside from the mechanical obstruction of glossoptosis, other factors can contribute to ventilation compromise in these patients. Understanding the site of airway obstruction seems to be critical for determining optimal therapy. There is a growing debate on whether awake [14-16] or slight sedation [13,17-19] endoscopic evaluation would be a better option for these patients. In our opinion, since the worst moment of obstruction in RS is during sleep, the sleep endoscopy would be the best method to evaluate obstruction in RS patients.

Sher et al. described four mechanisms of airway obstruction in 33 patients with craniofacial anomalies, including RS, from birth to 24 years of age, examined while awake. The mechanisms described are **type 1:** the tongue contacting the posterior pharyngeal wall below the soft palate (true glossoptosis); **type 2**: posterior contraction of the tongue towards the posterior pharyngeal wall, but the palate becomes sandwiched between the tongue and velum; **type 3**: medial contraction of the lateral pharyngeal walls; **type 4**: sphincteric, the tongue does not contact the posterior pharyngeal wall [14].

Yellon examined 14 children under light sedation and graduated epiglottis and base of tongue prolapse from 0 to 3 (Figure 1) [18].

De Sousa et al. evaluated 56 children with RS, examined while awake and graduated glossoptosis in mild, moderate and severe (Figure 2). They described a poor correlation between the severity of glossoptosis and the severity of clinical manifestations [15].

Manica et al. evaluated Yellon and de Sousa classifications as predictors of clinical manifestations classified according to Cole. Both have shown a low sensitivity and a moderate to high specificity to identify patients with a severe clinical manifestation [20].

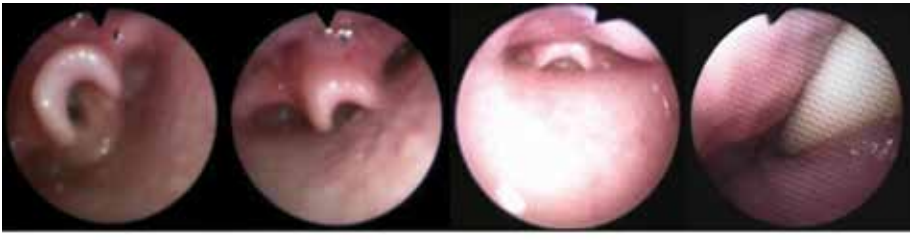

Figure 1. Epiglottis and base of tongue prolapse.

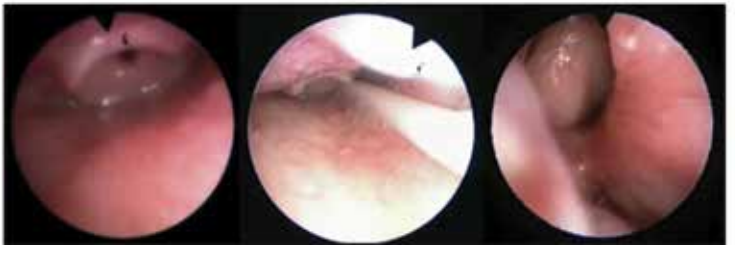

Figure 2. Glossoptosis.

2. Objective evaluation of airway obstruction

Clinical signs alone seem to be insufficient to ascertain the degree of upper airway obstruction, while the use of polysomnography (PSG) greatly improves the diagnostic accuracy of upper airway obstruction severity assessment [5].

PSG is the gold standard for the diagnosis of airway obstruction, particularly if the clinical picture is not clear. It is well known that young infants have central nervous system pauses in breathing and PSG is useful to differentiate them from obstructive pauses. However, it must be performed concomitantly to endoscopic evaluation, since it does not evaluate the degree of obstruction. An obstructive apnea index of 1 is chosen as the cutoff for the reference range and an apnea index of 10 is considered to be severe, diverging from adults [21,22].

Manica et al., while assessing the association of PSG parameters and clinical severity, reported that percentage of time with oxygen saturation <90%, percentage of time presenting with obstruction and sleep mean oxygen saturation were positively correlated with a worse clinical picture [23].

3. Feeding evaluation

Given the prevalence of feeding difficulties, care should be taken to evaluate feeding problems in infants with glossoptosis. Even in infants who seem to be doing well, care should be taken to detect silent aspiration. Videofluoroscopic swallow study and fiberoptic endoscopic evaluation of swallowing are the most common instrumental assessments for objective assessment of oropharyngeal swallowing function in the pediatric population. The videofluoroscopic examination provides dynamic evaluation of oral, pharyngeal, and upper esophageal phases of swallowing. The endoscopic evaluation provides direct visualization of pharyngeal and laryngeal structures before and after the swallow. The endoscopic evaluation has the advantage of avoiding exposure to radiation but it is not always easy to perform in the pediatric population.

Treatment

Management relies on the degree of upper airway obstruction and concomitant manifestations such as feeding difficulties and pulmonary infections.

Current alternatives include non-surgical (prone positioning, nasopharyngeal tube/stenting, prolonged intubation), or surgical options (tracheostomy, tongue-lip adhesion, mandibular distraction osteogenesis).

Conservative interventions

1. Positioning

In cases of mild airway obstruction, children can be managed by non-surgical treatment including lateral or prone positioning, in order to displace the tongue anteriorly [24]. However, studies showing effectiveness of this maneuver in improving apnea-hypopnea index or avoiding tracheostomy are still lacking.

2. Nasopharyngeal Airway (NPA)

Non-surgical airway management includes the insertion of a NPA, and many centers use it as the primary treatment for mild cases of RS [12,25]. Studies in specific populations have proven this approach to be well tolerated with significant improvement on sleep study parameters [26], but studies in RS population are scarce.

3. Continuous Positive Airway Pressure (CPAP)

Many centers advocate the use of this device in infants with moderate symptoms [19,27], while others sustain that CPAP attempt often fail due to a retrognathia exacerbation caused by the ventilation mask [6]. The role of CPAP in treatment is therefore unclear.

Surgical interventions

1. Tracheostomy

Tracheostomy is an effective measure of establishing a secure airway and is the main treatment for sleep apnea. Early tracheostomy is warranted by some specialists, claiming that catch-up growth of the mandible will possibly allow for decannulation within 1 to 2 years [6].

However, tracheostomy is associated with multiples complications, including tracheomalacia and suprastomal collapse development, chronic pneumonia, laryngeal stenosis, compromised social interactions, requirement for complex nursing care, and mortality related to mucous plugging [28-30]. Furthermore, tracheostomy seems to increase the cost of care in RS compared to other invasive therapies [31].

2. Tongue-lip adhesion (TLA)

The tongue-lip adhesion (TLA) procedure, or glossopexy, was introduced as an alternative to tracheostomy [32]. In TLA, the tongue is anchored to the lower lip and mandible ensuring an anterior lingual position to alleviate the upper airway obstruction.

This procedure is typically performed early in life and is reversed at around 12 months. Although it is frequently effective in relieving a tongue-base airway obstruction, several authors consider TLA a transient procedure because it often requires multiple additional interventions to achieve airway patency and adequate feeding [33,34].

The high success rate achieved with this procedure in the immediate postoperative course allows patients to be extubated and return home, but most of them still manifest mild to moderate respiratory distress after discharge [33,35]. The lack of long-term efficacy probably relates to the fact that TLA cannot correct the primary RS defect, i.e., micrognathia and consequent tongue retropositioning. Besides, TLA may lead to several complications, including dehiscence, tongue lacerations, injuries to Wharton's ducts, wound infections, scar deformation, and severe dysphagia with consequent aspiration pneumonia [34,36].

3. Mandibular distraction osteogenesis (MDO)

MDO exerts its therapeutic effect by bringing the tongue and the suprahyoid muscles forward by the gradual lengthening of the mandible, thereby increasing the size of the pharyngeal airway.

Many authors reported that MDO has a high rate of success in avoiding tracheostomy or in decannulation [37-39], and in improving apnea-hypopnea index [37,40,41].

A meta-analysis showed that MDO could achieve a success rate of 91.3% in the prevention of a tracheostomy and 97% in the alleviation of obstructive airway symptoms in children with RS. A lower success rate of 78.4% was reported for decannulation of tracheostomies, and unsuccessful decannulation can be attributed to complications with the distraction process or inherent anatomical defects that were unable to be detected previously [42].

However, MDO is not a consensus. Those that argue against this technique raise several arguments. First, there is the concept of catch-up growth of the mandible, and such would avoid the need for MDO in young infants. This principle of catch-up growth itself is not clearly established.

In a study comparing young infants who underwent MDO or TLA, Greathouse and colleagues found that the overall success rate was higher in the MDO group (90.5% versus 60%). Eventual postoperative tracheostomies occurred in 8.1% of the MDO group and in 33.3% of the TLA group [38].

Management of dysphagia

Because most RS infants have a difficult feeding, with prolonged feeding time and aspiration, placement of a nasogastric tube is often required. MDO apparently corrects not only the airway obstruction of RS, but also has a beneficial effect on swallowing and reflux [40]. In contrast, TLA seems to somewhat worsen the dysphagia [33].

Prognosis

The effects of airway obstruction at the tongue base include failure to thrive, developmental delay, heart failure, brain injury and sudden death [43,44]. The mortality associated with upper airway obstruction in Pierre Robin sequence varies from 7% to 25% [45-47].

Further studies are required to assess the long-term stability of MDO, and to evaluate its effectiveness against other conventional treatments in cases of obstructive sleep apnea in RS.

Conclusions

Many knowledge gaps persist regarding RS, highlighting the need for additional research in the genetic field, patient evaluation, severity classification of the disease, and outcome of therapy.

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Stuttering: What the ENT doctor should know

Sulene Pirana, MD.

Fluency, continuous and soft speak, is importante for communication, it depends on harmonic integration of neural processing envolved in language and motor act; speech production must be easily, reasonably quick and without having to stop and pausing a lot.

During normal language development some disfluency can occur, its named normal speech disfluency, some words and short sentences repetition, emission reviews, interjections use and syllables repetition but rarely sounds prolongation.

Speech disfluency is a organization disorder in sequential articulatory speech events with speech flow interruption – cluttering and stuttering (which is more often known as stammering in the UK). (Table 1 and Figure 1).

Type	Clinical
Developmental	Gradual beginning in childhood
Acquired	Abrupt onset in fluent individuals
Neurogenic	Brain injury – stroke, tumours, traumatic brain injury, Parkinson, Alzheimer
Psychogenic	Emotional, repetition of initial or tonic syllable, indifference to symptoms, disfluency without variations

Table 1. Stuttering types.

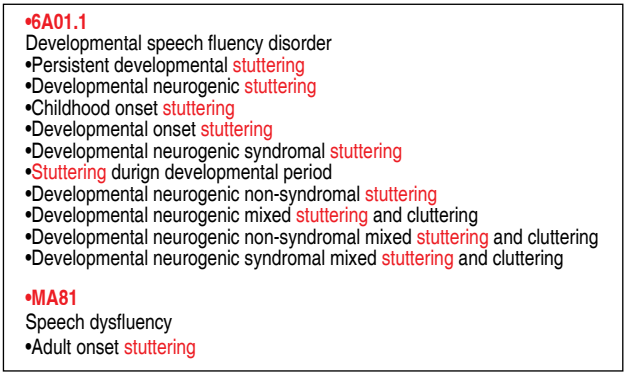

Figure 1. CID 11.

Cluttering is a fluency disorder characterised by a rapid and/or irregular speaking rate, excessive dysfluencies, disordered stress and pausing during speaking. It may co-exist with language or phonological errors and attention deficits. Cluttering is a different fluency disorder from stuttering, but it might occur alongside stuttering.

The most common form of stuttering is a neurodevelopmental disorder – developmental stuttering. It happens in children during language development and affects 5% of the world's population. The prevalence of chronical stutters is about 1% of the world's population, around 70 million people worldwide. About 5% of children between 2 and 5 years old have stuttering - boys 1:1 girls; 80% of spontaneous remission - more in girls, 20% stutters with different severity degrees. The chance to chronifies is 7% in girls and 34% in boys. The prevalence is woman 1: 5 men.

In about 60% of children who sutter, the sumptoms will remit by 16 yars of age. But many cases persist into adulthood, and given the importance of communication in the development of a child, tratment of stuttering in children requires eartly intervention.

Primary symptoms are disfluencies, involuntary disruptions in normal speech flow – disfluencies, that are classified as common and atypical (typical of stuttering); common may occur in people without stuttering, but in less than 10% of emissions. (Tables 2 and 3).

Common – CD	Atypical – AD
Hesitation	Monosyllabic word repetition
Interjection	Syllable repetition
Unfinished Word	Sounds repettion
Revision	Sound prolongation
Word repetition	Blocking
Segment repetition	Break
Sentence repetition	Sound or segment intrusion

Table 2. Disfluencies typology.

Disfluence	Clinical Presentation
Hesitation	silent: 1 – 2 seconds
Interjection	word or clause that does not relate to the text – so, if, ok, may
Unfinished Word	incomplete – he got some can... (dy), she li... (ves)
Revision	remakes the speech; frequently after na unfinished word
Word repetition	take, take, take the ball
Segment repetition	repetition of at least 2 complete words – I will , I will
Sentence repetition	my dog ran, my dog ran
Monosyllabic word repetition	me, me, me
Syllable repetition	re-re-re-repetition
Sounds repettion	s-s-s-s-sleep
Sound prolongation	Fffffork
Blocking	/cat
Break	silence greater than 2 seconds
Sound or segment intrusion	tsts, ririri, tongue popping

Table 3. Disfluencies: Clinical presentation.

What causes stuttering? For centuries, stuttering was believed to envolve abnormalities in the tongue or laryns. But treatments tha focused on the tongue or laryns have not demonstrated consistente efficacy in improving stuttering symptoms. The pioneering work of Orton and Travis postulated that stuttering may arise from abnormal cerebral activity.

There were too wrong theories of ambiental and psychological causes, one the most famous was the diagnosogenic theory – stuttering started when parents in general misdiagnosed their children as stutterers when actually they only presented normal disfluence. Parents commited mistake again trying to control their children disfluent speech with rejection, tension – pathological stuttering development.

Wendell Johnson, Iowa University, 1939, made several experiments, interviewed dozens of stuttering children's mothers and advocatted that stuttering is undoubtedly a learned conditioned response – the diagnosogenic theory. One of his unpublished study is named nowadays as – "monsters study".

Acquired stuttering causes are stroke, cranioencephalic traumatism, pre, peri or postnatal lesions. The etiology of developmental stuttering is polygenic multifatorial; organic base works in conjuction with environmental factors and personal characteristics. (Figure 2).

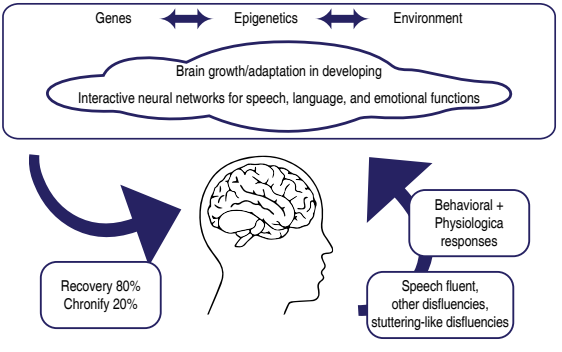

Figure 2. Multifatorial etiology of stuttering.

Social factor provided if there is an organic predisposition – family or school environment facilitating stuttering onset; jittery environment, people who speak fast or talk with a complexity much greater than it is suitable for children.

It has been proved that emotional problems do not cause stuttering; emotional factors can be considered aggravating. Stuttering is a neurological disturbance related to speech and language slow maturation neural processing. (Figure 3).

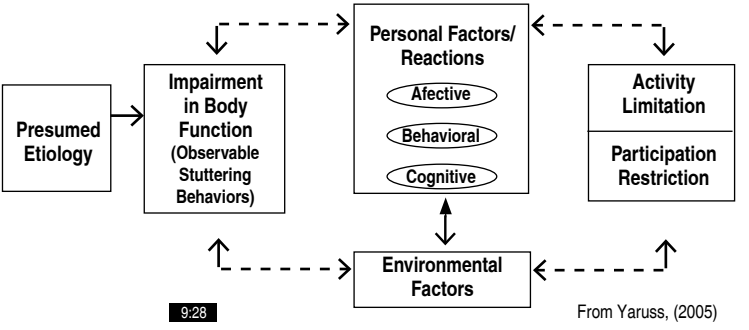

Figure 3. Components of the Stuttering disorder.

Because many people who stutter speak fluently the majority of the time, stuttering is thought to be a disorder of the structure and/or function of the brain that transiently disrupts speech production. Fluent and effortless speech production depends on connections between areas that perform auditory processing, planning and motor execution – motor auditory integration – matching sounds you hear and sounds generated by your speech output. The disruption occur between thinking the word and planning the speak motor act; the time between them is about 450msec.

The upper longitudinal fascicle (ULF) dorsally interconnected regions involved in cortical speech processing in left hemisphere:
– hearing: upper temporal gyrus – phonological and auditory processing
– inferior frontal gyrus – articulatory speech planning
– dorsolateral pre-motor cortex – auditory-motor integration
– motor cortex – speech performance

Tractography show significant differences in robustness and in the pattern of interhemispheric asymmetry of white matter and in the density of ULF fibers. In stutterer ULF fibers penetrate subtle in superior temporal gyrus where auditory and phonological speech processing takes place.

Functional image studies (FMRi) show more active auditory cortex in fluent people; stutterers present greater volume and activity of right hemisphere. To compensate for connectivity deficits of left hemisphere?

Neuroimaging studies show anatomical and functional diferences in stutterers compared to fluente controls, specifically in the motor and auditory regions and in the basal ganglia. These changes increase with the duration of stuttering. In adult stuttering there are hyperactivation of regions in the right hemisphere: abnormal coordiantion between speech planning and execution áreas. Are these anatomical and functional changes cause or adaptations?

Failure to develop left-hemispheric dominance for speech is a long-standing theory; other implicate the motor system more broadly, postulating hyperactivity of the right

(language non-dominant) cerebral hemisphere. As knowledge of motor circuitry has advanced, theories of stuttering have become more anatomically specific, postulating hyperactivity of premotor córtex, either directly or through connectivity with the thalamus and basal ganglia. Others theories target the auditory and speech production systems. Stuttering induced widespread overactivations of the motor system in both cerebrum and cerebellum, with right cerebral dominance. Stuttered Reading lacked left-lateralized activations of the auditory system, wich ar thought to support the self-monitoring of speech, and selectivity deactivated a frontal-temporal system implicated in speech production. Induced fluency decreased or eliminated the overactivity in most motor áreas, and largely reversed the auditory-system underactivations and the deactivation of the speech production system. Thus stuttering is a disorder affecting the multiple neural systems used for speaking.

Doctor Gerald MacGuire – psychiatrist and researcher at Califórnia University – demonstrated changes in bases nuclei core circuitry neurotransmitter (dopamine), that generate the temporal cues that initiate and chain speech movements. Variations of fluency can be explained by the greater or lesser involvement of the base nuclei. The age of stuttering onset: between 2 and 3 years old are the same age in which the base nuclei circuits are in full development and dopamine receptor concentration major changes: D1 e D2. Avaliations using PET-Scan showed indreased dopamine precursor. Dopamine administration increases disfluency; dopamine antagonists improve fluency.

Speech production depends on base nuclei function, they act mainly in situations of spontaneous speech, especially when the message presents great content and its involvement tends to decrease in situations that do not involve spontaneous speech (singing, speaking with another accent, syllabic speaking, speaking in metronomic rythm, reading in chorus) and in situations where there is little content in speech (talking to animals, talking to small children, speaking alone); these situations usually induce fluency in stutterers. (Figure 4).

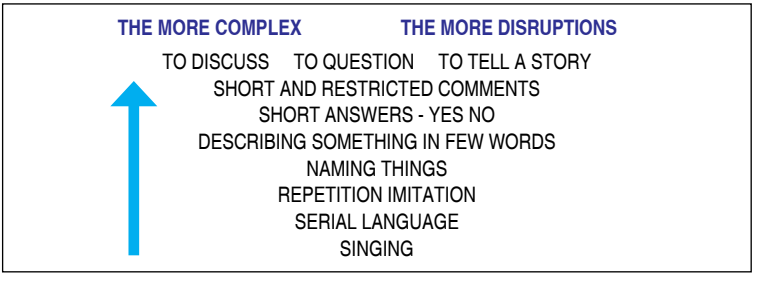

Figure 4. Fluency and linguistic context.

Doctors Dennis Dranya and Changsoo Kang, NIDCD – National Institute on Deafness and Other Communication Disorders, discoverd genetics causes of developmental stuttering – genes GNPTAB, GNPTG e NAGPA mutations; a metabolic cause of sturttering. A global epidemiological study demonstrated that its responsible for approximately 1 in 6 cases of stuttering.

Stanford scientists determine 3d structure of stuttering-linked enzyme, the UCE – uncovering enzyme that is encoded by the gene nagpa, acts on the golgi apparatus that process digestive proteins that will be sent to lysosomes. Oligodendrocytes full of lysosomes are induced by neurons to bring to surface an important protein that will be used in myelin sheath production. Efficiency loss in lysosomal mediated intracellular

protein transportation leads to reduction in growth rate and myelin renewal resulting in loss of integrity in bundles of white matter important for fluent speech production. Mutations in UCE are related to discrete metabolic changes in mice and persistent stuttering of development in humans.

Genetics analysis of DRD2 – dopamine receptor gene prevalente in the brain, showed an increased of a specific allele in stutters. Functions of the identified genes include neuro-metabolism, embryonic transcription regulation behavior modification.

One recente case report suggests stuttering as a pediatric auto-imune neuropsychiatric disorder associated with streptococcal infections (PANDAS). The hypothesis is that the antibodies created to fight the streptococcal infection cross-react with the developing basal ganglia.

There are no cure for stuttering; stuttering treatment is speech therapy; it is indicated for children who stutters for more than 6 months or early if they are in the risk group for chronification. (Table 4). Neuronal plasticity reduces the risk of persistence. Take action near the rise of stuttering streaming up 98-100% the chance of fluency recovery.

	Greater risk	Lesser risk
Gender	Male	Female
Time of stuttering	More than 3 months	Less than 3 months
Age of onset of symptoms	4 years old or more	Until 3 years old
Familial history of sttutering	Closer parents	Extended family
Child temperamento	Give up talking	Don't give up talking
Associated physical symptoms	Present	Not presente
Duration of longest disruptions	More than 1 second	Less than 1 second
Disfluencies typology	More AD	More CD
Onset of speech therapy after rupture initiation	After 1 year	Less than 1 year
Number of repetitions per episodes	More than 2	1 or 2
Muscle tensions during speech	Present	Not present
Difficulties in language, speech and oral motricity	Present	Not present
Social and emotional interferences	Present	Not present
Another factores that increase the risk for chronification	Prematurity, low birth weight, absence of breastfeeding, sleep disorders	

Table 4. Risk indicators for persistent stuttering.

While children often recover, stuttering may also spontaneously disappear much later after years of dysfluency. These rare cases of unassisted recovery in adulthood provide a model of optimal brain repair outside the classical windows of developmental plasticity. Speech therapy shifts the altered right lateralization activation in the inferior frontal and the precentral gyrus to the left homologue. Conversly, the focus of activation in the cerebellum shifted the other way, from the left to the right.

Stuttering can often be transiently alleviated by a variety of interventions, collectively termed fluency inductions. These are either auditory stimulations (for example chorus Reading, masking and shadowing) or speech-pattern changes (such singing, prolonged speech, rhythmic speeche, whispering and shouting).

In young children, treatment may involve combinations of indirect approaches that aim to modify the environment via parents and thereby have an impact on fluency, attitudes, feelings, fears and language, or direct approaches that involve working with the child to change individual speech behaviours. The use of indirect rather than direct

approaches distinguishes treatment for stuttering in young children from those used for older children and adult interventions. Historically, there have been two broad philosophies within the field, with a distinction between stuttering modification approaches (stutter more fluently), which aim to reduce avoidance behaviours and negative attitudes and thereby modify stuttering episodes, and fluency-shaping approaches (speak more fluently), which teach new and controlled speech production patterns. These more fluent patterns are learned in formal practice sessions before gradually being generalised to normal conversational settings with these interventions seeking to achieve complete fluency for the people who stutter. These approaches to intervention may have become less defined in current practice, with interventions commonly drawing on a range of influences.

Pharmacological treatment is not effective: antidepressants show no or minimal benefit; anxiolytics like benzodiazepines show some improvement in severity and antipsychotics (dopaminergic blockers), like lurasidona, are showing promising results, but only in adults stutterers.

Negative effects of stuttering are not generally observed in the first year following onset, those who continue to stutter into adulthood can experience marked disruptions to their qualify of life. Psychotherapy is an important adjuvant when there are psychological problems related to communications disturbances – behavioral aspects of stuttering, impact on daily life, role of speak situation, atitudes, fears and thoughts about speech. (Figures 5 and 6). (Table 5).

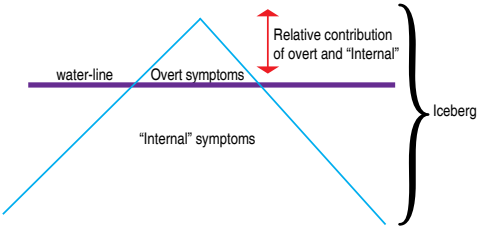

Figure 5. Sheehan's stuttering iceberg.

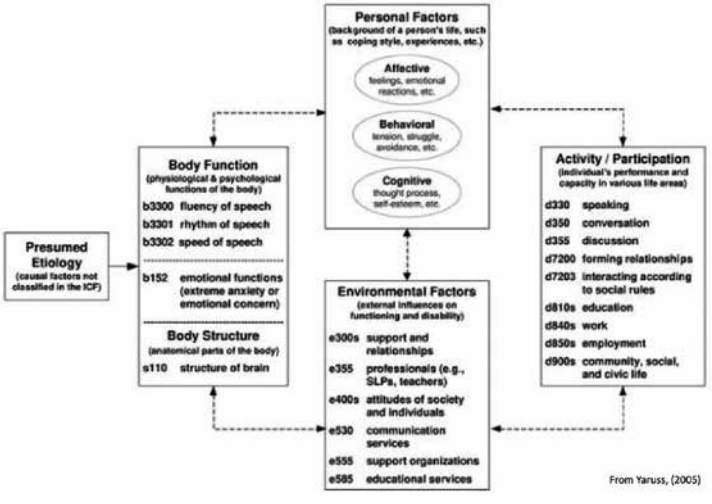

Figure 6. The International Classification of Functioning.

People who stutter do more than just stutter, personal histories by people who stutter highlight the broad impact of the disorder: stuttering interferes with school/work (79%) and social/family interactions (64%); many feel embarassed about stuttering (70%) and avoid speaking situations (82%). This is true even after treatment.

Listen carefully to your child
Remain natural while the child speaks
Set aside time to talk to the child, without distractions
Speak slowly and without haste, without however losing the naturalness of speech
Encourage everyone in the family to be a good listener
Create the most peaceful and relaxed environment possible
Avoid calling attention to stuttering during daily interactions
Accept the child as he/she is
Do not react negatively, do not criticize and do not punish the child when he/she stutters

Table 5. Talking to a stutterer child.

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PHARYNX

Pediatric OSA: Outcomes of T&A and results of the CHAT Study

Ron B. Mitchell, MD.

Obstructive sleep apnea (OSA) is associated with respiratory events that can range from complete cessation of airflow (also known as apnea) to oxygen desaturation and airflow restriction (also known as hypopnea). These respiratory events are calculated per hour and presented as an index, known as the apnea -hypopnea index or AHI. In children, AHI levels below 1 are normal, 1 to 5 is mild, moderate is 5 to 10, and more than 10 is severe OSA. Pediatric OSA is diagnosed between birth and 18 but is most common in children who are 3-8 years old, during the time of maximal hypertrophy of the tonsils and adenoids. Obstructive sleep apnea syndrome (OSAS) is often used in recognition that any decision to recommend T&A should not be based solely on polysomnography findings but also on clinical history, examination, and the likelihood that surgery will improve sleep and lead to improvements in day- and nighttime symptoms such as attention deficit hyperactivity disorder (ADHD), irritability, cognitive dysfunction, insomnia or daytime fatigue. In adolescents, some suggest continuing to use the children's cutoff numbers for OSA while others suggest using adult criteria (AHI less than 5 is normal and more than 30 is severe OSA in adults). The prevalence of OSA in children is 1-3%. However, this rate can increase to 80% in children with Prader Willi syndrome or Down's syndrome and 60% in craniofacial syndromes or neuromuscular disorders [1-3].

The first line surgical treatment of OSA in children is tonsillectomy with or without adenoidectomy (T&A). Adenotonsillar hypertrophy is the most common etiology of OSA in children and several studies have shown improvements in respiratory sleep parameters, quality-of life, behavior and healthcare utilization after T&A [4-7]. Battacharjee et al. [8] reported on a multicenter retrospective study of 578 children in 8 pediatric sleep centers in the United States and Europe who had a T&A for OSA with pre- and postoperative polysomnography. T&A resulted in a significant reduction in AHI from a mean 18 to 6 but only 27% had complete resolution of OSA. Older age, chronic asthma and obesity were predictors of persistent OSA. Thus, T&A was associated with a significant improvement in OSA in most children but resolution in a minority. These studies showed an association, but not causality, between T&A for OSA in children and improvements in a variety of outcomes measures. However, the positive outcomes of surgery may also be seen by a period of observation. The growing child may, over time, see enlargement of the pediatric airway either by an increase in the size of the naso- and oro-pharynx, or by a decrease in adenotonsillar hypertrophy or by both. This could lead to resolution of OSA without the need for T&A.

A recent multicentered prospective double-blind study (Childhood Adenotonsillectomy Trial; CHAT study) looked at causality. CHAT was a well-designed and rigorously conducted randomized controlled trial with wide geographic and racial representation and high follow-up rates. Children with OSA were randomized to observation as well as to T&A [9]. The primary outcome measure in the CHAT study was change in executive function that was not different between T&A and a 7-month period of watchful waiting as measured by neuropsychological testing. Normalization of

polysomnography was much higher in the T&A groups versus the observation group (79% vs 46%). While the OSA cure rate of T&A reached 85% in normal- weight children with mild OSA, a high percentage of children with moderate to severe OSA and/or obesity had residual OSA. There was also a higher rate of persistent OSA in African Americans compared to Caucasians [8]. T&A did reduce symptoms and improve secondary outcomes of symptoms, behavior and quality-of-life as compared with 7 months of observation [9]. The conclusions from the CHAT study was that T&A is highly effective at normalizing polysomnography, reducing symptoms and improving quality of life. However, in children with mild OSA and mild symptoms a period of observation may also lead to resolution of the sleep disorder.

There is an ongoing debate about the efficacy of T&A for mild OSA [11]. The Pediatric Adenotonsillectomy Trial for Snoring (PATS) is an ongoing multicentered randomized controlled study comparing the outcomes of children with mild OSA that undergo T&A to observation over a 12-month period. The results are likely to be published in the coming years as a primary and several secondary papers. The PATS study is likely to increase our understanding of the best ways to manage children with mild OSA.

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Tonsillectomy: Intracapsular vs. total resection

Caroline M. Kolb, MD, **Santiago Rengifo**, MD and **Udayan Shah,** MD.

Outline

I. A brief history of tonsillectomy.
II. Modern tonsillectomy devices and techniques.
III. What is an intracapsular tonsillectomy?
IV. Advantages and disadvantages of intracapsular tonsillectomy.

V. Efficacy in management of tonsillar disease.
VI. Critiques: Regrowth, cost and surgical time.
VII. Conclusion.

I. A brief history of tonsillectomy

There is a wide range of procedures used to remove enlarged or infected tonsils. The different techniques in use today and throughout the history of tonsillectomy in Western medicine indicates the absence of a clearly superior technique. Tonsillar diseases have affected the human race throughout recorded history. In the first century AD, Celsus removed diseased tonsils using blunt finger dissection or a sharp hook and knife. The fossae were then "washed out with vinegar and painted with a medication to reduce bleeding."

From the mid-19th century until the earlier part of the 20th century, sharp removal with knife, dissectors, scissors, tonsillotomes or guillotines, were used for the complete removal of the tonsils (tonsillectomy) or partial removal of the tonsils (tonsillotomy). The patients were either unanesthetized, under local anesthesia, or anesthetized briefly with ether. Hemostasis was achieved with gargles or painting the fossae with medications. The significant improvements in general anesthesia by the mid-20th century allowed surgeons to perform tonsillectomy with careful dissection using knife, scissors, and/or dissectors with hemostasis using ties or suture ligatures.

II. Modern tonsillectomy devices and techniques

When assessing surgeon preference for devices, we looked across three distinct geographic regions of the United States in 2009 to query device preferences. Overall, approximately 28% of surgeons used primarily monopolar techniques, 22% use bipolar instruments, 27% use coblation, 16% use microdebriders, 4% use the jPK plasmacision device, and 4% use other means. The jPK device is no longer in production, but has been replaced by the PlasmaBlade™ Soft Tissue Dissection Device. Plasmacision devices are not commonly used today in the United States.

Today, most tonsillectomies are performed with careful dissection of the tonsil from its fibrous capsule by knife, scissors, dissector, or electrosurgery under general anesthesia. In the United States, tonsillectomy is rarely performed under local anesthesia. Hemostasis is largely achieved with suction electrocautery or sutures. The carbon dioxide (CO_2) laser, Mucosal Intact Laser Tonsillar Ablation (MILTA), diode laser, or radiofrequency treatments are other treatment modalities, but have not supplanted either the "cold" or "hot" methods for tonsillectomy.

Total, complete or extracapsular tonsillectomy (ECT) is typically performed using monopolar electrocautery by grasping the tonsil and retracting it medially, while dissecting within the fibrous plane between the tonsil and the pharyngeal constrictor muscles. Tonsillectomy by monopolar electrocautery is generally expected to cause less intra-operative bleeding than when using knife, scissors or dissectors, while greater pain is expected due to thermal effects when using monopolar cautery for excision and/or hemostasis.

Coblation is a common alternative to monopolar tonsillectomy, which is thought to be less painful than monopolar tonsillectomy. Coblation achieves tissue resection by ionizing protons in water, which breaks tissue apart, resulting in reduced thermal effect than that seen with monopolar electrocautery.

Microdebrider tonsillectomy is a form of intracapsular tonsillectomy performed with a powered instrument connected to a suction and irrigation source with a blade that can be set to rotate by oscillation. This tool continuously uses suction to remove blood and tissue from the surgical field. In the case of a partial tonsillectomy, the Microdebrider is useful in preserving the capsule of the tonsil. This capsule is an important barrier that prevents exposure of the pharyngeal muscles. This technique is comparable to digging out a canoe from a tree trunk. Microdebrider tonsillectomy is associated with reduced postoperative pain and fewer episodes of delayed hemorrhage and dehydration.

III. What is an intracapsular tonsillectomy?

Partial tonsillectomy, subtotal tonsillectomy, or intracapsular tonsillectomy are interchangeable terms describing the removal of most (approximately 95%) of the tonsil, while preserving a rim of lymphoid tissue within the capsule. The preservation of this lymphoid lining within the capsule can serve as a "biologic dressing" to reduce postoperative pain, decrease hemorrhage rates, and improve the rate of return to a normal diet following tonsil surgery.

Intracapsular tonsillectomy (ICT) may be performed for most tonsillectomy indications including obstructive sleep apnea, chronic tonsillitis or pharyngitis, upper airway resistance syndrome, and sleep-disordered breathing. Sufficient tissue removal to exteriorize the tonsillar crypts must be performed if ICT is to be effective for managing infections and tonsilloliths. ICT should not be performed when a biopsy is indicated or for the management of tonsil neoplasia. ICT can be performed using a noncauterizing microdebrider (Medtronic, Olympus), a cauterizing microdebrider (Olympus), or Coblation.

Microdebriders

Dissection can be performed by shelling out the lymphoid tissue with the microdebrider leaving a 2 mm height of remaining tissue. When using loupes, fibrous strands are more easily seen at the ideal margin of resection and depth of debridement. This depth of dissection allows additional tissue reduction with the suction bovie electrocautery, while protecting the tonsillar capsule and preventing exposure of the superior constrictor muscle as the lateral border of the tonsillar fossa. Hemostasis is achieved by blanching, turning the tissue white, rather than creating a thick, dark eschar. The spray setting of the suction bovie around 35 watts of power is recommended. The surgical technique for ICT using a noncauterizing microdebrider is shown in. (https://www.csurgeries.com/school/nemoursalfred-i-dupont-hospital-for-children/).

Coblation

Coblation is a method of intracapsular tonsillectomy that effectively reduces both large and small tonsils. The "loop off" technique truncates large tonsils from anterior to posterior utilizing ablate and coagulation functions as necessary. Ablate is used for tissue reduction of the remaining fibrous strands, and can be used to evacuate crypts adjacent to the pericapsular region. If less than 3 mm from the lateral pharyngeal wall, coagulation is used to reduce tissue further. Smaller tonsils are shaved down using a combination of ablate and coagulation, comparable to the technique used in shaving down shrubbery. In some cases, electrocautery may not be needed for Coblation tonsillectomy. Electrocautery for hemostasis may be required more often when the tissue is inflamed or infected.

IV. Advantages and disadvantages of intracapsular tonsillectomy

Most tonsil surgeons measure safety by postoperative bleeding rates and readmissions for pain and dehydration. A 2007 study comparing microdebrider-assisted intracapsular tonsillectomy (ICT) vs monopolar extracapsular tonsillectomy (ECT) showed decreased rates of delayed hemorrhage requiring operative hemostasis (0.5% for ICT vs 2.1% for ECT) and decreased rates of emergency department visits and readmissions for pain or dehydration (3% ICT vs 5.4% ECT). Less than 1% of patients required a revision tonsillectomy over the 3.5 year study period.

A 2017 meta-analysis comparing ICT vs ECT reviewed 15 randomized controlled trials showing significantly decreased postoperative bleeding, postoperative pain, and need for analgesics in patients undergoing ICT. The number of days to return to normal diet and activity were also significantly shortened in the ICT group.

In a systematic review by Zhang, thirty-two studies were used to compare clinical efficacy, cost-effectiveness, and post-operative morbidity of ICT vs ECT in pediatric patients with sleep-disordered breathing. Zhang found that certain factors like patient satisfaction and quality-of-life did not differ between ICT and ECT. However, the study concluded that ICT reduced the odds of secondary bleeding by 79% and decreased post-operative pain. In fact, ICT required less overall analgesia in all but one of the seven studies that monitored this outcome. This finding further supported the use of ICT in children. Additionally, compared to ECT, ICT reduced patients' return to normal oral intake by 2.8 days, and the odds of readmission were decreased by 62%. Results suggested the overall healthcare burden is reduced by ICT due to fewer post-operative complications and a decreased need for medical re-contact.

V. Efficacy in management of tonsillar disease

Chang, et al. demonstrated the efficacy of ICT vs ECT in treating pediatric obstructive sleep apnea by reviewing pre- and postoperative polysomnography results. The patients in the ICT group were younger with lower BMIs, larger tonsil sizes, and lower preoperative AHI scores compared to the ECT group. There were statistically similar improvements in the apnea hypopnea index (AHI) and minimum oxygen saturations between the two groups. This study concludes that ICT is a suitable option for treating pediatric sleep apnea in selected patients.

Mostavych expanded the review of pre and postoperative polysomnography results of ICT by evaluating the effectiveness of using microdebrider-assisted ICT on children with severe obstructive sleep apnea (OSA). The patients were a median age of 3.7 years at surgery and suffered from severe OSA, described as having an AHI above 10 or an oxygen saturation nadir that is less than 80%. Microdebrider-assisted ICT improved OSA in these patients by lessening obstructive apneas and hypopneas, arousal index, oxygen desaturation, snoring, and carbon dioxide level. Additionally, significant increases in oxygen saturation and oxygen saturation nadir were found in these patients.

VI. Critiques: Regrowth, cost and surgical time

Regrowth

Initial reviews of tonsillar regrowth rates between 0.8 to 16.7% were described by Acevedo et al. in a systematic review of tonsillotomies. They concluded that tonsillectomy offers distinct advantages over tonsillectomy in terms of postoperative morbidity, but regrowth rates were not yet sufficient for formal analysis.

Since the Acevedo study, Mueller et al. found that 6% required reoperation with 44% for pharyngitis, but at a substantially lower bleed rate associated with ICT (0.7%) compared to ECT (12%). A subsequent meta-analysis did find a 6-fold increased risk of developing residual tonsil tissue compared to ECT that may result in recurrent tonsillitis; however, there was no increased risk of recurrent tonsillitis in the ICT group compared to ECT group. There did not appear to be any difference between the microdebrider and Coblation techniques regarding postoperative pain and bleeding.

Cost

A discussion of cost must always keep in mind that patient safety is the most important factor in technique and device selection. It has been repeatedly shown that ICT is safer in terms of postoperative bleeding and shorter recovery times. Recently, the cost of ICT vs ECT was recently examined by comparing costs associated with the recovery time and complications of surgery including bleeding rates, readmissions, and regrowth for patients undergoing ICT. The cost analysis favored ICT as the less expensive option. Another cost study comparing ECT with monopolar electrocautery vs ICT with microdebrider in treating pediatric obstructive sleep apnea showed that ICT had an overall lower expected cost, but was less cost-effective in terms of effectiveness by quality-adjusted life year. When the failure rate of recurrent or residual obstructive sleep apnea was less than 3.12%, partial tonsillectomy would be more cost effective in this model. Overall, the evidence does suggest that aggregate costs appear to be lower with shorter recoveries and fewer complications and readmissions. A safe recovery outweighs the small differences in costs estimated between the two procedures in selected candidates.

Surgical time

Seven studies were evaluated in a meta-analysis comparing operating time for ICT and ECT. There was no statistically significant difference in surgical times; however, there was a high degree of heterogeneity and small sample sizes in the selected studies. Shah et al. analyzed multiple variables that affect surgical times and found that age, body mass index (BMI), trainee involvement, and surgical technique all factor into the equation. Patients under age 3, with lower BMI, and without trainee involvement tend to have statistically significant shorter procedures. Procedure times were shorter for microdebrider-assisted compared with electrocautery ($P<.001$).

VII. Conclusion

Intracapsular tonsillectomy should be considered for patients with obstructive sleep apnea and chronic tonsillitis or pharyngitis. ICT has an excellent safety profile with fewer bleeds, less dehydration, and fewer returns to the hospital, compared to extracapsular tonsillectomy. Surgeons may wish to consider traditional extracapsular techniques in patients with obstructive apnea who have small tonsils, and for patients with recurrent infections.

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Pediatric OSA and hypertension. Post-adenotonsillectomy changes

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Abstract

Sleep-disordered breathing includes a spectrum of upper airway disorders ranging from primary snoring to obstructive sleep apnea (OSA). In adults, untreated obstructive sleep apnea is associated with hypertension and other cardiovascular morbidities. In children, the first paper described high blood pressure (BP) among children with OSA in 1976. Since then, several studies have linked obstructive sleep apnea with blood pressure in pediatric populations and some literature show associations between blood pressure and obstructive sleep apnea in children, further studies are needed to clarify this clinical relevant issue.

The aims of this presentation review is to describe associations between blood pressure and obstructive sleep apnea in children, and to further investigate the effects of adenotonsillectomy (T&A) on blood pressure in children with obstructive sleep disorders. Subgroup comparisons on obese vs. non-obese and hypertensive vs. non-hypertensive children were also discussed.

Obese vs. Non-obese:

Among the children receiving T&A as treatment for OSA, nonobese children improved more than obese children did in terms of blood pressure. Obese children with residual OSA even had a higher diastolic BP after surgery. Obese children with OSA may benefit less from T&A in cardiovascular morbidities. It demonstrated that pediatric obesity interacted with OSA and contributed to cardiovascular parameter changes.

Hypertensive vs. Non-hypertensive:

Hypertensive children had significant improvement on all BP parameters after T&A. Shift of hypertensive status after T&A in children with OSA may occur. Decrease in BP among hypertensive children with OSA after surgery which may imply OSA as a major determinant for childhood hypertension. It becomes warranted to screen and treat hypertensive children with OSA as proper treatment not only eases their OSA symptoms but may also prevent future cardiovascular and end organ disease.

Key words: Adenoidectomy, Blood pressure, Child, Polysomnography, Sleep apnea syndromes, Tonsillectomy.

Introduction

Associations between obstructive sleep apnea (OSA) in children and elevated blood pressure have received increasing attention in recent years [1-19]. At the beginning, Professor Guilleminault reported children with OSA diagnosed by means of nocturnal polygraphic monitoring and described progressive development of hypertension in children may be associated with OSA [1]. The following researchers used office or ambulatory blood pressure (BP) monitoring and reported continually that BP was elevated in children with OSA than those without [2-19]. Previous studies suggested that at least in some children with OSA did have higher BP, and possibly causing further end-organ damages [2-19].

Hypertrophy of adenoids and tonsils are the main causes of OSA in children [20,21]. Nowadays, adenotonsillectomy (T&A) is still widely recognized as the most effective first-line therapy for childhood sleep apnea [22-26]. T&A is effective in the alleviation of OSA in children [22-26]. T&A also offers prominent improvement in a variety of sleep parameters [24]. Recently, literatures have focus on effects of T&A on blood pressure in children with OSA. Question is raised whether T&A play a significant role in reversing the cardiovascular sequelae of OSA [27-37].

The main purpose of this article is to elucidate associations between elevated BP / hypertension and childhood sleep apnea. The first part of the article reviewed previous studies pertaining to BP monitoring in children with sleep-disordered breathing/OSA. Another main purpose of this article is to clarify the effects of T&A on BP in children with OSA. In particular, this article describes results of BP changes after surgery in subgroups such as obese vs. non-obese children and hypertensive vs. non-hypertensive children.

BP monitoring in children with OSA

In adults, untreated OSA is associated with hypertension and other cardiovascular morbidities [38-41]. In children, associations between OSA and elevated BP/hypertension have been studies. Herein, we summarized several great studies addressing this issue. In 1976, professor Guilleminault and his colleagues firstly described eight children with OSA diagnosed by polygraphic monitoring with symptoms and signs such as loud snoring, excessive daytime sleepiness, decrease in school performance, abnormal daytime behavior, and progressive development of hypertension [1]. In 1998, Marcus et al. systematically studied office BP in 41 children with OSA and 26 children with primary snoring as control and found children with OSA had a higher diastolic BP than controls while no significant difference was observed in systolic BP between these two groups [2]. In 2004, Amin et al. compared 24-hour ambulatory BP measures in 39 children with OSA to 21 children with primary snoring [3]. Amin et al. found children

with OSA had significantly greater BP variability, a higher night-to-day systolic BP, and a smaller nocturnal dipping and concluded that OSA in children is associated with 24-hour BP dysregulation. Subsequent studies by Li et al. recruited large community-based cohort and measured ambulatory BP in children with OSA, primary snoring, and normal controls [5,7]. Results from Li's study group revealed OSA was associated with elevated daytime and nocturnal BP, and is an independent predictor of nocturnal hypertension [5]. In children with primary snoring, nighttime diastolic BP was significantly elevated compared to those in normal controls [7]. Hospital studies conducted by our research groups also confirmed that children with had a higher ambulatory BP compared to children without OSA [18,19].

Few studies addressed longitudinal BP changes in children with OSA [16,17]. Vlahandonis et al. recruited 40 children aged 6-11 years and tracked OSA and BP changes in these children years later [16]. At follow-up period, children with improvement in OSA was associated with improved BP control (16). Another large longitudinal cohort was from Li's study group [17]. Study by Li et al. enrolled 185 children with 4-year follow-up period and found changes in childhood OSA was associated with elevated BP independent of obesity [17]. These findings suggest that BP may be elevated years after OSA diagnosis, along with an increase of OSA. Therefore, proper diagnosis and management of OSA is highly desired.

Treating childhood OSA with T&A: an evidence-based medicine

Currently, T&A is still the first-line therapy for childhood OSA [20,42,43]. The effectiveness of T&A in treating OSA has been well documented. A large multicenter study by professor Gozal and his colleagues identified 578 children with OSA treated with T&A and reported a significant reduction of apnea-hypopnea index (AHI) from 18.2 to 4.1 event/hour [25]. Prestigious childhood adenotonsillectoy trial (CHAT) firstly conducted a randomized controlled trial and compared treatment outcomes between T&A and watchful waiting in children with OSA [26]. The CHAT study randomly assigned 464 children, school aged (5 to 9 years of age) with OSA into two treatment groups and confirmed T&A provides a favorable outcomes in polysomnographic findings over watchful waiting [26]. Our research group also had several publications about improvements of polysomnographic findings and quality of life after surgical treatment for OSA [44-47].

Until now, three meta-analysis have been published for polysomnographic outcomes after T&A in children with OSA [22-24]. The first work was from Brietzke et al. in 2006. A meta-analysis by Brietzke included 14 studies and reported a reduction of 13.92 events/hour in the AHI after T&A with 82.9% of children normalized their sleep data [22]. An updated meta-analysis in 2009 by Friedman et al. found the treatment success was only 59.8% when "cure" was defined as AHI <1 events/hour after surgery [23]. A recent meta-analysis was conducted by our research group in 2016 which included 51 studies with 3413 children [24]. Our meta-analysis found T&A offers prominent reduction of 12.4 events/hour in the AHI and improvement in a variety of sleep parameters [24]. The overall success rate in our meta-analysis was 51% for postoperative AHI <1, and 81% for AHI <5 [24].

Factors associated poor outcomes in polysomnographic results after T&A in childhood OSA have been explored. Obesity and the AHI before surgery are regarded as two major determinant factors for poor surgical outcomes [48-51]. A meta-analysis by Costa et al. in 2000 revealed T&A improves but does not resolve OSA in the majority

of obese children [51]. An updated meta-analysis in 2016 by our research groups also showed that postoperative AHI was positively correlated with AHI and body mass index z score before surgery by using meta-regression analyses [24].

Effects of T&A on BP in children with OSA

Since T&A is effective for improvement of OSA in children, clinicians are curious about whether T&A results in reversing adverse cardiovascular consequences as well. In recent years, effect of T&A on BP in children with OSA have received an increasing attention [27-37]. In 2008, Amin et al. for the first time demonstrated that there might be a change in BP after T&A in children with OSA [27]. Amin et al. observed a significant reduction of diastolic BP at 6 months after surgery in children with OSA [27]. However, in the same year, Apostolidou et al. reported no significant change in BP after surgery in Greek children with OSA [28]. In 2010, Ng et al. firstly reported the BP data derived from ambulatory BP monitoring after surgery in children with OSA [29]. In Ng's study, 44 children with OSA had a significant reduction of BP load after T&A [29]. Another recent study by Lee et al. in 2015 showed severity of childhood OSA and hypertension were both improved after T&A using office BP measurements [30].

Although previous studies have shed light on this issue, results from pertinent studies are limited and contentious [27-37]. Our research group are dedicated to this issue and announced 5 publications until now [31,33-36]. A 3-months follow-up study by our group enrolled 159 children underwent T&A and showed a significant reduction of overall diastolic BP from 65.1 mm Hg to 63.8 mmHg after surgery ($P = 0.04$) [34]. A 6-months follow-up study by our group enrolled 124 children underwent T&A and showed daytime systolic BP was slightly increased from 114.3 mmHg to 117.3 mm Hg and no change in other BP paramters [35]. We also compared ambulatory BP parameters between 3-months and 6-months follow-up period and observed 24-hour ambulatory BP findings did not differ significantly between the three- and six-month follow-up [36]. Our results reveal ambulatory BP changes after T&A among children with OSA may be minimal [31,33-36].

Recently, the prestigious CHAT study have published their data about BP outcomes after surgery [32-37]. In 2015, the CHAT group reported no significant change in systolic (from 43.5 to 42.9 percentile) and diastolic BP percentile (from 61.5 to 62.6 percentile) after surgery in children with OSA [32]. In 2017, the CHAT group reported no significant change in absolute value of systolic (change: 1.2 mmHg, 95% CI = -0.6 to 3.1 mmHg) and diastolic BP (change: 1.1 mmHg, 95% CI = -0.5 to 2.7 mmHg) after surgery in children with OSA [37]. Results from the CHAT's study also did not observe any difference in BP or BP percentile changes between children with OSA with surgical treatment or watchful waiting [32,37].

Effects of T&A on BP in obese vs. non-obese children with OSA

Our research group compared BP changes after T&A between obese and non-obese children with OSA [31]. We conducted a case-control study and recruited 39 obese and 39 non-obese children. In our cohort, non-obese group had a significantly decreased systolic and diastolic BP. In contrast, all BP parameters in the obese group were not significantly changed postoperatively [31]. We thus concluded that among the children receiving T&A as treatment for OSA, non-obese children improved more than obese children did in terms of BP measures.

Effects of T&A on BP in hypertensive vs. non-hypertensive children with OSA

Several literature compared disparities in BP changes between hypertensive and non-hypertensive children with OSA [29,30,33-35].

Ng et al. conducted subgroup analysis and analyzed ambulatory BP changes after surgery in hypertensive (n = 8) and non-hypertensive (n =36) children with OSA [29]. In Ng's study, 8 children with hypertension and OSA had the overall and nocturnal systolic and diastolic BP loads significantly reduced, while BP measures were not significantly changed in non-hypertensive children [29].

Lee et al. recruited 50 children with OSA [30]. Among these children, 17 children had hypertension, and the other 33 children had normal BP. In Lee's study, the median systolic and diastolic BP were significantly reduced in hypertension group (systolic BP: from 119.0 to 113.0 mmHg [P = 0.038]; diastolic BP: from 79.0 to 68.0 mmHg [P = 0.005]). The hypertension rate were also significantly reduced from 34% to 14% (P = 0.006).

Our research group had 4 studies comparing BP changes in hypertensive and non-hypertensive children with OSA [33-36].

In a hospital-based setting, we recruited 240 non-obese children with OSA and had office BP measure before and after T&A [33]. Among these children, 169 children were non-hypertensive, while 71 children were hypertensive. The whole cohort had a significant decrease in nocturnal diastolic BP (66.9 to 64.5 mmHg; 95%CI of difference, −4.1 to −0.7mmHg) and morning diastolic BP (66.9 to 64.4 mmHg; 95%CI of difference, −4.2 to −0.8mmHg). Postoperatively, hypertensive children had a significant decrease in all BP measures, including mean (SD) nocturnal and morning systolic BP (nocturnal: 107.5 [8.6]mmHg; morning: 106.0 [9.4] mmHg), systolic BP index (nocturnal: −4.3 [8.6]; morning: −5.7 [8.5]), diastolic BP (nocturnal: 65.1 [11.5]mmHg; morning: 64.4 [10.1] mmHg), and diastolic BP index (nocturnal: −10.7 [17.3]; morning: −11.6 [15.7]), whereas the non-hypertensive group had a slight increase in nocturnal systolic BP (103.8 to 105.9mmHg; 95%CI of difference, 0.4-3.9 mmHg) [33].

In another three hospital-based studies, we used 24-hour ambulatory BP measures for children with OSA before and after surgery [34,35]. Results from these 3 studies showed the 24-hour ABP change after T&A is small. Moreover, among children with preoperative hypertension, there is significant BP improvement after T&A surgery at both 3-month and 6-month follow-up period [34-36].

Conflicts of interest

The authors declare no conflicts of interest.

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NOSE AND SINUSES

Immunotherapy of allergic rhinitis

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Introduction

Allergic rhinitis (AR) is a disorder resulting from an IgE-mediated inflammation of the nasal mucosa. Typical symptoms, that affect the nose with rhinorrhea, nasal obstruction, sneezing and itching, with or without ocular involvement, may be described as seasonal and/or perennial, as intermittent or persistent depending on their onset and persistence. The severity is mild, moderate or severe according to the impact on quality of life [1]. AR is a global problem, affecting 10% to 30% of the general population and prevalence rates are increasing worldwide. Although not life threatening, the degree of severity of AR is detrimental for patients, by determining psychological effects, interference with social interactions, work/school performances and quality of sleep. This creates an economic burden not only for the affected person, but for the family and the society at large [2].

Symptoms of AR can be controlled with environmental measures, patient education to allergen avoidance, and pharmacotherapy. Pharmacotherapy includes antihistamines, mast cells stabilizers, antileukotrienes, decongestants and topical corticosteroids. Nevertheless, many patients continue to experience ongoing symptoms and impaired quality of life [3] even with this routine management. Environmental control and avoidance measures, although reduce the allergen load in some cases, often are not feasible or show limited clinical effect [4]. Patients with severe AR are seldom satisfied by pharmacotherapy alone, and this one is not always free from side effects [5, 6]. Finally, there is currently no evidence that pharmacotherapy alone can modify the natural course of the allergic disease, intended as a trend to increase in severity and develop comorbidities [7, 8].

Allergen immunotherapy (AIT) represents the only currently available strategy that targets the underlying pathophysiology, and may have a disease-modifying action. It consists in the progressive administration of the culprit allergens, in order modify patients' immune response against them, thereby ameliorating symptoms, but also delivering long-term clinical benefits which may persist for years after treatment discontinuation [9].

The immunological rationale, tailored to the specific IgE spectrum of each individual, makes AIT one of the best candidates for a precision-medicine approach, since: 1. the main immunological and molecular pathways at the basis of the disease are known; 2. the relevant molecules involved in allergic reactions are known and specific and sensitive standard diagnostic tests to precisely identify the IgE-mediated reactions exist; 3. standardized and highly characterized products for effective and safe AIT to target the mechanisms of the disease are available [10] (Figure 1). This open the way to tailored therapies on the basis of diagnostic and predictive biomarkers of response, even for primary and secondary prevention.

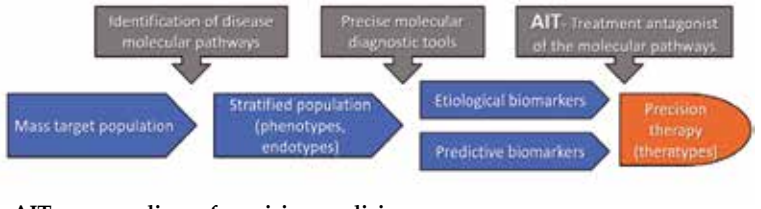

Figure 1. AIT as a paradigm of precision medicine.

Allergen extracts and administration routes

The allergen extracts for AIT usually differ in terms of composition and allergen activity because of the differences in manufacturing processing, therefore comparisons are difficult even when the same allergen sources are used. Standardized, purified and highly characterized allergen extracts have to be used and all manufacturers have their own in-house reference standard to control their biological activity by in-vitro methods and to guarantee stability and batch to batch consistency [11]. The determination of individual allergens (particularly the major allergens) with standardized, validated methods is highly recommended, however manufacturers utilize different measuring systems, thus direct comparison of specifications, including the amount of major allergen, among different products is little realistic [12].

Non-modified (native) purified extracts and chemically modified extracts (allergoids) can be used for AIT in routine practice. Allergoids are characterized by less reactive B-cell epitopes and reduced IgE binding (observable with immoblotting and EAST-inhibition assays), while their T-cell epitopes and their immunogenic action remain unaltered, with the purpose of taking advantage of a better safety profile [13]. The modified extracts can be obtained with chemical reactions of polymerization (with glutaraldehyde) or with selective substitution of intramolecular aminoacids (carbamylation of lysines). These last kind of allergoids, named monomeric, keep the same molecular weight of the native allergen as observed in SDS page bands and gain partial resistance to enzymatic degradation, this providing a different and peculiar pharmacokinetic profile going beyond the mere oro-mucosal absorption [14].

New attractive approaches under investigation focus on hypoallergenic recombinant allergens, B-cell epitope-based vaccine or immunogenic peptides, fusion of allergens with immune modifiers and peptide carrier proteins, but current data are somehow inconsistent and their real convenience remains controversial [15].

With AIT, allergen extracts are presented to the immune system either subcutaneously or sublingually. In the 80's, sublingual allergen immunotherapy (SLIT) was proposed as an alternative to subcutaneous allergen immunotherapy (SCIT) and raised the level of interest among practicing allergists and primary care physicians. The main purpose was to provide the increasing allergic population a new therapeutic easy-to-take intervention with an improved safety profile [16]. Alternative routes were bronchial (LBIT), oral (OIT), mainly abandoned for the occurrence of adverse events, and local nasal (LNIT) immunotherapy, being the last one recalled in recent years as an interesting option for localized AR [17, 18]. More recently, intralymphatic immunotherapy (ILIT), epicutaneous immunotherapy (EPIT), intradermal immunotherapy (ID) have been proposed with the scope of directly targenting districts with highly immune-competent cells and poor of effectors cells, but the real convenience of these routes is still under investigation [19].

Allergen extracts initially diffuse into local site tissue, where they are uptaken by antigen-presenting cells (APC) [20]. The speed of this process depends on the formulation of the extracts, particularly when depot preparations are used in SCIT, and hydrogliceric drops or tablets or lyophilized are used for SLIT [21]. In this latter case, the preparation is retained under the tongue for at least 1 minute and then swallowed. The dimension of the molecular allergen appears important to this process, therefore native allergens and small sized allergoids (monomeric) are facilitated to pass the mucosal barrier. Big sized allergoids, due to their polymeric nature, are preferentially administered by subcutaneous route [22]. Preparations for SCIT may be aqueous (usually for insect venom allergy and US countries) or depot extracts (especially in EU countries), physically adsorbed to a carrier (aluminum hydroxide, tyrosine or calcium phosphate), eventually associated to adjuvants [23, 24]. (Table 1).

Allergen extracts available for different AIT routes	**Subcutaneous (SCIT aqueous)**	**Subcutaneous (SCIT depot)**	**Sublingual (SLIT)**	**Local nasal (LNIT)**
	Native allergens	Native allergens Polymeric allergoids Monomeric allergoids	Native allergens Monomeric allergoids	Native allergens (powder)
New routes under investigation	**Epicutaneous (EPIT)**	**Intralymphatic (ILIT)**	**Intradermal (ID)**	**Liposomes**
Hypoallergenic variants	**Chemically modified** Monomeric allergoids Polymeric allergoids		**Recombinant DNA technology** Recombinant Allergens T-Cell Peptide Immunotherapy B-Cell Peptide Immunotherapy Contiguous overlapping peptides Hydrolyzed peptides Chimeric proteins	
Adjuvants	Tyrosine Calcium phosphate Aluminium salts TLR agonists Nanoparticles		VLPs (virus-like particles) Mannan PLA, polylactic acid Cellulose Vitamine D	

Table 1. Summary of product preparations for AIT.

Single AIT has become the preferred treatment for both SLIT and SCIT, mainly in European countries, however most allergic patients result poly-sensitized [25]. In these patients, preparations including mixtures of different allergen sources may represent an attractive approach. Mixtures of grass pollen and mixtures of tree pollen are frequently used in AIT and they appear effective [26]. Conversely, the use of different, non-taxonomically related allergens mixed in a single AIT product has been investigated only in a very limited number of studies [11]. Since the dilutional effect and the potential allergen degradation due to enzymatic activity of some allergens (house dust mites, molds and insects) can impair the properties of an extract, when prescribing an allergen mixture physician should limit the number of individual allergens to those belonging to the same or correlated homologous group [27].

The mechanisms of action of AIT

At the basis of allergic reactions there is an inflammatory response towards an allergen in a sensitized patient upon renewed exposure. AIT acts through a series of complex mechanisms in particular targeting type II innate immune cells, Th2 cells (which produce IL-4, IL-5, and IL-13), B cells and effector cells (mast cell, basophil, and eosinophil) [20].

Following administration of AIT, the allergens reach the local lymph nodes via free diffusion or taken up by dendritic or B cells [21]. The subsequent events include an early desensitization via rapid upregulation of histamine type 2 receptors, an activation of regulatory T cells (Tregs) that inhibit the T cell-mediated activation of B cells and the specific T-cell response to the allergen. Tregs migrate from the lymph nodes to the inflammation site and release IL-10 and TGF-ß switching off the immune response and attenuate local mast cells activity and other effector cells that contribute to allergic inflammation [28]. This phenomenon reinforces the induction of new (or boosting of preexisting) specific IgG antibodies that inhibit the allergen-antibody-mediated immune response, by preventing the binding of IgE-allergen complexes to B cells, DC and effector cells. In some circumstances, especially for SCIT, the increase of IgG1-4 titers correlated to the clinical success, whereas the induction of specific IgA has been observed in SLIT. In the long-term down-regulation of specific IgE production is observed [29].

These events in synthesis explain the nature of AIT as disease-modifying therapy, able to stimulate blocking antibodies, pro-tolerogenic cells and mediators to prevent the triggering of allergic responses and maintenance of inflammation in target tissues. In 1998, a landmark study demonstrated that allergoid tablets reduce the eye basal inflammation, and following specific provocation, in subjects allergic to house dust mites treated for two years [30] (Figure 2).

General considerations on AIT

It is recognized that AIT should be considered in case of clinically relevant AR symptoms, with or without conjunctivitis or asthma, suggestive of an allergen-specific IgE sensitization documented by positive skin test or laboratory assay [1,9,31]. This step ensures that the correct allergen preparation is used for AIT. Key point is the clear correlation between allergen exposure and symptoms occurrence. In some circumstances, nasal or conjunctival provocation testing may be useful to prove the clinical relevance of the allergic sensitization in the target organs [32]. When the mentioned tests are unable to precisely identify the culprit of the diseases the component-resolved diagnostics provide further information [33].

In general, AIT is indicated in subjects with moderate to severe AR sub-optimally controlled despite allergen avoidance and pharmacotherapy, but in less severe AR it is acceptable when patients do not tolerate the side effect of drugs or wish the benefit of long-term protection and potential disease-modifying effect [9].

Contraindications to AIT should be referred to the summary of product characteristics (SmPC), being the safety profile, preclinical and clinical data, strictly specific for each individual preparation, and wide difference exists in this sense. However, recognized general absolute contraindications include uncontrolled or severe asthma, active systemic autoimmune disorders, active malignant neoplasia, start of desensitization during pregnancy. Other conditions, representing relative contraindications, are partially controlled asthma, severe cardiovascular diseases, intake of beta-blockers, systemic autoimmune disorders in remission or organ specific, primary and secondary immunodeficiencies. In these cases, doctors should use AIT only when benefits outweigh potential risks, after a case-by-case discussion with the patient. Patients with severe psychiatric disorders and other conditions leading to expected poor adherence should contraindicate the beginning of an AIT course [9] (Table 2).

• Evidence of specific IgE-sensitization towards one or few clinically relevant allergen(s)
• Severity of symptoms and pharmacotherapy requirements
• Efficacy of avoidance measures
• Success and side effects of pharmacotherapy
• Comorbidities and contraindications
• Patients' preference and acceptability
• Patient's age and positive benefit/risk ratio
• Adherence to treatment
• Availability of high-quality standardized extracts with documented efficacy and safety

Table 2. Aspects to be considered before prescribing AIT.

Clinical efficacy of AIT in different age groups

In general, the efficacy of AIT is assessed using symptom scores (total symptom score, individual nasal and ocular symptoms, medication consumption scores, combined symptom-medication scores (frequently used as primary endpoints in AIT trials), health-related quality of life (HRQL), disease-control questionnaires, as well as other methods like visual analog scales, "well" or "severe days" along the allergy exposure period [34].

There is insufficient evidence to determine which of SCIT and SLIT is most effective [26,35,36]. Under a clinical point of view, AIT with standardized extracts is well characterized by numerous clinical trials showing effectiveness, and this is even more evident for SLIT, for which large trials involving hundreds of patients are nowadays available [37]. Meta-analyses suggest that both SCIT and SLIT are effective for AR, both in adult and in children, favoring a reduction in symptoms and anti-allergic medication use [26] (Table 3). Since substantial heterogeneity was found in these systematic reviews, owing to study designs, study populations and products evaluated, it is not possible to make generic recommendations and a broad transfer of the efficacy of some preparations to all others administered in the same way is not endorsed. Therefore, it is solicited to initiate a treatment with a specific product after an individual product-based evaluation of the evidence [9].

Concerning SCIT, robust evidence of efficacy in rhino-conjunctivitis caused by pollen allergy in adulthood is well-documented, while in childhood and adolescence only in a few trials. For house dust mite allergy, efficacy is documented by a number of controlled trials in adults and few controlled trials in children. For mold and animal dander allergy, only few and small controlled studies are available [26]. SCIT is recommended as a treatment option, in addition to allergen avoidance and pharmacotherapy, in controlled bronchial intermittent or mild persistent asthma, when a clear causal relationship exists between respiratory symptoms and the relevant allergen [38].

SLIT was largely investigated for grass pollen allergy and efficacy was documented in adult and young patients [39,40]. Upcoming evidences are also for weeds and trees allergy, like ragweed and birch [41,42]. New controlled trials, even including a large number of patients, on house dust mite allergy provide evidence of efficacy of SLIT in adults and children [43-46].

SCIT and SLIT are recommended for the treatment of seasonal AR in adults and children, since they have been shown to provide short-term benefit in moderate-to-severe disease sub-optimally controlled despite pharmacotherapy [9]. The evidence for short-term benefit of continuous SCIT is stronger for seasonal than for perennial AR.

Pre/coseasonal schedules benefit from a shorter course but some data suggests that continuous therapy may be more effective.

SLIT should be taken either continuously or pre-/coseasonally starting at least 2 months and ideally 4 months prior to the start of the pollen season in order to provide short-term reductions in symptoms and rescue medication. At least 3 years of treatment are recommended to get benefit after discontinuation. The evidence of efficacy of SLIT in perennial disease is less robust but convincing [9].

The evidence of efficacy is limited in the pediatric population below 5 years of age [47]. Concerns exist on the ability in early childhood to promptly refer the onset of severe side effects with SCIT, therefore AIT it should be considered as a therapeutic option only in limited cases. Side-effects to a sublingual monomeric allergoid were recorded at a rate of 0.071/1000 doses in a group of children with a mean age of 3 years [48]. In preschool children older than 5 years, some studies are available and since repeated injections may be stressful, SLIT may represent an option in this age class [49]. In any case, it is advisable that the decision to start the treatment has to be taken case-by-case (on the basis of health-related quality of life impairment and expected treatment acceptance) involving care-givers' judgment. For school age children and adolescents more data are available, especially for grass pollen, although there are no consistent results for other allergens [50,51]. Meta-analyses of SLIT in children and adolescents reported significantly improvement (Table 3), but well-designed and powered studies are solicited by the European Medicines Agency within the pediatric investigations plan, with an emphasis on long-term efficacy [52-54].

The safety and tolerability of AIT

AIT consists in the administration of an allergen extract to a allergic patients and this may results in adverse reactions of allergic nature.

SCIT is a safe and well-tolerated treatment when the injections are given in a medical setting by experienced personnel trained in the early recognition of systemic reactions and their management with immediate access to resuscitation equipment [9]. Systemic reactions to SCIT can range between mild-to-severe involvement of the skin, upper and lower airways, gastrointestinal tract, or cardiovascular system, up to anaphylaxis. Recognized risk factors are current infections, mast cell diseases, a high degree of sensitization, excess dose escalation, beta-blockers use, overdose of allergen extract, high-intensity physical exercise. Those for fatal reactions include uncontrolled asthma at the time of injection, dosing or injection mistakes, delay or inadequate administration of epinephrine during anaphylaxis, a prior history of anaphylaxis, administration during peak allergy seasons, use of native extracts, rapid induction regimens. This was confirmed by a European real-life, prospective, survey performed by members of the Immunotherapy Interest Group of EAACI on 4316 patients in France, Germany, and Spain, but it was concluded that SCIT for inhalant allergy is generally safe in adults and children with only a low number of systematic reactions (2.1% of all SCIT-treated patients) [55, 56]. With conventional build-up schemes this percentage is even lower (0.1–0.2%). An important finding from the published surveys was that only 14% of reported systemic reactions had begun 30 min after the injection, this fact raising debate on whether all patients receiving SCIT should be prescribed epinephrine autoinjectors [57, 58]. Redness, itching, or swelling at the injection site are often experienced in 26–86% of subjects but local measures or oral antihistamines may easily control these reactions. Conflicting data exist on the risks of prior large local reactions in anticipating systemic reactions [59].

Author	Condition	Population	Studies (n)	Participants		Effect Size SMD (95% CI)		Heterogeneity I^2	
				Active	Placebo	Symptoms reduction	Medication reduction		
Wilson 2003	SLIT Rhinitis	Adults and Children	21	484	475	-0.42 (-0.69, -0.15)	-0.43 (-0.63, -0.23)	73%	44%
Olaquibel 2005	SLIT Rhinitis	Children	6			–0.44 (–1.22, 0.35)	-	-	-
Penagos 2006	SLIT Rhinitis	Children	10	245	239	-0.56 (-1.01, -0.10)	-0.76 (-1.46, -0.06)	81%	86%
Calderon 2007	SCIT Seasonal rhinitis	Adults and Children	15	1645	1226	-0.73 (-0.97, -0.50)	-0.57 (-0.82, -0.33)	-	-
Compalati 2009	SLIT HDM Rhinitis	Adults and Children	8	194	188	-0.95 (-1.77, -0.14)	-1.88 (-3.65, -0.12)	92%	95%
Di Bona 2010	SLIT grass Rhinitis	Adults and Children	19	1518	1453	-0.32 (-0.44, -0.21)	-0.33 (-0.50, -0.16)	56%	78%
Radulovic 2011	SLIT Rhinitis	Adults and Children	49	2333	2256	-0.49 (-0.64, -0.34)	-0.32 (-0.43, -0.21)	81%	50%
Meadows 2013	SCIT Rhinitis	Adults and Children	17	659	525	-0.65 (-0.85 to -0.45)	-0.55 (-0.75 to -0.34)	57%	57%
Meadows 2013	SLIT Rhinitis	Adults and Children	42	2440	2379	-0.33 (-0.42 -0.25)	-0.27 (-0.37 to -0.17)	42%	49%
Feng 2014	SCIT cluster Rhinitis	Adults and Children	4	103	77	-5.91 (-13.68, 1.87)	-1.27 (-2.83, 0.29)	89%	94%
Yang 2016	SLIT cedar Rhinitis	Adults and Children	4	389	336	-0.94 (-1.75, -0.14)		93%	
Dhami 2017	SCIT Rhinitis	Adults and Children	16	632	499	-0.648 (-0.86, -0.43)	-0.521 (-0.75, -0.28)	62%	64%
Dhami 2017	SLIT Rhinitis	Adults and Children	41	2285	2187	-0.485 (-0.60, -0.36)	-0.311 (-0.43, -0.18)	69%	57%
Feng 2017	SLIT Rhinitis	Children	26	1147	1065	-0.55 (-0.86, -0.25)	-0.67 (-0.96, -0.38)	90%	83%
Li 2018	SLIT tablet Rhinitis	Adults	7	883	923	-0.33 (-0.54, -0.13)	-	74%	-
Mosges 2019	SCIT Rhinitis	Adults and Children	8	591	324	-1.9 (- 2.8, -0.9)		97%	

Table 3. Metanalyses on the efficacy of AIT in allergic rhinitis.

Undesirable effects during SLIT are relatively common (from 40 to 70% in controlled trials), mainly at local application site (oromucosal and gastroenteric), of mild/moderate intensity, transient and occurring most frequently during the treatment initiation [58]. However, recently, large trials even in children found a not negligible risk of treatment discontinuation related to severe local reactions (3 to 10% of patients) [60].

These bothersome side effects can actually impair compliance or require antiallergic medications. Some isolated cases of eosinophilic esophagitis have been reported [61]. Severe systemic reactions seem considerably less likely than with SCIT, although the overall rate of any adverse reactions is similar at least for native unmodified allergens extracts.

Higher doses and/or increased cumulative doses of AIT may be more effective, but may be associated with more side-effects, thus the decisions on dose and product must be made balancing efficacy and tolerability [62]. The majority of adverse events in SLIT develops at home without any medical observations, therefore patients should be thoroughly informed about how to recognize and manage reactions. With native high dose allergen-based tablet SLIT, it is encouraged to perform the first administration in doctors' office, on the other hand a recent FDA warning recommended epinephrine concomitant prescription and use-training to face the eventual occurrence of home severe reactions or anaphylaxis [63]. With modified allergen extracts no cases of anaphylaxis have ever been reported in literature or pharmacovigilance databases, and this event is virtually excluded by the low IgE-binding profile, responsible also for the very low incidence of mild to moderate local and systemic reactions even at very high doses [64, 65].

In conclusion, the benefits of AIT, regardless of the administration route, have to be weighed against the real risks of rare life-threatening systemic allergic reactions and fatal anaphylaxis through rigorous evaluation of safety data for each product from clinical trials and post-marketing surveillance. It is essential to identify predictors of risk for serious reactions in order to implement preventive measures in clinical practice.

Long term and preventive effects of AIT

For individual products some controlled, open studies have shown that AIT has preventive characteristics, with a potential long-term effect on the progression of the allergic disease. Some evidence supports reduction in the onset of new sensitizations and the likelihood of progression from rhinitis to asthma (secondary prevention) (Figure 2). As a consequence, it is clear that young patients with early manifestations of allergic symptoms are potentially an important target group for AIT intervention [66].

One of the first landmark evidences comes from the Durham's study, published on the New England Journal of Medicine in 1999. Grass-pollen SCIT along three to four years induced a prolonged clinical remission accompanied by a persistent alteration in immunologic reactivity [67]. Other prospective studies with grass pollen and mite SCIT suggested that a 3 years course produces prolonged remission of symptoms after discontinuation.

Preliminary data supporting the long-term benefits of SLIT came largely from small and/or non-randomized controlled trials. Most of them followed patients for 1- or 2-years during treatment [68]. On the other hand, being the persistence of the therapeutic effect after discontinuation a pivotal reason to support the beginning of an AIT course, the EMA currently recommends controlled designs involving 3 years of therapy with a 2-year follow-up period off-treatment [69]. Some of the available evidence with grass pollen SLIT demonstrated a sustained effect in double blind randomized studies [70]. Some data suggest that also HDM SLIT provides sustained protection for at least 1 year after 1 year of therapy [71]. Interestingly, a single open, pharmacotherapy-controlled trial in mite-allergic adults followed-up for a total of 10 to 12 years provided preliminary data that SLIT might provide 7-8-years long-term protection after discontinuation of 4- 5-years course [72].

Recently, either SCIT or SLIT were effective compared to placebo over 2 years, but these were insufficient for long-term protection as measured 1 year after discontinuation [73].

Regarding the preventive effect on asthma development, in the open prospective 'Preventive allergy treatment (PAT) study', a SCIT preparation containing seasonal pollen allergens, was shown to reduce the risk of developing allergic asthma in AR subjects. This effect was detectable 7 years after discontinuation of SCIT compared to subjects receiving symptomatic treatment only [74].

The preventive effect of SLIT on asthma onset has also been observed, but mainly in open studies [75, 76]. A recent huge controlled double-blind trial (the GAP trial) with grass pollen tablets given for three years to 810 children with AR without asthma, followed-up for further 2 years without treatment, failed to reach the primary endpoint of observing reduced risk of asthma development, but found a significantly reduced risk of experiencing asthma symptoms or using asthma medication at the end of trial [60].

A recent large retrospective analysis, based on German longitudinal prescription databases to assess the real-world long-term efficacy of grass pollen SLIT, revealed that the treatment was associated with slower AR progression, less frequent asthma onset, and slower asthma progression in respect to a control group not having received AIT [77].

There is currently weak evidence for a preventive effect of AIT in the prevention of new sensitization, mainly in the long term. A systematic review subgroup analysis showed a tendency towards an effect in children and adolescents after three years of AIT, supporting the rationale for future high-quality trials [78].

The evidence of sustained clinical effect and long-term benefit of AIT after cessation, in view of the potential side effects, cost and the necessary patient commitment, is an important consideration for recommending AIT over standard pharmacotherapy. The most recent revision of the literature suggests that 3 years of either SCIT or SLIT for grass pollen provides clinical benefit and immunological changes consistent with allergen-specific tolerance sustained for at least 2-3 years after cessation, therefore the administration course should be continued for a minimum of 3 years. Gaps in the evidence remain regarding the long-term efficacy of AIT for perennial AR and in children [79].

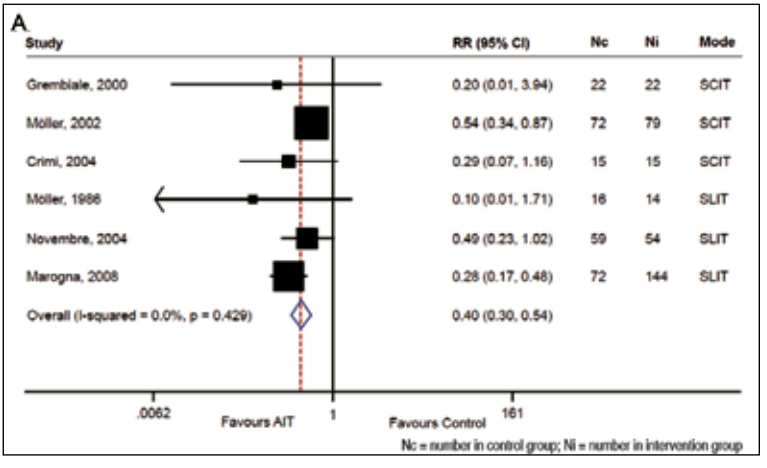

Figure 2A. Meta-analyses of effectiveness of AIT in short-term prevention of asthma in those with allergic rhinitis.

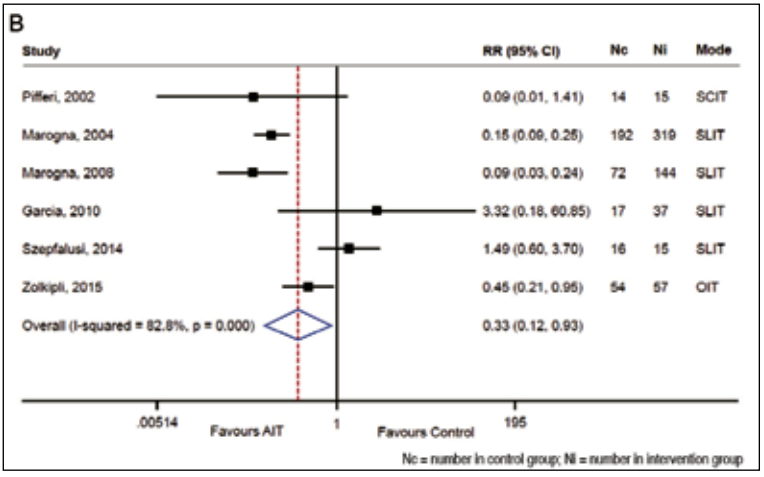

Figure 2B. Short-term prevention of allergic sensitization.

AIT in polysensitized patients

Epidemiological data indicate that the majority of patients with AR are poly-sensitized (with in vivo or in vitro demonstration of IgE hypereactivity to different allergens). AIT is equally effective in mono-sensitized and poly-sensitized patients if the relevant allergen is selected [80].

After exclusion of irrelevant co-sensitizations due to cross-reactivity (for instance, profilins), the clinical evaluation should be directed to establish if these subjects are mono-allergic (with only 1 allergen driving symptoms) or actually poly-allergic (when symptoms are elicited by multiple different allergens) by means of the history, or the component-resolved diagnostics or the use of specific provocation challenges [81].

Poly-sensitized mono-allergic patients are recommended to receive AIT selected for the specific allergen responsible for their symptoms. AIT with a single allergen extract seems to be less effective in poly-allergic patients, however when positive to biologically related allergens, a single allergen preparation or a mixture of 2 homologous allergens can be used. Separate AIT preparations for 1 to 3 of the clinically most important allergens can be used in poly-allergic patients to not homologous allergens (Figure 3).

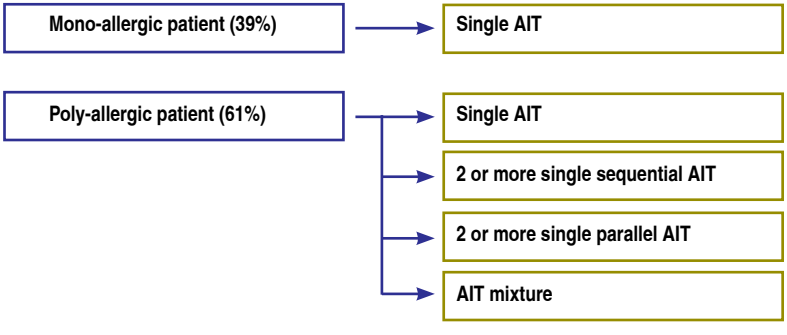

Figure 3. AIT options in mono-allergic and poly-allergic patients.

Unmet needs and future development

Allergic respiratory diseases represent a significant burden for individual patients as well as for national health care systems due to the direct and indirect related costs. Subjects with AR have a 3.5-fold higher relative risk of developing bronchial asthma within less than 10 years [82]. Treatment consist of symptomatic medications and allergen avoidance, but often are not resolving. AIT is the only option currently available with disease-modifying perspectives related to the long-term protection and preventive effect on disease deterioration, progression and development of complications. The costs of AIT are not irrelevant in respect to other options, but there is somehow evidence that this significant investment can be cost-neutral after 6-7 years on average (break-even point) [83]. Of course, this depends on multiple clinical factors and decision analysis models can assist the physician in properly customizing patient counseling with regard to treatment options [84].

Several cost-effectiveness analyses have shown that SCIT and SLIT are economically advantageous when treatment adherence and patients' compliance are respected. Recent investigations documented high rate of treatment drop-out irrespective of the form of administration, despite the frequent misperception of physicians [85]. Improving AIT adherence is one of the most important future goals and new approaches aimed at improving patient's convenience with shorter courses, while improving or maintaining efficacy and reducing the risk of systemic side-effects are welcome [86].

In conclusion, despite AIT represents a well-established, evidence-based therapy and great progresses have been achieved in products development, a number of barriers still exist to its wide diffusion. Efforts should be done to spread the knowledge of AIT benefits in areas with low awareness. Facilitation of regulatory environment in different countries is strongly encouraged. Improvement in diagnostic tool and identification of proper biomarkers is crucial to the selection of patients ideally candidates to AIT.

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Phitoterapy in rhinosinusitis treatment

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Introduction

Rhinosinusitis, an acute or chronic inflammation of the nose and paranasal sinuses. is a highly prevalent condition affecting 2 to 8% of the adult population. Episodes of rhinosinusitis are associated with significant reduction of quality of life, increased used of medications and high health-care utilisation. Due to the burden of disease and

its wide range of complications, rhinosinusitis is considered among the world's most debilitating diseases.

Current treatment for rhinosinusitis includes antibiotics, corticosteroids, antihistamines, and sinus surgery; however, these treatments do not eradicate the underlying cause and may create resistance. Growing scientific evidence suggests that herbal medicine (phytotherapy) may be helpful as an adjuvant treatment in rhinosinusitis. Herein, we reviewed current literature and determined the role, efficacy and safety of phytotherapy in the treatment of acute and chronic rhinosinusitis and establish the qualities of herbal drugs as demonstrated by in vitro and in vivo experiments.

Effects of phytotherapy in rhinosinusitis

Our literature review on articles focused on phytotherapy in the treatment of acute and chronic rhinosinusitis, including clinical trials, case reports and case studies, indicated that herbal medicines can have mucolytic, antiviral, antimicrobial, anti-inflammatory and secretolytic effects in experimental animals and humans. Phytotherapy has found to be efficacious in reducing the symptoms of acute and chronic rhinosinusitis in children and the adult population in vivo, demonstrating a high level of tolerability and safety. Herbal products have shown improvements in performance compared with previous formulations.

The antimicrobial effects of phytoneering herbal drugs in vitro have been assessed on several bacteria including Staphylococcus aureus, Streptococcus aureus, Streptococcus pyogenes, Escherichia coli and Haemophilus influenzae. Phytoneering products demonstrated bactericidal effects on Gram positive and negative bacteria, and antiviral effects against adenovirus C subtype 5, human rhinovirus B subtype 14 and the long strain of respiratory syncytial virus, in all of which the dry extract was significantly superior to oral drops.

Common herbs used in phytotherapy for rhinosinusitis

Common herbs used for phytoneering herbal drugs include yellow gentian root, cowslip flowers, common sorrel, elderflower, Sambucus nigra and verbena officinalis. Yellow gentian root grows wild in southern Europe and the mountains of southern Central Europe. The medicinally used parts of gentian are the driedrhizomes and roots of the plant. Bitter substances are the main ingredient of yellowgentian. Verbena officinalis is an annual to perennial plant and is native to Europe aswell as North and South Africa, the Americas, Central Asia and the Middle East. Sambucus nigra is found almost everywhere in Europe and Central Asia. The elder flowers are used medicinally. Common sorrel is found all over theworld. The leaves are used medicinally. Among others, sorrel contains flavonoids and hydroxylcinnamic acid derivatives such as gallic acid and ferulic acid derivatives, for which antiphlogistic, antimicrobial, and antioxidant properties are described. The natural range of perennial cowslip encompasses Europe, Central Asia and the Middle East. Both the root and the flowers have medicinal uses. Cowslip flowers contain flavonoids and are responsible for the yellow color of the flowers.

Pharmacodynamic properties of phytotherapy

The pharmacodynamic properties of phytotherapy in the treatment of acute and chronic rhinosinusitis related to the main indication include mucosecretolytic effects, anti-inflammatory effects, antiviral activities and antibacterial activities. The mucosecretolytic effects are based on an increased chloride ion secretion over the respiratory

epithelial cells that lead to a hydratization of the airway surface liquid (Cho et al. 2019, Kreindler et al. 2012) and on an increased ciliary beating frequency (Zhang et al. 2014). Together, these effects facilitate the removal of thick mucus from the paranasal sinuses. The exact anti-inflammatory mode of action is unknown at present and certainly multifaceted as usual with herbal drugs. One possible mechanism contributing to the anti-inflammatory effect is the inhibition of several inflammatory cytokines (Seifert et al. 2014). A potential underlying mechanism of the antiviral effects is the inhibition of viral neuraminidase, a key enzyme in viral replication, spread, and pathogenesis (Seifert et al. 2013). Antibacterial effects have been shown in animal models for bacterial rhinosinusitis, demonstrating a complete eradication of bacteria in the sinuses (Stierna 2014, Ismail 2005).

Clinical efficacy of phytotherapy in rhinosinusitis

Clinical efficacy of herbal drugs for rhinosinusitis has been demonstrated in two double blind, placebo-controlled, multi-centre phase III clinical trials (Jund et al., 2012) and asa pooled analysis combining data from the ARhiSi-1 and ARhiSi-2 trials (Jund et al., 2015). In the pooled study, 589 patients with acute viral rhinosinusitis were randomly divided into two groups: 294 patients were given 160 mg ofthe dry extract BNO 1016 contained in herbal extract 3 x daily, while 295 patients were given a placebo 3 x daily. Total duration of treatment was 15 days. The clinical symptoms were confirmed bysonography of the sinuses (Jund et al., 2012). A significant and clinically relevant superiority was demonstrated for BNO 1016 versus the placebo ($p < 0.0001$) following treatment over 15 consecutive days, resulting in a significantly lower MSS. Considered individually, herbal therapy showed improvement in all five major symptoms of rhinosinusitis including headache, facial pain, postnasal drip, rhinorrhoea and nasal congestion (Jund et al., 2012; Jund et al., 2015). The safety of herbal therapy has also been evaluated. Reported side effects were epistaxis and nasal itching.

The efficacy of herbal therapy has been also studied in children. In a prospective, multi-centre, non-interventional and randomized clinical trial for the treatment of post-viral acute rhinosinusitis in children, Popovich et al. (Popovich and Koshel 2018) treated 65 children between 6 and 11 years of age with herbal therapy as a supplement to standard saline irrigation and symptomatic therapy. The control group contained 55 children of the same age group. Symptoms were assessed by the physician and the patients. Patients in the treatment group recovered significantly faster from acute post-viral rhinosinusitis compared to the control patients. During treatment, patients self-assessed that rhinorrhea symptoms improved significantly with herbal therapy when compared to the control group. No adverse occurred during the study period. A similar study has been conducted in 184 children aged 6 to 11 years (Popovich &Beketova 2018). Patients were included in a randomized controlled study with two parallel groups. Both groups received standard treatment including Weber's douche and symptomatic medicine on therapeutic grounds. Isotonic sea salt solution was applied four times daily for 10 days. The intervention group received phytotherapy three times daily as add-on therapy. Physicians evaluated nasal congestion, nasal discharge, post-nasal drip, headache, and facial pain; significant improvements were detected in three out of five symptomatic parameters under combined treatment including herbal therapy as assessed by the physicians. Furthermore, the frequency of the transition of viral rhinosinusitis to the post-viral phase tended to decrease. No adverse reactions to the herbal medicine occurred during the study period.

Conclusion

In conclusion, the current literature suggests that phytotherapy can be considered an effective and safe form of ancillary treatment for rhinosinusitis. In particular, herbal drugs made with the technique of phytoneering have proven effective in acute rhinosinusitis. Taken together, the available clinical and non-clinical data on phytotherapy provide thorough evidence that this treatment is effective in treating the symptoms of acute uncomplicated inflammations of the paranasal sinuses (acute uncomplicated rhinosinusitis). Furthermore, its use has been proven very safe and well tolerated in both adults and children.

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Nasal wash. Always the same?

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Brief history

The application of solutions in the nasal cavities for clinical treatment of diseases of the nose and paranasal sinuses is a secular practice, whose probable origin is in the

Indian tradition of the Yogis and Ayurvedic Hindus, in which a technique called "jala neti" was carried out, even without scientific data to prove its effectiveness [7,10]. This technique consisted of cleaning the nasal passages with a simple solution of warm water and salt, in order to facilitate nasal drainage and eliminate mucus and toxins that accumulate in that region.

At the beginning of the 20th century, there was the publication of one of the first scientific works on the subject, produced by Wyatt Wingrave, in which various treatment regimes for saline nasal irrigation were described. And in 1926, Proetz proposed that nasal irrigation with solution would improve mucociliary function.

Importance of nasal lavage

Nasal lavage is a procedure that rinses the nasal cavity, done with aqueous hypertonic or hypotonic solution, conservatively, with minimal adverse effects, being a very low cost technique that generates potential benefits in a simple way [13]. This form of treatment has been improved over the years due to the concern with the overuse of antibiotics [7].

Nasal lavage with saline is used as adjuvant therapy in the treatment of colds, allergic rhinitis, and rhinosinusitis. Thus, the use of nasal irrigation has the potential to reduce the prescriptions of antibiotics, in addition to corticosteroids and mucolytics, for acute and chronic nasosinusal infections.

Humidification is one of the several benefits reported on the practice of nasal lavage with saline [13]. As one of the functions of the nose, in addition to heating and filtering the air, humidification is essential for the proper functioning of the nose and can be impaired by low humidity in the dry climate, artificially heated environments or even by air pollution, which they can generate symptoms such as itching, sneezing, nasal obstruction and even progression to nasosinusal infections.

When it comes to the effect of nasal irrigation with saline solution on mucociliary clearance, some studies show that saline solutions are effective in increasing mucociliary clearance and reducing inflammatory mediators such as interleukins, prostaglandins D2 and histamine in nasal secretions, reducing the score symptoms of patients and the use of oral antihistamines [12,20].

Nasal irrigation method

Currently, the market offers different methods for performing nasal lavage, the most used of which are nasal sprays, syringes, neti pots and squeeze bottles.

There is no consensus in the literature as to which method is best, but studies have shown that high-volume nasal irrigation with positive pressure presents superior results when compared to low volume and / or low pressure (sprays, aerosols). Low pressure devices do not reach the middle meatus region in more than 50% of the nasal cavities. And squeeeze bottles, which achieve better distribution of the applied solutions compared to high volume and low pressure (syringes, neti pots) [5,23].

Composition of solutions

Despite the development of evidence on the efficacy of nasal lavage with saline solution, there are still few studies dealing with the role of different solutions on the market that investigate the impact that these solutions with different compositions and pH can have on the functionality of the mucosa.

The composition of the nasal saline solution is influenced by the sodium chloride tonicity, added minerals and temperature [19]. These authors reported findings that suggest that hypertonic saline is more effective in increasing the frequency of ciliary beating and in decreasing edema in the nasal mucosa. However, this solution is associated with greater patient discomfort.

Calcium ions are known to imply the regulation of ciliary beats, while potassium is involved in healing, magnesium acts to control local inflammation resulting from allergy, bicarbonate reduces mucus viscosity and zinc has been shown to assist in the epithelial repair process.

A study carried out in 2016 concluded that normal saline induces epithelial cell death in vitro, which may have potential damage to the nasal mucosa [3]. In addition, it has an acidic pH that is harmful to the ciliary beat. However, this solution is widely used for nasal lavage and no harmful effects have been reported in patients.

In general, due to the few studies and the diverse conclusions, there is no consensus on the ideal composition of saline in the current literature.

Temperature

The impact of temperature on nasal lavages is a poorly studied subject. It is known that the frequency of the ciliary beat can vary depending on the temperature, however the ideal temperature for performing nasal lavage is not known.

A randomized study was carried out in order to determine the effect of nasal lavage at two different temperatures on the measurement of nasal mucociliary transport time, using the saccharin test. It used 78 healthy volunteers, on the first day a baseline saccharin test was performed and on the second the individuals were divided into two groups: nasal lavages at 20 and 37°C. There was improvement in mucociliary transport in both groups, however in the group with the highest temperature presented a shorter mucociliary transport time [17].

Disinfection

A survey conducted in 2012 showed that 50% of the nasal wash bottles and 40% of the irrigation fluids used by patients showed bacterial contamination by presenting positive cultures for Acinetobacter, gram-negative bacilli and coagulase-negative staphylococci despite cleaning with hot water and soap [14].

Due to the importance of nasal irrigation, this study aimed to investigate the possibility of bacterial infection and the effectiveness of microwave disinfection. According to the results, the disinfection done in the microwave for a period of 1.5 to 2.0 minutes was effective in combating bacterial colonization when done by the patient under supervision. Despite explaining in detail how to perform the process, patients who performed the process without supervision returned the irrigation bottles with a high incidence of contamination.

At the conclusion of the research, it was not possible to determine whether the risk of contamination was due to the inadequate performance of the procedure by the patient without supervision or if the risk is secondary to new contamination depending on the time after disinfection. It should be noted that despite the presence of a positive bacterial culture, there were no patients with a demonstration of clinical infection.

Lactate Ringer

The composition of lactate ringer has lower concentrations of potassium and calcium and high potential to alkalinize, which makes its electrolytic composition more

similar to blood plasma. Just like the sodium chloride nasal products, those of lactate ringer are also recommended to make secretions more fluid, which facilitates their elimination. They are also indicated in all situations of dryness of the mucosa.

The saline solution of lactate ringer shows a significant improvement in mucociliary clearance times in relation to the 0.9% saline solution. In addition, it is considered a nasal humectant of extreme quality because its composition corroborates minor irritating effects on the respiratory mucosa, guaranteeing hydration and nasal comfort with minimal burning [4].The lactate ringer has no side effects and is low cost. It also showed that it has a better mucociliary clearance time than isotonic saline after nasal septum surgery [21].

Sea water

A study carried out in 2016 aimed to compare the frequency of ciliary beat and the speed of repair of epithelial wounds in response to three types of isotonic saline solutions: normal 0.9% saline (pH 5.21), undiluted sea water (pH 7.29) and 30% diluted sea water (pH 7.9) [3].

The in vitro results showed that undiluted sea water significantly increased the frequency of ciliary beating and, more discreetly, increased the speed of repair of epithelial wounds, both when compared to diluted sea water and normal saline solutions.

A possible explanation for these results may be the mineral composition of sea water, which remains preserved in the undiluted solution, in addition to having an alkaline pH that favors the ciliary beat as demonstrated in vitro. In the diluted solution, the mineral content presented is lower and therefore not as significantly effective.

Xylitol

Xylitol is a natural sugar, found in the fibers of fruits and vegetables, derived from the catalytic hydrogenation of xylose and composed of 5 carbons. Currently, it has attracted the attention of the scientific community for presenting promising results in nasal lavage aimed at the treatment of chronic bacterial infections, such as rhinosinusitis [11].

To better understand how this substance, it is necessary to better understand the mechanism of action of xylitol on the bacterium *S. pneumoniae* [1].

Bacteria have carbohydrates as their energy source, they have 21 complex systems of sugar-dependent enzymes. This fact demonstrates the importance of carbohydrates for bacteria. Among these systems, S.pneumonie uses the Fructose-Phosphotransferase system (FPS) for the degradation and utilization of carbohydrates.

Since bacteria are unable to break down xylitol, it enters a "futile cycle" through FPS. In this cycle it is then phosphorylated into xylitol-5-phosphate and becomes toxic. In this way, the bacterium's adherence to the host's mucous membranes is reduced (given the dependence on carbohydrates and proteins to bind cells), there is also the inhibition of glycolytic enzymes, the inhibition of bacterial growth and consequently the survival time of this microorganism.

In addition, xylitol in concentrations greater than 4.5% alters the osmolality of the nasal mucosa making it hypotonic in relation to sodium chloride by the increase in water at the site, which provides an increase in innate immunity on the surface of the pathways aerial.

In addition, nasal irrigation with xylitol is more tolerated and has better results when compared to nasal lavage with saline in patients with chronic rhinosinusitis [22]. It has also been observed in patients with allergic sensitization presenting with rhinitis, that the use of xylitol irrigation reduced the symptoms of rhinorrhea. Finally, the nasal lavage with this natural sugar during the postoperative period improves nasal congestion [7].

Conclusion

Irrigation with nasal saline plays an important role in the treatment of various diseases of the upper airways. It is a beneficial treatment that can be used by all age groups, has low cost and has adverse effects.

Studies have shown that:

– large volume irrigation provides good irrigation of the nasal cavity;
– stable isotonic solution, slightly alkaline pH optimizes the trophic recovery of the respiratory epithelium, sea water seems to provide a definite advantage in many clinical situations and one factor that can not be neglected is the correct adherence to therapy in the preparation of the solution and the maintenance and hygiene of the devices;
– clinically the literature still fails to prove the superiority of one product over another.

Nasal lavage in children has good results in the adjuvant treatment of rhinitis and rhinosinusitis, however it is very important to be careful with the technique of application with the middle ear.

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Diagnosis and endoscopic management of pediatric nasal encephaloceles

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Background

An encephalocele is a protrusion of brain and meninges through a cranial opening, while a meningocele is a protrusion of the meninges alone [1,2]. Prevalence of congenital encephaloceles ranges from 1 in 3,000 to 1in 30,000 live births in North America and Europe. They are more common in Southeast Asian countries, with a reported incidence of 1 in 6000 live births [3]. They can present as a nasal or nasopharyngeal mass in an infant or child as part of a group of congenital midline nasal masses including nasal dermoids and gliomas (nasal cerebral heterotopia). These defects can arise due to an anterior neuropore anomaly during development [4]. Dermoids and epidermoids represent up to 60% of these lesions, and up to 20% of dermoids can contain intracranial tissue [4,5]. Approximately 30% of gliomas present as intranasal masses [4] and the majority no longer have intracranial connections except for a fibrous stalk in 15%. The differential diagnosis can be broad and includes polyp, papilloma, hemangioma, fibroma, lipoma, sarcoma, lymphoma, schwannoma, and carcinoma [4]. Magnetic resonance imaging (MRI) is the imaging of choice for the diagnosis and differentiation of midline nasal masses.

Clinical presentation:

Encephaloceles can be classified through the site of cranial defect: occipital, cranial vault, frontoethmoidal (also known as sincipital), and basal (which includes transethmoidal, transphenoidal, sphenoethmoidal, sphenomaxillary, frontosphenoidal / spheno-orbital) (Table 1) [2]. Encephaloceles with extension into the nose, nasopharynx or sinuses often present with nasal obstruction, feeding difficulty, sleep disordered breathing, cerebrospinal fluid (CSF) rhinorrhea, recurring meningitis, septal deviation, widened nasal root, or increased intraocular distance [6,7]. Additional associated findings can include hypertelorism, morning glory syndrome (a congenital dysplasia of the optic nerve described in 67.7% of basal encephaloceles), median cleft face syndrome, or hydrocephalus [8]. Physical exam of the nasal cavity usually reveals a mucous membrane covered mass that is soft, pink, and non-pulsatile. Encephaloceles with

extension in to the nose are often superior and lateral to the anterior end of the middle turbinate [2, 6] (Figure 1), whereas, those with extension into the nasopharynx may not be seen without flexible nasopharyngoscopy. Endoscopic examination will also help visualize nasal anatomy, detect the presence of CSF rhinorrhea, and help locate the lesion in the nasal vault. Biopsy should not be performed due to possible intracranial communication [9].

		Site of herniation	Location of mass
Occipital			
Cranial Vault			
	Interfrontal		
	Anterior fontanel		
	Interparietal		
	Posterior fontanel		
	Temporal		
Frontoethmoidal			
	Nasofrontal	Fonticulus nasofrontalis	Forehead: nasal bridge
	Nasoethmoidal	Foramen cecum	Nasal bridge
	Naso-orbital	Medial orbital wall	Orbit
Basal			
	Transethmoidal	Cribriform plate	Intranasal
	Transphenoidal	Between ethmoid and sphenoid	Nasopharynx
	Sphenoethmoidal	Craniopharyngeal canal	Nasopharynx
	Sphenomaxillary	Superior and inferior orbital fissure	Pterygopalatine fossa
	Frontosphenoidal/ spheno-orbital	Orbital roof, superior orbital fissure	Orbit

Table 1. Classification of Meningoencephaloceles / Encephaloceles [6,9,11].

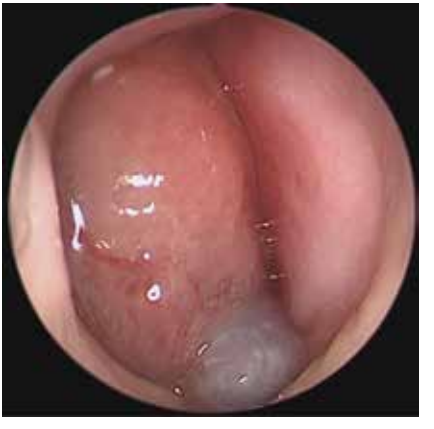

Figure 1. Anterior rhinoscopy of a 6-year old boy with a right sided nasal ecephalocele with nasal lining and a clear bluish portion inferiorly. It is filling the nasal cavity and pusing the septum to the left.

Preoperative evaluation

Imaging studies are crucial for preoperative planning. A thin-cut, high resolution computed tomography (CT) scan allows for detailed examination of the skull base

including detection of multiple skull base defects (Figure 2A) and can be used for image-guided surgery. An MRI is necessary for fluid and soft tissue characterization of the mass, including outlining the contents of the sac and examining for brain irregularities such as herniation of the brain seen in encephaloceles [10, 9] (Figure 2 B); it is also helpful to evaluate the presence of any cerebral blood vessels encased or in near proximity to the mass [7].

Ophthalmology evaluation including visual fields and intraocular pressure is a useful baseline examination and is particularly helpful in patients with preoperative visual symptoms or if imaging shows that the optic nerve, orbit or cavernous sinus is closely related to the mass. Endocrine evaluation is recommended in patients with transphenoidal basal encephaloceles as endocrine disturbances, typically of the hypothalamic-pituitary-adrenal axis, can occur.

Treatment

Indications

Treatment for congenital encephaloceles and meningoceles is surgical [9], but indications, timing and type of approach has not been standardized. The ultimate goal of surgery is to improve the nasal airway, eliminate communication of the sinonasal cavities with intracranial structures, to decrease the lifetime risk of future infections and to prevent cosmetic deformities [10]. Benefits of surgical repair must be weighed against the increased risk and difficulty of surgery in younger patients. The risk of meningitis over time in children with unrepaired encephalocele/meningoceles has not been quantified. Some have observed a low risk of infection before 5 years of age, and argue that repair can be deferred in asymptomatic children until endoscopic approaches are easier (about 2 or 3 years old) [11]. More recently, others are recommending surgical management as early as possible given the low morbidity and mortality of the surgery compared to the risk of meningitis [7].

Untreated encephaloceles can impact craniofacial development. Earlier removal of large masses with large skull base defects may help prevent development of telecanthus [12]. Urgent surgical intervention should be considered if patients present with a persistent CSF leak, recurrent meningitis or worsening neurologic or respiratory status. Safe and successful excision of these masses requires a multidisciplinary approach with neurosurgery, neuroradiology, and anesthesia.

Surgical approach

The surgical approach depends on the type and location of the defect but can include any combination of extracranial, transcranial, transnasal endoscopic or transpalatal methods [8]. Occipital and cranial vault encephalocele approaches are beyond the scope of this chapter as these locations require large open approaches requiring a craniotomy with cranial reconstructions. For frontoethmoidal encephaloceles that extend intracranially, a frontal craniotomy via a bicoronal incision is recommended to excise the mass and repair any dural or skull base defects. For intranasal components of frontoethmoidal and basal encephaloceles endoscopic/endonasal approaches are preferred [13], at times with a lateral rhinotomy approach to improve access.

Specific endoscopic approaches include direct paraseptal, trans-ethmoid-pterygoid-sphenoidal, and trans-ethmoidal-sphenoidal-petro-clival [7]. Endoscopic techniques have been possible in children as young as 2 years old [14]. Advantages of endoscopic approaches include avoiding external scars, no brain retraction, and improved visualization.

The endoscopic direct paraseptal approach can be used for lesions located anterior to the cribriform plate and lateral to the cecum foramen [7]. Trans-ethmoid-pterygoid-sphenoidal approach, which includes an ethmoidectomy, is employed for defects located in the cribriform plate and ethmoidal roof. Trans-ethmoidal-petro-clival approaches are employed for defects located in the petro-clival or petro-occipital regions.

Transphenoidal encephaloceles are especially challenging to resect because they often contain important neurologic structures such as the pituitary gland or optic pathways. For this reason, mortality rate is over 50% and morbidity is over 70% [15]. In cases with a concurrent cleft palate or where transnasal endoscopic exposure is limited or where the encephalocele is located in the nasopharynx, a transpalatal approach provides easier access to skull base defects and decreases the chance of damaging functional tissue [8,15,16]. For children with no preexisting cleft palate and who are very young, a combined transnasal and transoral approach can be used [17] as well as a transphenoidal sublabial microsurgical technique [18].

Endoscopic endonasal surgical technique

Surgical technique for endonasal approaches in pediatric patients are similar to those in adults. The patient is positioned supine with the head of bed elevated 30 degrees; a shoulder roll for next extension may improve access to the anterior ethmoid and frontal sinuses. The nose is decongested with oxymetazoline (0.05%). The middle turbinate and the sphenopalatine artery are blocked with 1% lidocaine with 1:100,000 epinephrine for hemostasis. Depending on the needed exposure, visualization, and pyriform aperture width, 4 mm and 2.7 mm endoscopes with 0, 30, 45, and 70-degree lenses are used. The middle turbinate may need to be removed for exposure. Nasal mucosa is incised and stripped off the enceophalocele including a cuff around the bony defect, which will allow future onlay grafts to adhere to the skull base. This nasal mucosa can sometimes be peeled off the encephalocele on either side and left attached to the surrounding nasal/nasopharyngeal tissue; this tissue can then be used as an overlay mucosal flap over the defect. Then, the encephalocele is reduced using bipolar or monopolar cautery [11,19,20]. Image guidance is useful for complete excision, especially with complex defects, multiple defects, and incompletely pneumatized sinuses.

Skull base reconstruction techniques

For small defects (<1 cm), fascia, fat, muscle, mucosa, cartilage, bone or a combination can be used. Cartilage and bone can be taken from the vomer and posterior cartilaginous septum, middle turbinate (if it is removed), or from the sphenoid rostrum. If a larger bone graft is needed, a calvarial bone graft can be used (Figure 2C).

For larger defects with high flow CSF leaks, vascularized tissue is recommended. This includes sinonasal flaps and scalp flaps. Sinonasal flaps include nasoseptal, inferior turbinate, and middle turbinate flaps. Other options include pericranial, galeopericranial, and temporoparietal fascial and temporalis flaps.

Reconstruction material can be used as inlay or onlay grafts. Inlay grafts are placed between dura and skull base and require elevation of dura from bone. Reconstruction options include abdominal fat, acellular dermis, and fascia lata. Onlay grafts are placed extracranially as a free graft or a pedicled vascular flap (nasoseptal flap, turbinate flap, regional flaps). These congenital skull base defects are typically small, anteriorly-located, and tend to approach midline where the crista galli would impede inlay graft placement. Thus, for endoscopic approaches, onlay grafts are preferred.[9] Reconstructed defects are often reinforced with tissue glue like Tissel and absorbable packing.

Nasoseptal flap

The nasoseptal flap (NSF) is one of the most commonly used flaps for skull base reconstruction. It is a mucoperichondrial/mucoperiosteal flap raised from the nasal septum with a pedicle based off the posterior septal branches of the sphenopalatine artery. The NSF is a reliable technique that has been shown to decrease CSF leaks in adults and children [21]. The size of the NSF in children may limit its use. A study of head CT scans shows that although the width of NSFs is adequate in any age, the length may be age dependent [21].

Antibiotics

The use of antibiotic prophylaxis for endoscopic skull base surgery in both children and adults is varied [22, 23]. One prospective study in adults suggests that 24-48 hours of postoperative antibiotics is sufficient in prevention of infection, regardless of the presence of a CSF leak [24]. Another author describes the use of clindamycin irrigation in the nose during the surgery and administering oral antibiotics for 2-3 weeks postoperatively [20]. In our practice, we administer intraoperative antibiotics and consider postoperative antibiotics if packing or a lumbar drain is left in place.

Lumbar drain

Some advocate routine placement of a lumbar drain in children as they are unlikely to adhere with CSF leak precautions postoperatively. However, this is not our practice as lumbar drain placement can cause infection, lengthen hospital stay and restrict movement. We recommend it is used selectively if hydrocephalus or a high pressure CSF system is suspected [7] or if an early CSF leak occurs postoperatively [9].

Pediatric considerations for surgery

Until age 6 or 7 years, the nasal aperture is much narrower than in adults and can limit access for endoscopic endonasal approaches or make surgical approaches more difficult. The intercarotid artery distances at the skull base are also narrower in children. Additionally, sinonasal and skull base growth centers, if disturbed, can impact craniofacial growth. The sphenoid sinus is not completely pneumatized until age 14, but this is not a contraindication for endoscopic skull base repairs [25]. Studies indicate that sphenoid pneumatization is progressive, with planum and sellar floor occurring by age 6 to 7 and superior clival after age 12 [25].

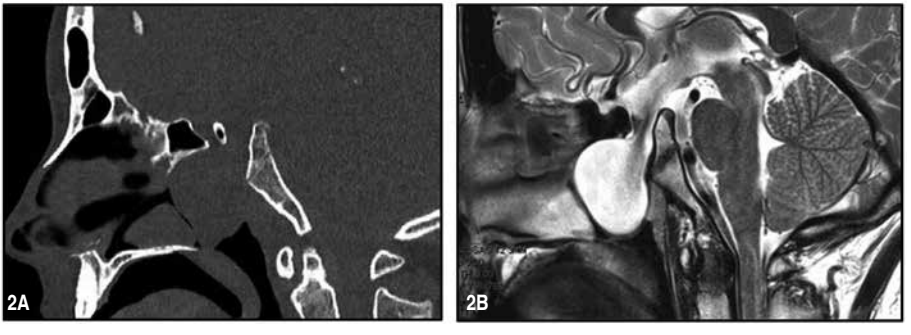

Figure 2A. Congenital Basal Encephalocele in a 17 year old male that was followed since infancy. Figure A shows a CT sagittal cut showing 2 skull base defects at posterior to the sphenoid sinus and anterior to the clivus with a bony rigde between the 2 openings. Figure B. Shows a T2-weighted MRI showing a large fluid filled mass extending into the nasopharynx that is consistent with cerebrospinal fluid.

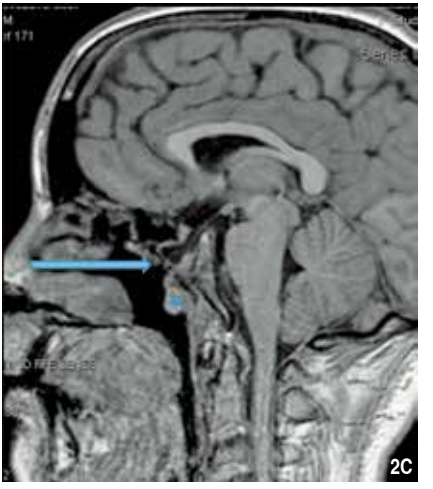

Figure 2C. Shows post-operative MRI T1-weighted image after the encephalocele was reduced to the clivus; the bony defect was repaired with an overlay pericranial bone graft (blue arrow showing the black linear hypodensity) secured with a single screw and flaps from the nasal lining of the encephalocele (blue star showing redundant nasal lining over the bone graft).

Complications

Overall, post-surgical prognosis is good with a surgery-related mortality rate of 3% [8]. Deaths reported in case series were often due to aspiration pneumonia and meningitis [8]. Location is not a significant predictor of outcome but isolated nasal encephaloceles without other defects such as holoprosencephaly or ventriculomegaly have a better prognosis [26].

Postoperative complications include impaired sinonasal function, neurovascular injury, CSF leak, CNS infection and damage to CNS tissue. Lastly, there is concern for long lasting cosmetic defects such as telecanthus. Endoscopic approaches seem to have little impact on craniofacial growth but data is limited [27]. Sinonasal complications include synechiae, nasal obstruction, nasal stenosis, chronic sinusitis, septal perforation, and change in olfaction. Younger children more frequently sustain minor trauma to nasal mucosa due to their smaller nasal cavities. Some recommend placing intranasal Silastic sheeting between the septum and turbinates to prevent iatrogenic synechiae [9]. Nasal alar erythema has also been reported in young children [13]. The external nasal skin can be very sensitive to the heat of the endoscopes and to stretching needed to fit instruments into the nasal cavity. A short course of postoperative antibiotic ointment helps prevent desquamation and scarring. Neurovascular morbidities can result from intraoperative hemorrhage, stroke and cranial nerve dysfunction/injury (i.e. vision loss, diplopia). Other complications include epiphora and seizures. Due to proximity to the pituitary gland, transphenoidal encephalocele repairs could cause diabetes insipidus and panhypopituitarism.

Conclusions

Pediatric encephaloceles and skull base defects can be repaired using an open, transpalatal, or endonasal endoscopic approach. Endoscopic repair has been shown to be

effective and safe and is becoming increasingly common. Much like adult skull base repairs, pediatric skull base defects can be repaired with either an onlay or inlay graft. Graft material will depend on the size of the defect and severity of the CSF leak. NSFs have been shown to be useful in children. Intraoperative image guidance has facilitated safe and complete excision of these lesions. Applications of new advances such as 3D printing may also help facilitate surgical planning and reconstruction [28]. Future work will be needed to assess long term outcomes of endoscopic resections on recurrence and complication rates, and effects on craniofacial development.

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Congenital nasal pyriform aperture stenosis

Hassan Ramadan, MD, MSc, FACS, FARS.

Introduction

Congenital nasal pyriform aperture stenosis (CNPAS) is one of the etiologies for congenital nasal airway obstruction and neonatal respiratory distress. It is an uncommon entity, first described in 1989 by Brown et al. [1]. Presentation can be variable depending on the severity of the narrowing. Infants can be asymptomatic, but also can present with cyclic cyanosis during feeding [2,3]. In its most severe form, CNPAS can cause life-threatening respiratory compromise [2-3]. CNPAS can present as an isolated anomaly or it can be associated with other craniofacial anomalies.

Anatomy, embryology and pathogenesis

CNPAS is the anatomical narrowing of the nasal bony pyriform aperture which is the narrowest and most anterior opening of the bony nasal airway [3]. It is thought to result from overgrowth of the nasal process of the maxilla at approximately 4 months in fetal development [4]. Another less accepted theory defends that CNPAS results from medialization of the normally shaped maxilla [5]. In either theory, the result is an increased nasal airway resistance with obstruction.

CNPAS can occur as an isolated anomaly, or it can be part of a syndromic constellation such as absence of the anterior pituitary gland, submucous cleft palate, hypoplastic maxillary sinuses, or prominent central incisor (mega-incisor) [6] (Figure 1). The most common associated craniafacial anomaly is solitary median maxillary central incisor (SMMCI), with reported incidence of 40-75% of CNPAS cases [7]. Intracranial anomalies can also occur as part of the holoprosencephaly sequence. Endocrine abnormalities involving agenesis or hypoplasia of the hypothalamus and anterior or posterior pituitary gland can also occur in up to 25-45% of patients with SMMCI [8]. Other syndromes that have been associated with CNPAS include Noonan Syndrome, hemifacial microsomia, and heminasal aplasia [9].

The exact etiologies of craniofacial anomalies are not known. However, factors that increase the risk of embryological defects may play a role in development of CNPAS. Maternal diabetes mellitus (MDM) may be one of those [10]. MDM is known to double the rate of congenital anomalies including congenital heart disease, genitourinary, gastrointestinal and musculoskeletal anomalies [11]. Other studies suggest that hyperglycemia during pregnancy may lead to orofacial clefts, facial deformities and defects

in neural tube closure [11]. Given the high incidence of congenital anomalies, including craniofacial and neural tube defects in these infants, MDM may be a risk factor for CNPAS [10].

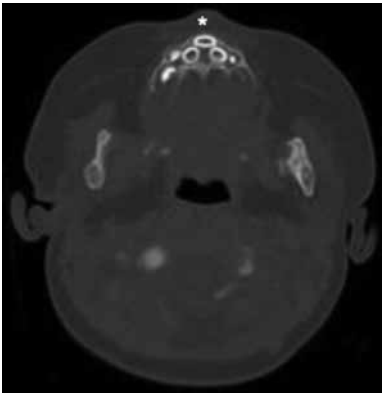

Figure 1. High-resolution CT image revealing central maxillary "mega-incisor" (white asterix).

Clinical presentation

Clinical presentation in patients with CNPAS can be variable. In some mild forms, infants can be asymptomatic. More severe forms present at birth with acute respiratory distress. Patients with associated syndromes also may have accompanying symptoms specific for other findings.

In a recent case series of 20 CNPAS patients by Shah et al. [10], the average age at presentation was 65 days (range of 1-906 days).

Neonates are obligate nose breathers until 4-6 weeks of life, and thus they can have a myriad of symptoms including labored breathing, feeding problems, recurrent cycles of cyanosis, and apnea relieved by crying [3]. Because the signs and symptoms of respiratory distress are often nonspecific, the diagnosis of pyriform aperture stenosis may not be considered initially [3].

Diagnosis

Once nasal obstruction is suspected, a thorough head and neck examination is warranted. Inability to pass 6 or 8 french catheter confirms nasal obstruction. Nasal anomalies presenting with airway obstruction include bilateral posterior choanal stenosis/atresia, bilateral lacrimal duct mucoceles, hypoplasia of the nasal alae, and CNPAS [12]. Nasal endoscopy using pediatric 2.4 mm flexible nasopharyngoscope after proper nasal decongestion and suctioning should be performed. In case of CNPAS, the endoscope can't be introduced past the nasal vestibule, with normal anterior nasal septum. Other associated craniofacial anomalies should be noted during a thorough physical examination. For instance, absence of upper lip frenulum will alert clinicians to the possibility of SMMCI [13]. Cleft palate and/or lip, hypotelorism, and microcephaly can be present especially when associated with craniofacial syndromes [6].

The gold standard test to diagnose CNPAS is maxillofacial CT scan with thin 1-2 mm cuts. Scan allows definitive evaluation of the nasal cavity including the pyriform aperture, nasal bones, and choanae. It helps in ruling out and differentiating other causes

of nasal obstruction, including obstruction from nasal septal deviation, choanal atresia or stenosis, or nasolacrimal duct cysts. Pyriform aperture width of less than 11 mm is diagnostic of CNPAS [3,6] (Figure 2). In two recent studies [9,10], CT scan was obtained in all infants who were diagnosed with CNPAS. The average narrowing of the pyriform aperture was between 5.3 and 6.41 mm.

MRI brain is usually considered when intracranial anomalies are suspected, like in cases of microcephaly and holoprosencephaly. However, even in cases of isolated CNPAS, MRI brain showed anomalies in 25% of the cases, including hypothalamic hamartoma, grade 1 germinal matrix hemorrhage, and bilateral grade IV germinal matrix hemorrhages concurrent with subarachnoid and subdural hemorrhage [9].

Diagnostic algorithm is suggested in figure 3.

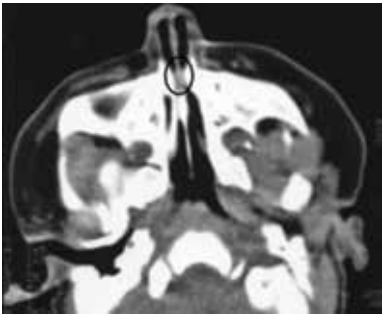

Figure 2. High-resolution CT image revealing bony stenosis at the pyriform aperture (narrowest area circled).

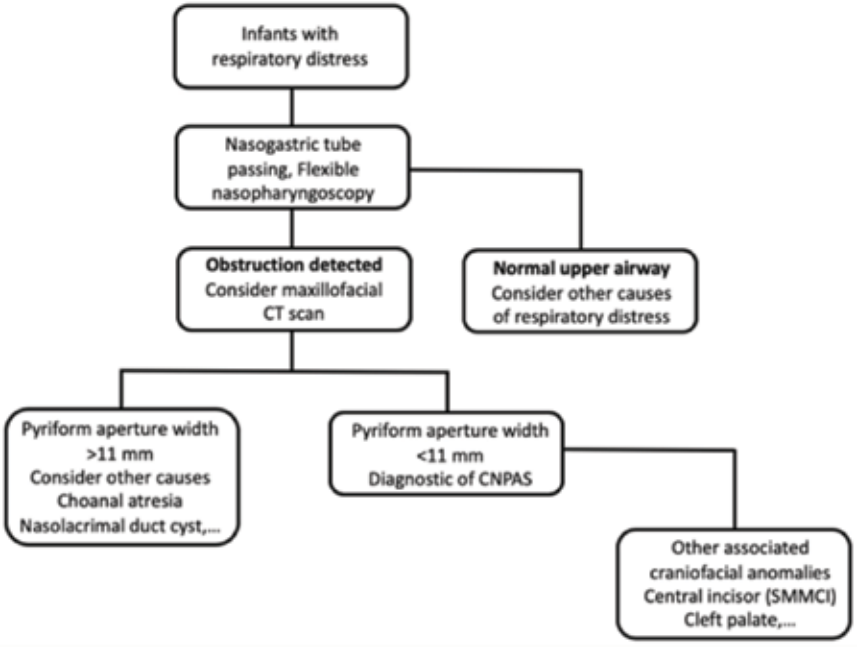

Figure 3. Diagnostic algorithm for congenital nasal pyriform aperture stenosis (CNPAS).

Management

Management of the airway

Patients with severe CNPAS usually present with respiratory distress at birth. They may need emergent intubation. However, respiratory distress can be relieved with oral airway as well. McGovern nipple is frequently used [12]. This is an intraoral nipple with a large opening by cutting its end off, secured in the mouth with ties around the infant's head [12]. If oral airway is not effective, intubation may be required. Tracheostomy is done when long term intubation is expected due to delay in repair, or due to other syndromic anomalies.

Conservative management

Medical management includes topical nasal saline sprays, short-term topical decongestants like neosynephrine or oxymetazoline, nasal steroids in the form of aerosolized nasal steroid spray, or antibiotic/steroid drops, specifically ciprofloxacin 0.3%/dexamethasone 0.1% otic suspension drops [3,6,10]. Success rate of the medical conservative treatment depends on the overall respiratory stability of the infant, and it can be up to 50% [10]. This treatment can be tried for minimum of 15 days as long as patients are stable, and can be continued for up to a year if successful (average successful medical treatment is 100 days) [10].

Surgical management

Patients who fail medical treatment or present with severe respiratory distress are good candidates for surgical repair. Patients who require surgery typically have cyclical cyanosis, apneic episodes, poor growth and failure to strive. Those patients are usually diagnosed at an earlier age [10]. One study [10] showed that patients with CNPAS who were successfully managed conservatively were diagnosed at an average age of 113 days, as compared to those who required surgical repair were diagnosed at an average age of 17 days. Of note, multiple studies [2,6,10,14] have shown no difference in pyriform aperture width between infants managed surgically and medically.

Nasal dilation is an option to consider before proceeding with more invasive procedures [15]. It is done under general anesthesia using various rigid dilators (e.g. Hegar cervical dilators), starting with 2 mm and going up to 4 mm diameter dilators. Patients may require more than one dilation. The rationale behind that is thought to be outfracturing and crushing of the inferior turbinates which allows more airflow in.

A more invasive and definitive treatment is bony drill-out. There is no standard surgical approach for repair of CNPAS, but the most commonly used one entails widening of the pyriform aperture by drilling the bony inlet while taking care to prevent injury to the nasolacrimal ducts and tooth buds. This allows 1-2 mm widening of the aperture on each side. It is most commonly done through a sublabial approach which allows an optimal exposure. Various types and sizes of bone drills or bony curettes can be used. It is important to protect the nasal mucosa to prevent synechiae and restenosis. This is followed by post-operative stenting for 1-4 weeks using 3.5 mm tubes. The optimal duration of stenting is still not determined and varies by surgeons' experience. Reduction of the inferior turbinates is often performed simultaneously prior to stenting. Duration of stenting should be weighed against potential complications of nasal stents which are mainly alar injury, vestibular stenosis, columellar tear, and stent dislodgement or blockage. Revision surgeries may also be needed in cases of restenosis secondary to intranasal synechiae.

A modified endoscopic assisted extramucosal approach [16] has also been described. A limited small sublabial incision is coupled with endoscopic endonasal visualization. This allows more accurate assessment of the nasal airway and better visualization of the nasolacrimal duct while maintaining an extramucosal dissection.

Novel treatment modalities have been reported with good success such as rapid maxillary expansion [5]. This technique allows widening of the nasal base, leading to reduction in nasal airway resistance It has shown good results and may become standard treatment for CNAPS in the future.

Treatment modalities are summarized in Table 1.

Treatment of CNPAS		
Medical	topical nasal saline sprays topical decongestants (neosynephrine, oxymetazoline) nasal steroid spray or drops	two weeks trial up to 50% success
Surgical	nasal dilation	2-4 mm dilators
	sublabial drill-out	Gold standard
	endoscopic assisted	
	rapid maxillary expansion	
Adjuvant	inferior turbinate outfracture	
	nasal stenting	1-4 weeks

Table 1. Summary of treatment modalities.

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Image guidance in choanal atresia

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Outline

I. Background.
II. Anatomic considerations.
III. Surgical approach considerations.
IV. Understanding image guidance.
V. Surgical technique.

I. Background

Choanal atresia (CA) is a congenital deformity causing nasal obstruction at the level of the choana, usually by membranous and/or bony septae that fail to recanalize during fetal development. The condition was first described by Johann Roederer in 1755 and occurs in 1 in 7,000 live births.

The cause of choanal atresia is unknown, but both genetic and environmental factors may contribute to the condition. CA is not unique to the human race: this diseasealso may affect domesticated camelids (alpacas and llamas). The regulatory gene CHD7 in alpacas has a homologue frequently associated with CHARGE syndrome in humans, and CHD7 mutations cause similar clinical manifestations in camelids.

The deformity has been linked to the use of thyroxin in women with maternal hypothyroidism in early pregnancy, where the risk ratio was found to be slightly increased at 3.14 for choanal atresia. However, it is unclear if thyroid treatments or thyroid disease were a factor. Additionally, infants with choanal atresia may have syndromes such as the CHARGE, Treacher Collins, Crouzon, and Tessier syndromes.

In 1979, B.D. Hall originally described the CHARGE association as a group of congenital anomalies that were associated with choanal atresia in 17 children [(3)]. That same year, Hittner et al. reported a similar association between colobomas and other congenital anomalies in 10 children with choanal atresia [(4)]. The acronym CHARGE referring to the non-random association between Coloboma, Heart defects, Atresia choanae, Retarded growth and development, Genital hypoplasia, and Ear anomalies / deafness was not established until 1981 by Pagon et al. [(5)]. Furthermore, the CHARGE association was not officially recognized as a "syndrome" until the CHD7 gene was discovered to be the site of the mutations leading to CHARGE abnormalities [(6)].

In 1854, Carl Emmert described the first surgical treatment for choanal atresia using a transnasal curved trocar. Surgical navigation in choanal atresia was introduced two decades ago, when Caversaccio and Hausler described the first image guided repair in 2000 [(7)]. In 2004, Ayari et al. demonstrated that choanal atresia repairs could be improved with CT-assisted resection of the atretic plate to prevent inadequate resection or re-treatment of stenosis caused by neo-osteogenesis [(8)].

II. Anatomic considerations

Narrowing in patients with choanal atresia may be bony and/or membranous, but is often a combination of the two. In normal human development, the medial aspect of the choanae is formed by the posterior edge of the vomer, the posterior-inferior boundary by the palate bone, and the lateral boundary by the thin perpendicular plate of the palatine bone and the thick pterygoid process [9]. The height of the normal newborn choana is approximately 8mm with a width of approximately 6mm [10]. The nasal cavity of patients with CA has been found to be narrower in terms of anterior bony width, anterior interorbital distance, and bony choanal aperture width. Posteriorly, CA patients have thickening of the vomer and a decrease in the nasopharyngeal vertical distance [11].

Diagnosis of CA is by physical examination. Anterior rhinoscopy will show mucoid obstruction of the nasal airway. Failure for nasal airflow to move a cotton wisp held outside of the nare indicates nasal obstruction, as does the failure to fog a mirror via nasal airflow. Inability to pass a trans-nasal catheter into the nasopharynx indicates CA. Transnasal fiberoptic examination shows closure of the nasal airway by a mucosally covered plate.

Non-contrast enhanced computed tomography (CT) is an excellent diagnostic tool for the assessment of CA. The hallmark of CA is a champagne flute appearance caused by the lateral nasal walls and vomer forming the curved base of the champagne flute [12].

III. Surgical approach considerations

The goal of choanal atresia repair is to widen the choana in order to improve the airway, which is crucially important for nasal breathing in newborn infants. While 6 x 8mm represents the normal opening in a newborn's choana, the width is limited laterally by the thick nasal walls. Bilateral choanal atresia is not geometrically resolved by creating a posterior window. Optimal airway patency demands resection of the posterior aspect of the vomer. Opening the vomer anteriorly opens the depth of the choanal region (see Figure 1) and has long been the mainstay of the surgical approach to safe choanal atresia repair.

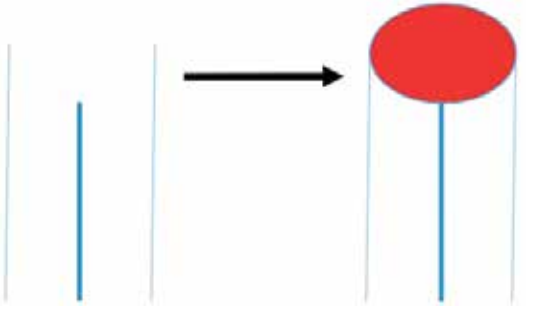

Figure 1. Opening the vomer anteriorly allows increased three-dimensional space in the posteriorly nasopharynx (thin blue lines = lateral nasal walls, thick blue lines = vomer).

While axial expansion is important, the skull base angle is also crucial for maximizing the three-dimensional assessment of the nasal airway and minimizing risks of

intracranial injury. In patients with CHARGE syndrome, the skull base angle slopes more quickly from anterior to posterior, thus limiting the nasopharyngeal diameter. In a study of 24 neonates with bilateral choanal atresia (BCA), the mid-nasal skull base height was 18.55mm in children with isolated BCA group vs 17mm in children with CHARGE-associated BCA (p=.053). The skull base slope was found to be 3.55 degrees in children with isolated BCA vs 5.33 degrees in children with CHARGE-associated BCA, but the sample size was too small to detect a difference [13].

While image guidance does significantly improve safety in choanal atresia repair, special consideration must be given to the neonatal population. Approximately 25% of children with CA have concomitant comorbidities to include otitis media with effusion, upper and lower respiratory tract diseases, cardiac anomalies, and gastrointestinal tract disorders. Children with BCA have significant correlations with cardiac disorders, CHARGE, obstructive sleep apnea, hematological problems, and prematurity or failure to thrive. These patients require a surgical team skilled in the care and perioperative management of complex pediatric disorders.

IV. Understanding image guidance

Currently, there are two main types of navigation systems that are commonly used for image-guidance in endoscopic sinus surgery: the infrared (optical) systems and the electromagnetic systems. While these systems use different technologies, the information provided regarding anatomical structures, position/size of lesions, and location of critical structures such as the carotid artery and optic nerve is very similar [14]. Additionally, both systems allow for real-time detection of surgical instruments throughout the procedures [15].

An endoscopic transnasal approach with image guidance allows the surgeon to repair bilateral choanal atresia in even the smallest neonates. By providing real-time localization of important structures, one can create larger openings with lower rates of complications at the skull base, lateral nasal wall, and orbit [12]. As choanal atresia is a relatively uncommon condition, few centers have large case volumes and image guidance can improve surgical safety in these low volume locations. Fellows, residents, and other surgical trainees can obtain surgical experience with supervision enhanced by image guidance. As choanal atresia is frequently associated with other congenital anomalies, image guidance can facilitate repair in patients with complicated choanal atresia, such as craniofacial syndromes or revision surgeries.

The accuracy of modern devices is excellent, even in pediatric populations. In 2015, Bergeron & Leclerc conducted a retrospective study on the precision of the calibration of the optical Stryker Neuronavigation ENT 2.0 system during endoscopic sinus surgery in children versus adults [16]. This study compared 38 adults and 21 children and found that there was no statistical difference between the two groups [16]. The precision of calibration in children was equivalent to the precision of calibration in adults. There was a mean precision of 0.7 mm in both groups with no major complications occurring during the procedures [16].

Limitations of image guidance are its cost, and the training required to use these systems. Training is generally straightforward, and with routine use across multiple surgical specialties, the cost consideration may be mitigated by the improved outcomes seen for patients.

V. Surgical technique

While newer electromagnetic devices such as the Medtronic StealthStation™ navigation system offer multiple emitters to allow for image-guided surgery in even the smallest infants, older systems can also be tailored for use in neonates and low-birth weight infants. Shah et al. describe a bilateral choanal atresia repair on a 2.1kg ten-day old infant using a completely transnasal endoscopic approach with the Stryker® surgical navigation system. A modified placement of the face mask allow allows for fitting to small infants. Under endoscopic visualization with image guidance, the mixed bony and membranous plate is punctured with a curette, then dilated with sounds to 8 French size. Back biting forceps are then used to resect 2mm of the posterior vomer. Eventually, the choana was widened to 4x4mm using true cut forceps. Topical Ciprodex drops were placed intranasally to discourage edema and stenosis [12].

An "inchworm" technique was utilized to fit the mask. The electrodes are compressed when there is available space on the bony skull with loops of non-adherent LED lights floating above the patient. The anatomic points are fitted using manual point-to-point registration with the facemask as the tracking device while maximizing the number of LEDs in the surgical field. Accuracy of 2mm is desirable and calibration can be checked between central incisors and the anterior middle turbinate [12].

Stents are an option employed by some surgeons to prevent stenosis. While some surgeons tout earlier discharge, less granulation and decreased numbers of re-operations with stenting, others find that stents cause more granulation, increased postoperative complications, and increased re-operations. A systematic review with meta-analysis examined 15 studies and found that success rates for bilateral choanal atresia repair are similar with and without the use of nasal stents. These authors did find that stents may be associated with more complications including alar injury, vestibular stenosis, columellar tears, and stent dislodgement or obstruction [17].

Stents may be useful when there is a thicker atretic plate or large amounts of bony exposure, although there is no current strong evidence to support their routine use. If stenting is desired, a modified RAE endotracheal tube stent conforms better to the natural angulation present at the nasal vestibule, where there is a natural downward turn. After placement, the end of the tube is trimmed so that its leading edge lies flush with, or just behind, the nostril opening. The stent is sutured into position with a transcolumellar suture through bilateral stents. Straight endotracheal tubes may impinge upon alar tissue, potentially resulting in pressure necrosis [18]. One case series describing the successful use of mometasone furoate-eluting stents to prevent re-stenosis in 3 patients shows early promise [19], however, more studies will be needed before this technique can be recommended.

Conclusion

Image guidance technology is very useful in creating wider nasopharyngeal openings with improved surgical safety. While image guidance is not a substitute for anatomical knowledge, it can be of special help in small infants, syndromic children, and in cases of re-operation and distorted anatomy. While image guidance does have some potential limitations, consistent use may optimize outcomes with more precise, safer surgery.

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Surgery for choanal atresia with a stentless folded-over-flap technique

Antonio Carlos Cedin, MD, PhD.

Since the first report of surgical treatment, in the middle of the 19th century, different techniques and approaches have been described.

There is only unanimity that the correction of bilateral atresia should be carried out as early as possible.

Regarding the ideal surgical procedure, it should provide adequate functional choanal patency, avoiding harm to any structure in development, enabling shorter surgery and hospitalization time with a minimum of morbidity and mortality [(2)].

I described a new endoscopic technique for surgical correction of choanal atresia using flaps fixed with fibrin glue to avoid the use of nasal stents or packing [(3,4)].

Surgical technique

The surgical procedure was carried out under general anesthesia, using propofol and remifentanil or propofol and sevoflurane. All patients were intubated with orotracheal tubes. I used a 4-mm 30° endoscope.

The septum, the atretic plates, and the sphenopalatinum foramen area were infiltrated with a 1:80,000 xylocaine and epinephrine solution, using a 1-mm syringe and a spinal needle. Additional vasoconstriction was obtained with cottonoid pads soaked in 0.5% oxymethazoline.

The resections were carried out by anteroposterior removal of the vomer using endonasal surgical instruments, such as cutting forceps, angled dissectors, curets, micro chisels, Freer type scalpels (with aspiration), and Blakesley-Weil type forceps.

In younger patients, otological surgical scalpels and Belluci-type scissors were chosen for the fashioning of flaps from the mucosa. Resection of the vomer and the removal of part of the medial pterygoid process is crucial for maintaining choanal patency in the long term follow up.

This technical detail is especially important in children with bilateral atresia, in whom the juncture of the widened vomer with the medial projection of the pterygoid processes determines the characteristic delta shape, contributing in a more significant way to the re-stenosis [2,3,6].

The mucosal flaps to protect the raw areas, fixed with fibrin glue, lead to a reduction of local bleeding, granulation tissue, and also scars. Consequently, there is a reduction in the rate of re-stenosis and an improvement in success rates [4,7].

This technique for correction of the atresia is performed according to the following steps:

Unilateral atresia (Figure 1).

1- Removal of the mucosa from the posterior septum and from the nasal face of the atretic plate (Figure 1A).

2- Removal of the vomer and the atretic plate preserving the pharyngeal mucosa of the atretic plate and contralateral side of the posterior septum (Figure 1B).

3- Fashioning the flaps from the preserved pharyngeal mucosa of the atretic plate by *"H"* shaped incisions (Figure 1C).

4- Using fibrin glue over the flaps (Figure 1D).

5- Folding over the flaps on the raw areas (Figure 1E).

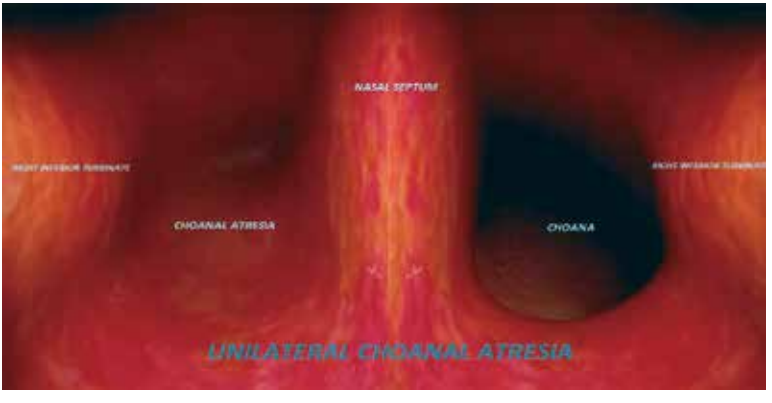

Figure 1. Unilateral choanal atresia.

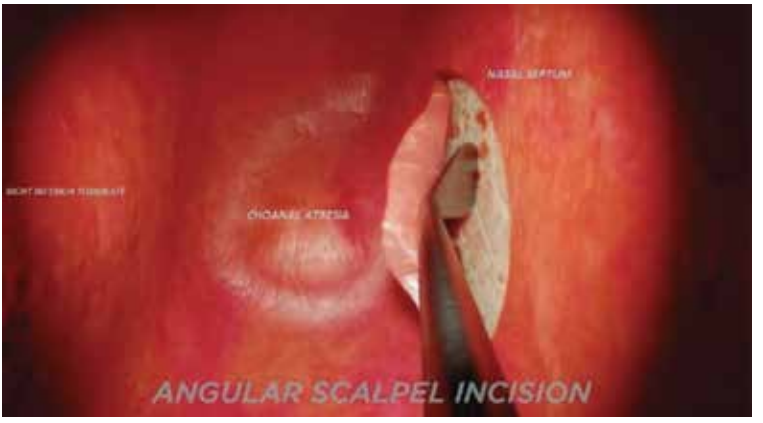

Figure 1A. Angular scalpel incision.

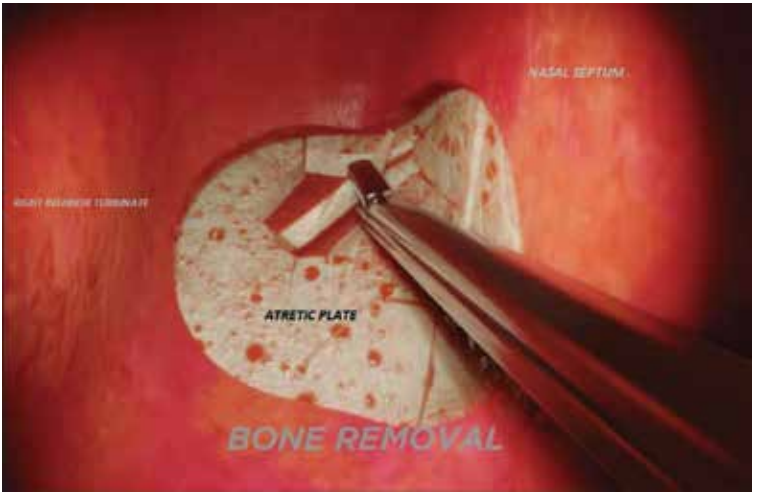

Figure 1B. Bone removal.

Figure 1C. H-shaped posterior mucosa cut.

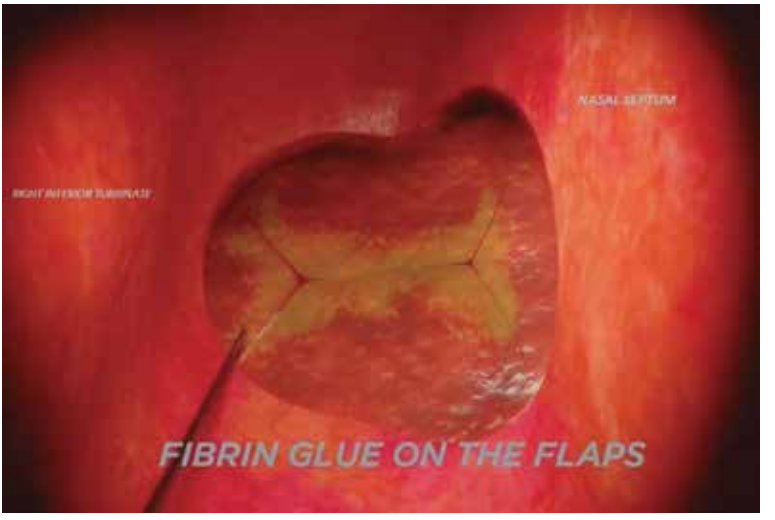

Figure 1D. Fibrin glue on the flaps.

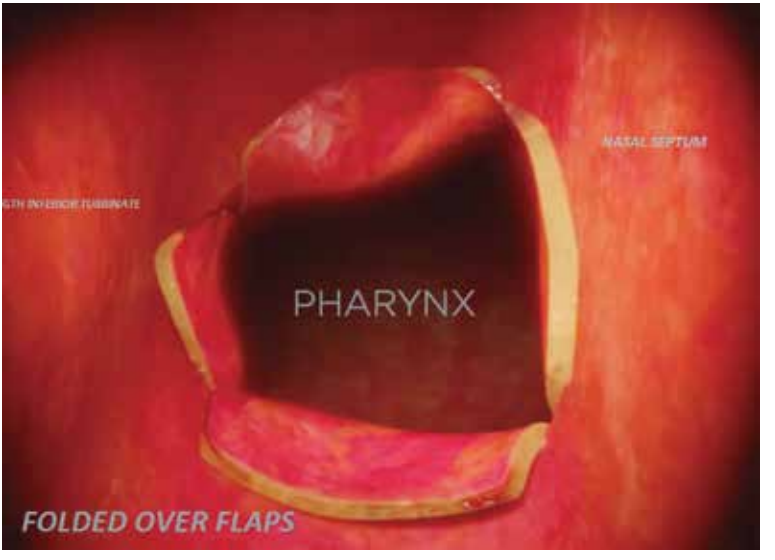

Figure 1E. Folded over flaps.

Bilateral atresia (Figure 2).

Removal of the vomer and the bony bilateral atretic plates, preserving only the mucosa of the pharyngeal face of the atresia and of the septum (Figure 2A).

Folding the flaps over the raw areas of the removed atretic plate and vomer and fixed them with fibrin glue (Figure 2B).

Figure 2. Bilateral choanal atresia.

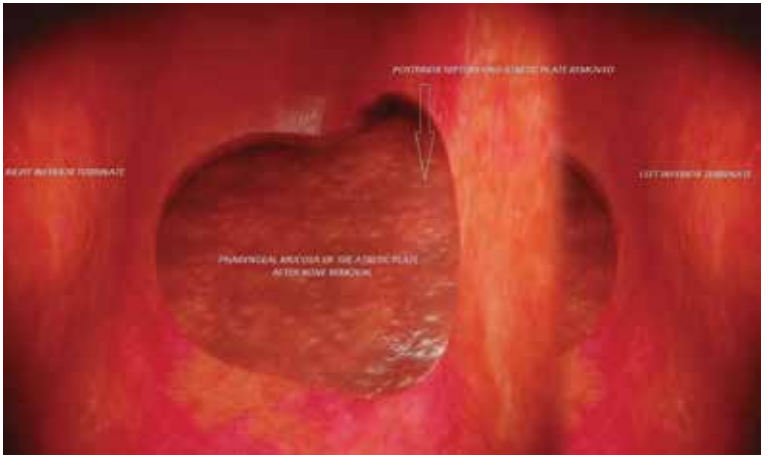

Figure 2A. Posterior septum and atretic plate removed, preserving only the mucosa of the pharyngeal face of the atresia and of the septum.

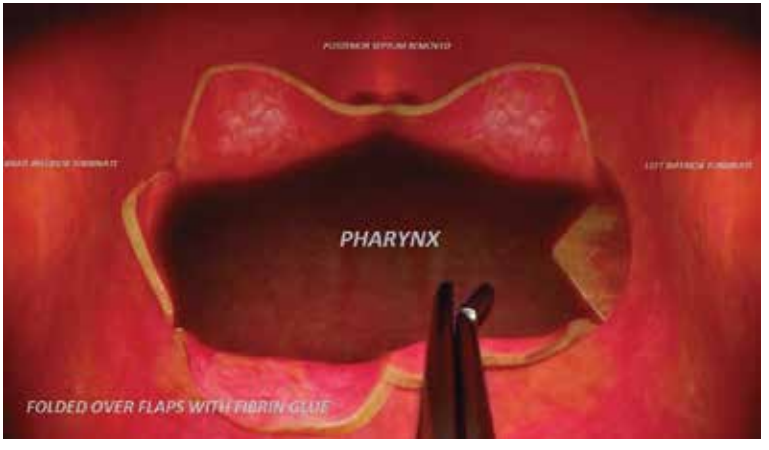

Figure 2B. Folded over flaps with fibrin glue.

However, there still is no consensus in the literature as to the ideal technique for managing this malformation [5].

I studied prospectively 21 patients to analyze the efficacy of my technique with long-term follow-up. In the postoperative period, the use of packs or stents is not necessary with any patient. Mouth feeding may begin on the first postoperative day.

There was need of only 1 revisional surgery for repair restenosis in 2 patients of this group. They were newborn with bilateral atresia.

All the patients who underwent surgery had satisfactory functional patency of the choanae, without respiratory discomfort in the follow-up from 6 months to 10 years. Definite choanal patency was confirmed with nasal endoscopy and CT.

The width of the new choana was nearly the same as that of the rhinopharynx in the axial view of the CT.

These results were analysed in comparison with those of other authors, selected by a systematic review of the literature a statistical analysis was done with the objective of determining if the use of flaps fashioned from mucosa, as part of surgical correction, diminished the number of restenosis (Table 1). The statistical analysis showed that the possibility of failure of flap thechniques was 9.25% compared to 30.0% of those that did not use them. The success rate with the use of flaps was 90.75% compared to 69.98% without the use of flaps. The odds ratio of 0.2376 (IC95%[0.1370;0.4120]) confirmed that the chance of surgical failure of techniques with the use of flaps was 23.76% of that of the risk to those without the use of flaps (Table 2).

There is a statistical significance between low rates of failures and the use of flaps.

	Technique		Restenosis	
Study	Flap	Nonflap	Flap	Nonflap
Anderhuber W, Stammberger H, 1997	0	7	0	1
Josephson GD et al., 1998	0	15	0	2
Saetti R et al., 1998	0	30	0	8
Wiatrak BJ, 1998	0	13	0	3
Gordts F et al., 2000	0	26	0	10
Dedo HH, 2001	18	0	2	0
Holland BW, McGuirt Jr WF, 2001	0	23	0	17
Rombaux P et al., 2001	0	38	0	23
Stamm A at al., 2001	33	0	6	0
Uri N, Greenberg E, 2001	7	0	1	0
Holzmann D, Ruckstuhl M, 2002	8	0	0	0
Khafagy YW, 2002	0	7	0	2
Van Den Abbeele T et al., 2002	0	40	0	6
Rombaux P et al., 2003	0	7	0	1
McLeod IK et al., 2003	0	6	0	0
Pasquini E et al., 2003	14	0	1	0
Triglia JM et al., 2003	0	58	0	3
Ayari S, 2004	0	20	0	12
Gujrathi CS et al., 2004	0	52	0	5
Schoem S, 2004	13	0	0	0
Bergonse et al., 2005	0	16	0	1
D'Eredita R, 2008	0	4	0	3
König AM, 2006	4	0	0	0
Önerci TM, 2006	24	0	3	0
Schraff AS et al., 2006	0	57	0	24
Sharma RK et al., 2006	0	13	0	6
Gosepath J et al., 2007	0	41	0	15
Yaniv E et al., 2007	17	0	1	0
Nour YA, 2008	14	0	0	0
Cedin AC; 2009	21	0	2	0
Total	**173**	**473**	**16**	**142**

Table 1. Surgery with Flap vs. Nonflap.

						CI 95%
	WITH FLAP	WITHOUT FLAP	Qui-SQUARE	p	(odds ratio)	(odds ratio)
Restenosis	16(9,25%)	142(30,02%)	29,5831	0,0000	0,2376	[0,1370;0,4120]
Success	157(90,75%)	331(69.98%)				
Total	**173(100%)**	**473(100%)**				

Less restenosis with flaps (p<0,001).

Table 2. Surgical success.

These results should be interpreted considering the limitations in the quality of the studies due to the lack of availability of controlled, randomized and blind trials, as would be normally required for more valid statistical evidence. However, we can consider that they corroborate a general impression from different authors, with show that these of mucosal flaps provides more successful surgery in the treatment of congenital choanal atresia and the use of nasal stents may be associated with more complications [6-8].

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Neonatal nasal obstruction: Congenital nasal pyrifirm aperture stenosis (CNPAS)

Scott R. Schoem, MD, MBA, FAAP.

Introduction

Congenital nasal pyriform aperture stenosis (CNPAS) was first described by Douglas in an adult patient in 1952. Brown et al. in 1989 reported the first known case in a neonate. This fetal developmental anomaly results in excess bone at the junction of the lateral nasal process of the maxilla, the horizontal process of the maxilla and the anterior nasal spine inferiorly. There is no yet known cause embryologically for isolated CNPAS. However, when associated with solitary median maxillary central incisor, this is part of the holoprosencephaly spectrum including absent upper labial frenulum, hypothalamo-pituitary axis abnormalities, and absent corpus callosum. CNPAS occurs in 1 in 25,000 births, less common than choanal atresia.

Clinical presentation

The presentation may range from mild to severe obstruction with cyclical cyanosis, respiratory distress and difficulty feeding similar to choanal atresia. The anatomical difference is anterior nasal obstruction rather than posterior nasal obstruction as seen in choanal atresia. Since stenosis usually allows passage of at least minimal air, the neonate may pass the "mirror fog test" but not allow passage of an 8 fr catheter. Flexible nasal endoscopy results may be variable but usually does not allow passage on at least one side. The child should undergo genetic and endocrine evaluations.

Radiology

Belden et al. established the computed tomography (CT) radiographic criteria with less than 11 mm width of the pyriform aperture as diagnostic of CNPAS. Wormald et al. determined that if the width is less than 5.7 mm, surgery is required to provide relief of respiratory distress. Brain MRI is warranted to assess for absence of corpus callosum. (Figure 1).

Treatment

Management depends on the degree of clinical severity and whether the CNPAS is isolated or syndromic. If isolated and mild, topical oxymetazoline and topical steroid drops may be sufficient as a bridge for a few weeks to provide symptomatic relief. If syndromic with multiple airway abnormalities, the neonate may require tracheotomy to provide a safe airway. Dilation has been reported to be successful in several cases to avoid surgical repair. When there is a reasonable chance of surgical success due to isolated but severe CNPAS, surgery may be performed through a sublabial incision elevating the submucosa off the nasal floor and medial maxilla, drilling down the bone until a 4 mm inner diameter endotracheal tube may be inserted and used as a stent for a few days. Some surgeons prefer not to place a stent. When the child is syndromic and has multiple multilevel airway anomalies, the most prudent course is to place a tracheostomy and defer surgery on the nasal deformity until the child is a little older. (Figures 2 and 3).

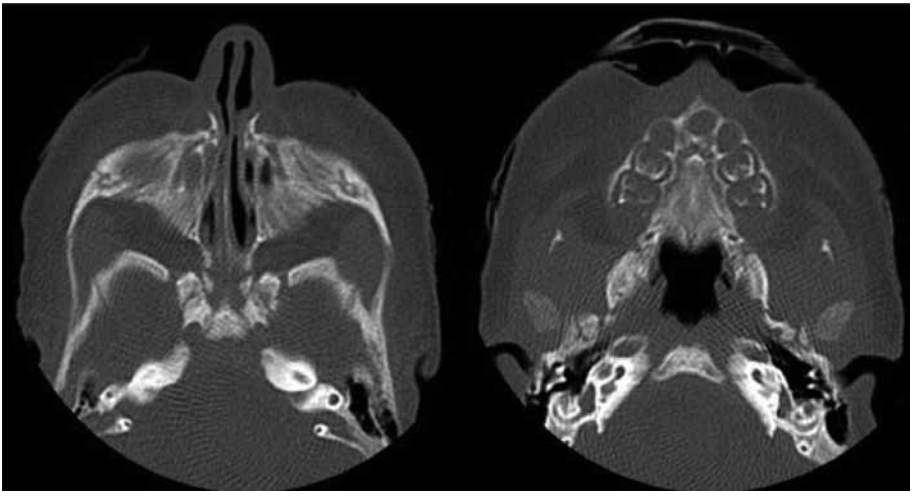

Figure 1. CT scan CNPAS.

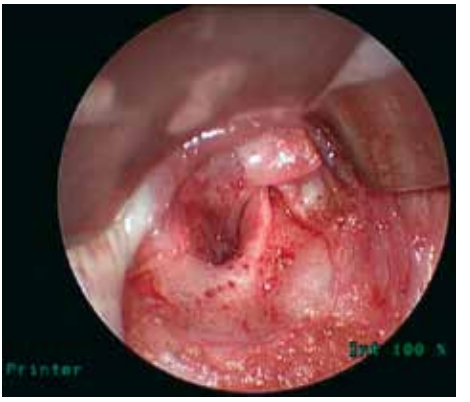

Figure 2. Endoscopic CNPAS.

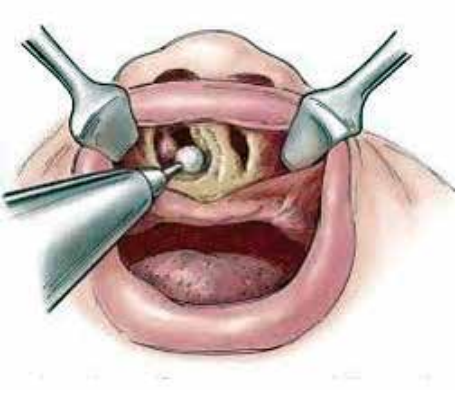

Figure 3. Surgery CNPAS.

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Dacryocystorhinostomy

Ian Selonke, MD, **Vinicius Fonseca**, MD, Prof, **Rafaela Sobreiro**, MD, Prof, and **Helen Mocelin**, MD, Prof.

Introduction

Since Toti's description of external dacryoscystorhinostomy (DCR) in 1904, most surgeries for clearing the lacrimal ducts system have been performed externally, which requires a facial incision in the lateral nasal wall, with the dissection of the orbicularis oculi muscle and the orbital periosteum, normally performed by ophthalmologists [1,2]. Although intranasal approaches to the lacrimal sac have been described since 1893, by Cadwell, due to endonasal access difficulties the technique became obsolete. Due to the development of endoscopic tools for nasal surgeries in the last decades providing high resolution images and offering excellent visualization inside narrow nasal cavities, the endonasal access has risen again the interest of researchers and surgeons in the lacrimal sac approach [4,5].

External DCR as well as internal DCR are surgical procedures that present good results to solve nasolacrimal obstruction. Several studies comparing them found success rates over 90%, without a significant difference between both approaches, however, failures still occur in approximately 5% to 10% of cases [6-9]. The main reported failures include nasal polyps and/or sinus diseases, canaliculus stenosis, sump syndrome (functional obstruction, with residual liquid accumulated in the lacrimal sac), inappropriate bone removal around the lacrimal sac, adherence between the lacrimal drainage ostium and the middle turbinate or other endonasal structures and the scaring of lacrimal drainage ostium [10,11].

The endoscopic technique described previously was performed by opening the lacrimal sac, in the lateral wall, anterior to the middle nasal concha, being the axilla of the middle turbinate the superior limit to the flap incisions, local described for the majority of the authors as the upper limit of the sac [12-15]. From the moment that it was demonstrated that the upper portion of the lacrimal sac commonly extend over the axilla of the middle turbinate and not only anterior to it, the making of the mucosal flap above the axilla of the middle turbinate enlarging the flag to 5mm has eased the marsupialization of the upper portion of the lacrimal sac, resulting in better surgical outcomes [16-19].

Welham and Wulc revised two hundred and eight (208) DCR procedures that needed re-approach and found out that the main reasons for the surgical failure were the errors related to the size and location of the ostium bone. They have also reported that incomplete overture resulted in the formation of a residual lacrimal sac, with consecutive infections and recurring symptoms, even in the presence of a patent ostium [20]. When Lin et al. evaluate the causes for DCR failures, whatever external or endoscopic ones, they observed that the inadequate removal of adjacent bone to lacrimal sac was the third most common cause linked to surgical failure. Being this the only variable correlated to the applied surgical technique [11].

Despite the superior lacrimal sac extension being well described in the literature [16-19], a challenge to endonasal surgeons is the demarcation of correct surgical margins for incision of the mucosa for posterior osteotomy above axilla of the middle turbinate. That is due to the great anatomic variation found in the lacrimal drainage system, also well described in literature. Thus, the pre-operatory evaluation, either by dacryocintigraphy, CT scan, transillumination optical imaging, or CT by dacryocisto-

gram (CT – DCG) is fundamental to help the surgeon concerning the extension and complete overture of the lacrimal sac [4,21,22].

Anatomy of the lacrimal system

Figure 1 illustrates the anatomy of lacrimal system.

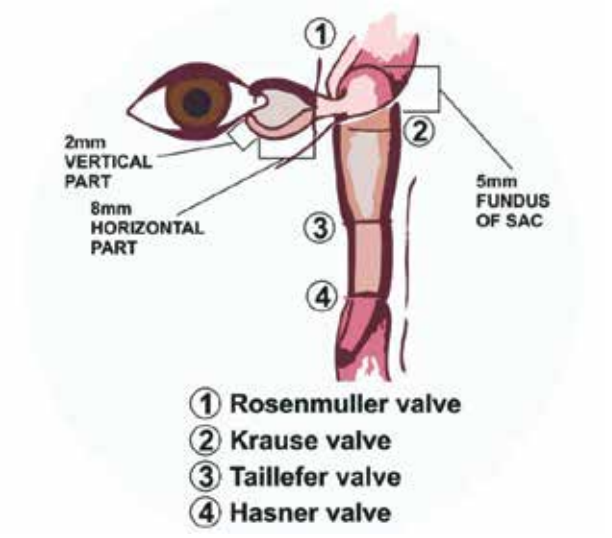


Figure 1. Lacrimal system.

The excretory lacrimal system drains the tear through superior and inferior lacrimal puncta, inferior and superior canaliculi, lacrimal sac and nasolacrimal duct. The blinking reflex also plays and important role in the lacrimal flux – it is called the lacrimal pump mechanism [19].

The lacrimal sac has an oval shape, measuring on average, 14mm high by 10mm wide. The lacrimal fossa is formed posteriorly by the lacrimal bone (thin and easily removed) and anteriorly by maxillary bone (thick and resistant). Both parts merge in a vertical suture, which can be surgically identified by an endoscopic technique. In the lower part of the bone begins the nasolacrimal duct, which flows into the inferior meatus about 10 mm posterior to the lower concha head. The lacrimal duct opens and tear flows through the lacrimal sac, in the junction of the upper third with the two inferior thirds.

The main complaint that takes people to evaluate the lacrimal duct is tearing. Unfortunately, it is a general and unspecific complaint, being necessary an ophthalmologist and an otorhinolaryngology's assessment to the differential diagnosis.

The cause of obstruction must be determined to a correct surgical approach whether it is high or low lacrimal obstruction. Imaging exams such as dacryoscintigraphy and dacryocistography help confirm the diagnosis after a thorough multidisciplinary clinical evaluation.

In cases of congenital lacrimal duct obstruction, it is paramount an interaction among the pediatrician, ophthalmologist and the otolaryngologist to a successful diagnosis and therapy. Normally a massage or an early probing can avoid a future DCR.

Congenital nasolacrimal duct obstruction is the most common cause of pediatric epiphora and can occur in almost 20% of newborns [23]. Almost all the cases (85-95%) are resolved without surgery or medication, until 1 year of age [24,25]. The cases that are not resolved spontaneously during the first year of life can require surgical intervention [26]. The most common surgical procedure used to treat nasolacrimal duct obstruction in children is probing, which is a safe and effective technique [27].

This technique consists in establishing a connection between the nasolacrimal duct and the nares by removing the obstruction at the distal duct. This is achieved by passing a probe through the punctum (variety of probes may be used for this procedure), along the canaliculus to the lacrimal sac, and down into the nares. The probe is first placed nearly perpendicular to the eyelid through the lacrimal punctum, then quickly turned to follow the course of the canaliculus parallel to the lid margin. Bone is felt when the probe encounters the bony medial wall on the medial side of the lacrimal sac. The probe is then turned 90 degrees and passed into the distal duct, through the obstruction into the nares. In most infants a popping sensation is felt as the probe passes through the obstruction [27,28] (Figure 2).

The presence of metal-on-metal contact when a second probe is passed into the nares to palpate the probe in the nasolacrimal duct can confirm that the probe has been passed successfully, and may help confirm that a nasolacrimal duct cyst or other abnormality is not present. Most doctors perform some sort of irrigation using a cannula after probing to ensure patency of the duct [28].

The reported rate of probing success is within 80–90% range in children aged less than 3 years, and remains high until 3 years of age, at this point success rates start to decrease [26-27, 29-30].

An alternative to the conventional blinded probing, especially in older children can be a surgical intervention by the introduction of an endoscopic probing in the nasolacrimal system [23,31-32]. It allows visualization of the lower end of the nasolacrimal system and of nasal anomalies such as the atresia, cyst, stenosis, and false probe passage [27] (Figure 3).

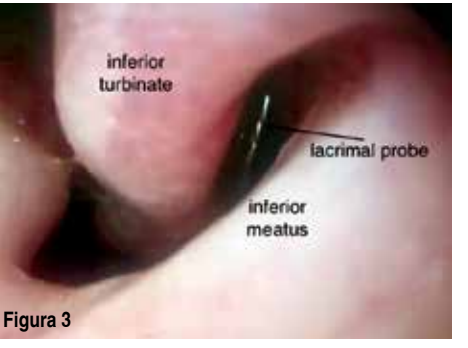


Figure 2. Image of the dilation of left eye inferior canaliculus with Bowman probe.
Figure 3. Endoscopic vision of left nostril showing the exit of a Bowman probe in the inferior meatus after canalization.

Complications such as bleeding may occur, which is common postoperatively, and can usually be controlled by digital pressure or home use of topical vasoconstrictors.

Many practitioners of this technique prescribe a short course of topical antibiotics with or without corticosteroids. Pain can usually be controlled with oral medications, and most infants recover quickly following the procedure [27].

For patients who have already tried the probing without success, patients with recurrent episodes of dacryocistitis with or without cutaneous fistula or those older than 3 years, it is recommended the Dacryocystorhinostomy (Figures 4 and 5).

Figures 4 and 5. Images of patients with dacryocistites and cutaneous fistula respectively.

Endoscopic dacryocystorhinostomy. Surgical technique

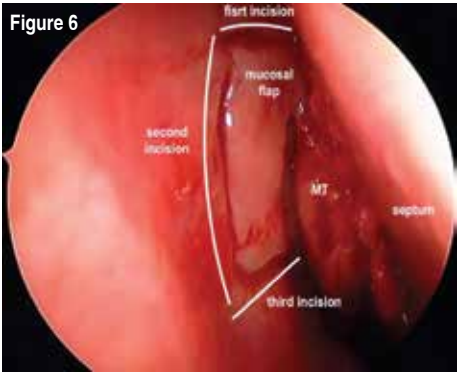
Preoperative care

The patients must be instructed to suspend the ingestion of acetylsalicylic acid or other non-hormonal anti-inflammatory drugs for at least 7-10 days before surgery. Other medicines that alters blood clotting (ex.: antiplatelet and any anti-coagulation drugs) also have to be suspended. In the presence of an acute nasal inflammatory process, antibiotics and oral corticosteroids are used. The risks and benefits of a surgery should be discussed with the patient, as well as the necessity of periodical post operatory revisions. Specific hospital consent must be signed. Always highlighting the possibility of use of a silicone tubing (silastic or other) in the lacrimal pathway, to be removed around a month after the procedure [19].

Under general anesthesia the patient is placed supine in a surgical table flexed approximately 30 degrees and the head rotated towards the surgeon (it is suggested in a unilateral surgery that the side should be shown and agreed with the patient while awake). A surgical video system is assembled to the surgery coupled to a 4 millimeter, zero or thirty-degree optic. After, a submucosal infiltration is performed in the nasal cavity septum (with xylocaine 2% with 1: 100,000 adrenaline) frontal process of maxilla, uncinate process, axilla of the middle turbinate and middle turbinate in the side to be operated. When necessary a septoplasty is performed to make easy the visualization of the middle turbinate since its head to the insertion in the axilla, as well as the frontal process of maxilla.

Insert neurosurgical patties soaked in a vasoconstrictor solution of adrenaline 1:4,000 in the surgical site mucosa. The first incision is made horizontally parallel to nasal floor, extend the incision in the axilla of the middle turbinate approximately 5 to 10 mm, approximately onto the line of the frontal process of maxilla. Turn to a second incision parallel to the first one, a bit lower, this line should be made between the half of middle turbinate or a two-thirty lower to the axilla of the turbinate, delimiting a flap which size correspond to the superior two-thirties of middle turbinate. Its extension

begins in the insertion of the uncinate process to the maxillary line of frontal process of maxilla. One must pay attention to the insertion of inferior turbinate, being careful to not injury it when making the flap. The third incision must be vertical and perpendicular to the nasal floor, joining the two first incisions, approximately 5 to 10 mm anterior to the insertion of uncinate process (Figures 6 and 7).



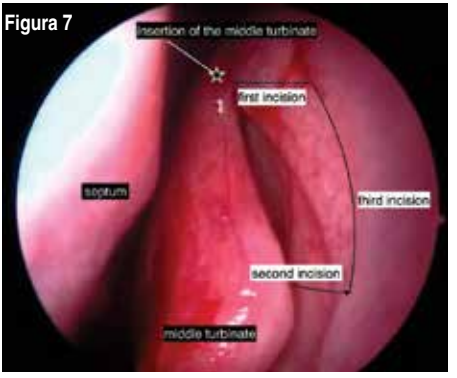


Figure 6. Endoscopic view of left nasal cavity, the white line delimitates incisions to create the mucosal flap. And the arrow draws the second incision.
Figure 7. Endoscopic view of left nasal cavity showing the 3 incisions in the DCR.

After performing these incisions, the subperiosteal mucosal flap with a posterior pedicle is raised to expose the maxillary frontal process to its articulation with the lacrimal bone. With delicate movements of a Cottle tweezers or a ball probe the lower articulation between the frontal process of maxilla and the lacrimal bone near the insertion of the middle turbinate is identified. At this point a Kerrinson punch is used to delicately remove a portion from anterior and medial bone of the frontal maxillary process, going up progressively to the bone in the insertion of the middle turbinate. The resection is done upwardly once it is believed to be the easiest way to expose the lacrimal sac. Bone density is thinner at the bottom and the use of Kerrinson is very efficient, since the ascending maxilla is thicker as it gets closer to the insertion of the middle turbinate. Thus, in case it is not possible to perform the osteotomy in this region using a Kerrinson punch, it makes necessary the use of a chisel or even a drill to a wider exposition of lacrimal sac (Figures 8, 9 and 10).

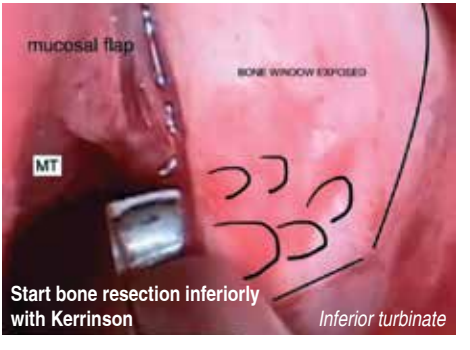
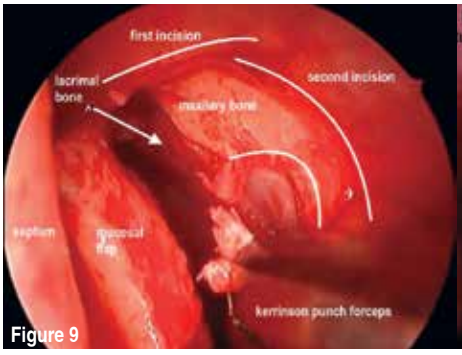


Figure 8. Endoscopic view of left nasal cavity, showing where an osteotomy will be performed with a Kerrinson punch.



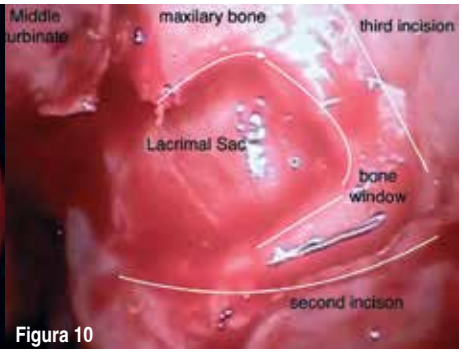


Figure 9. Broad view of mucosal flap, and the suture between the lacrimal bone and the maxillary bone.
Figure 10. Endoscopic view of left nasal cavity, exposing the lacrimal sac after opening of a bone window.

After exposing the lacrimal sac, a solution with xylocaine and vasoconstrictor is infiltrated in it. The objective is to dilate lumen as well as reduce bleeding after incision in the lacrimal sac. At this moment it is possible to visualize whether there is reflux of the sac content through inferior and superior lacrimal puncta or not. In the first situation, it is thought of a low obstruction favoring the result of DCR even without the use of silastic or Crawford probe. When the reflux cannot be seen favors a high obstruction at the height of Rosenmueller Valve, lacrimal puncta or even in the canaliculi. In these cases, it is necessary to reconstruct the lacrimal canaliculi with a Crawford probe (Figure 11, 12 and 13).

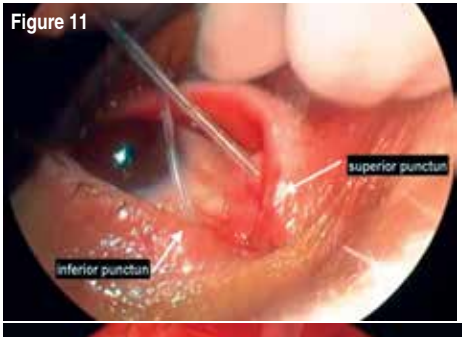
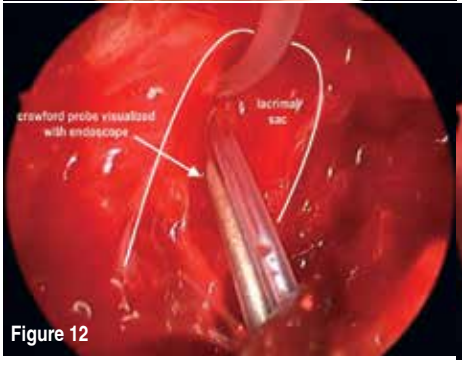
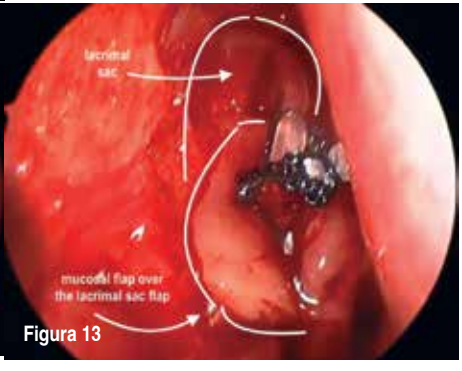


Figure 11. Probing superior and inferior pubtuns with crawford probe.
Figure 12. Crawford probe visualized with endoscope.
Figure 13. Repositioning of the mucous flap over the lacrimal sac flap,and below the silatic probe.





The fourth incision is performed right in the lacrimal sac also vertically perpendicular to the palate, parallel to the third incision, in the antero-medial face of lacrimal sac, take care not to cut or cause an iatrogenic lesion in the lateral superior face of lacrimal sac, avoiding trauma in the insertion of common canaliculi in the lacrimal sac floor (Figure 14).

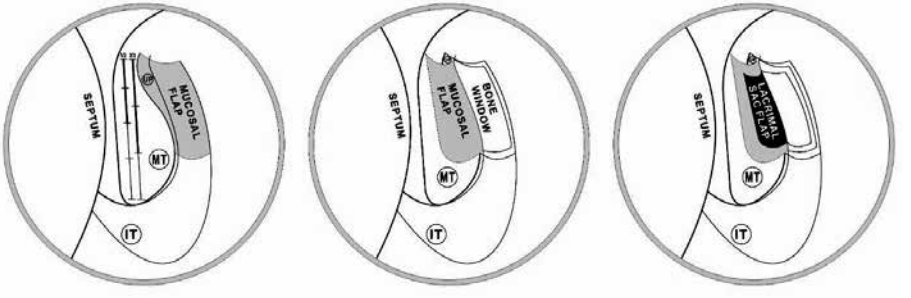


Figure 14. Drawing of the sequence of formation of mucosal flap, bone window and lacrimal sac flap.

After marsupialization of lacrimal sac, the opening of common canaliculus is identified with a Bowman probe after dilation and catheterization of upper and lower lacrimal canal. Both canaliculi are probed with Crawford lacrimal probe leaving them tied inside the nose.

Post operatory care

The post operatory care is the same as in any endoscopic sinus surgery. The recommendation is to sleep with the headboard raised. Avoid blowing the nose and performing vigorous physical efforts for about 10 to 14 days. It is important to wash the nose with saline solution. Frequently oral antibiotics are recommended (amoxicillin/clavulanic acid) for 5 to 7 days. Ophthalmologic drops with antibiotic and corticosteroids are prescribed for about 14 days. In case a silicone tube has been inserted, it is commonly removed in the doctor's office, from four weeks after surgery.

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Endoscopic sinus surgery in children

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Definition

Functional endoscopic sinus surgery (FESS) is a minimally invasive surgical treatment which uses nasal endoscopes to enlarge the nasal drainage pathways of the paranasal sinuses to improve sinus ventilation [(1)].

Historical milestones

– 1901, Berlin - Alfred Hirshman – first visualization of the nasal passage; he used a modified cystoscope.
– 1910, M. Reichart performed the first endoscopic sinus surgery using a 7 mm endoscope.
– 1925, Maxwell Maltz, MD created the term "sinuscopy," (the endoscopic method of visualizing the sinus).
– In the 1960s, Harold Hopkins – developes the Hopkins' rod optic system - the starting point of emergence and development of endoscopic sinus surgery.

– Endoscopic sinus surgery began in Europe with techniques described by Messerklinger and Wigand. The Messerklinger technique (1978) involves initially opening up the anterior area where the sinuses drain, the ostiomeatal complex. Wigand (1981) described increased access into the sphenoethmoidal recess by removing the posterior portion of the middle turbinate [2,3].
– Heinz Stammberger promoted the Messerklinger technique in Europe and then in America with David Kennedy in 1985 and 1986.
– 1989, Gross et al. published one of the first case series documenting functional endoscopic sinus surgery in the pediatric population [4].
– 1994, Poole suggested the term pediatric endoscopic sinus surgery (PESS) to mean FESS performed in pediatric population [5].

Problems

When we refer to FESS in children it is very important that the practitioners have a very good knowledge of the anatomy and development of the nose and the paranasal sinuses. ESS is more difficult in children than in adults, because of the children's smaller features [6].

An important difficulty of PESS is the tiny and thin intranasal features, or fragile anatomy of children. The high risk of injury to important anatomical elements requires a good ability of the surgeon to use the surgical instruments, as well as a rigorous control of both intraoperative and postoperative bleeding [7,8]. Wolf et al.[9] studied the development of the nasal sinuses in the skull and divided children into four stages corresponding to four age groups (first group – new born and infants to one year, the second group of children from one to four years, the third group of children from four to eight years and the fourth group, from eight years to twelve years), each group with certain caracteristics; he also described the clinical importance for PESS. Ramadan et al. [10], said that the results of endoscopic sinus surgery in children are age dependent because of the anatomy (that makes the procedure more difficult) and because of the immature immune sistem.

Initial concern that FESS may influence children's face growth has been overcome by a number of studies. Senior et al. [11] evaluated facial growth using CT scan images and volumetric analysis on patients who underwent sinus surgery due to orbital cellulitis and abscess, and re-evaluated the patients 4 to 10 years later and found that is not statistically significant difference between the sinus volume from the operated side to the non-operated side. Marcela R. Bothwell et al. [12] used quantitative anthropometric evaluation - 12 locations on the face were selected for measurements: nasion-gnathion, nasion-subnasale, nasion-stomion, zygion-zygion, endocanthion-endocanthion, tragus-nasion - right and left projection, tragus-subnasale - right and projection, tragus-gnathion -right and left projection. The measurements were repeated 3 times at each location. Different types of surgery were used for middle meatus antrostomy, ethmoidectomy either anterior or anterior/posterior, or a combination of procedures. There was no evidence that facial growth alteration will become clinically significant 10 years after FESS surgery. The same results reported Hebert RL and Bent JP [13] in 832 patients - no evidence of facial growth alteration.

Another problem was related to the need for surgical instruments and endoscopes corresponding to the age of the child. The 4.0 mm diameter endoscope is commonly used , but, if the child's anatomy is too small to accommodate the 4.0 mm endoscope, the 2.7 mm diameter endoscope can be used. The disadvantage of the 2.7 mm telescope is that it is more fragile and can be easily broken. Regarding the miniaturized versions of adult sinus surgery instruments, these are presently available from se-

veral manufacturing companies. From endoscopic sinus surgery performed with the surgeon looking directly through the optical telescope, to nowadays, when the use of digital cameras monitoring the surgery and microdebrider is part of the routine.

The role of imaging in PESS is very important. It is widwely accepted that CT scanning is the gold standard for imaging of the paranasal sinuses. CT scanning in the axial and especially coronal plane is the standard criterion for evaluation, with scanning intervals of 3 mm in the coronal plane. CT examination should not be a routine examination in order to not expose the child to unwarranted irradiation; it is a crucial imaging method and it is reserved especially when a complication is suspected.

MRI is helpful if further soft tissue delineation is needed to differentiate polyps, tumors, or allergic fungal sinusitis. It is also helpful if intracranial extension is suspected on CT scanning or clinical examination.

The role for plain radiography of the paranasal sinuses in children in preparation for endoscopic sinus surgery (ESS) is limited. Also, image guidance systems are used widely by otolaryngologists. Usefulness of image guidance systems is reserved especially for complex or complicated cases [14].

Indications

After the publication of the first studies studies on PESS, there appeared the need to standardize the indications of this type of surgery. Thus, in September 1998, in Brussels after the Consensus Meeting, the members of the Consensus Panel preferred to divide the indications for sinus surgery into absolute and possible indications [15].

Absolute indications are as follows:

1. complete nasal obstruction in cystic fibrosis caused by massive polyposis or closure of the nose by medialization of the lateral nasal wall,
2. antro-choanal polyps,
3. intracranial complications of sinus disease,
4. mucoceles and mucopyoceles,
5. orbital abscesses,
6. traumatic injury of the optic canal,
7. dacrocystorhinitis secondary to sinusitis,
8. fungal sinusitis,
9. some meningo-encephaloceles,
10. some neoplasms.

Possible indications are as follows:

1. Chronic rhinosinusitis that persist despite optimal medical management, and after exclusion of any systemic disease, endoscopic sinus surgery is a resonable alternative to continous medical treatment.
2. Optimal medical management includes 2 to 6 weeks of adeqate antibiotics (intravenous or oral) and treatment of concomitant diseases.
   Newer data from the literature classifies the indications as follows [16]:
   – In complicated acute and chronic rhinosinusitis.
   Complications
   – orbital involvement (cellulitis, abscess),
   – osteomyelitis of the frontal sinus (Pott's puffy tumor),
   – intracranial involvement (meningitis, epidural abscess, brain abscess).
   - Cystic fibrosis with worsened pulmonary function.
   - Nasal polyposis.
   - Fungal sinusitis.

Recent literature includes indications of FESS and surgical resection of anterior tumors in the skull, including juvenile nasopharyngeal angiofibroma.

The only absolute contraindication to surgery is the inability to undergo general anesthesia and a relative contraindication is an incomplete workup or inadequate maximum medical therapy.

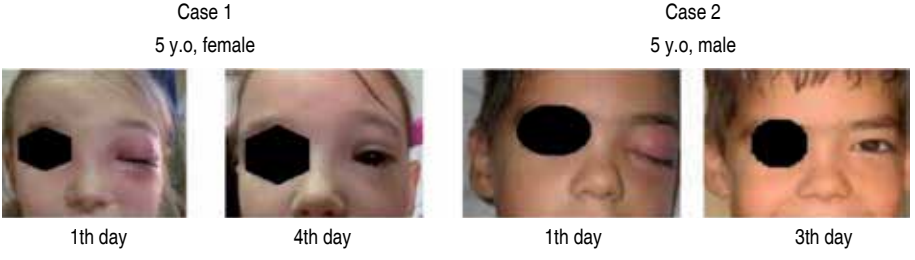
Regarding second look, the role is controversial. Can be considered in young children who are unable to clear their noses themselves, or children with severe risk factors or persistant disease (CF, ciliar diskinezia, allergic fungal sinusitis). Mitchell et al. [17] reported that second- look procedure has no value on the clinical outcome of PESS. According to Ramadan [18], adhesions and a scarred, narrow maxillary sinus ostium were the most common cause of failure in children after ESS. Presence of asthma at a younger age contributed to the failure in some of these children. Lazar et al. [19], found that postoperative synechiae are the most common postopertaive complication, irrespective of the age of the patient and consitute about 43%.

Basically, there were two major goals of surgery: (a) to re-establish a patent physiologic communication between the diseased paranasal sinuses and the nasal cavity with the least invasive procedure and (b) to preserve normal anatomy of nasal and sinus mucosa as possible. So, the aim of PESS was drainage procedure rather than extirpation procedure [20].

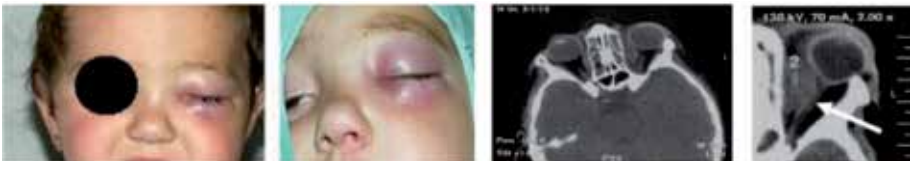
Complications of sinusitis in children

Coming back to indications, if we talk about acute rhinosinusitis, surgical interventions (including FESS), are usually considered for patients who have otherwise failed maximal medical therapy (antibiotics, corticosteroids, saline irigations) [21]. The main indications is complications of acute rhinosinusitis in children – orbital complications (cellulitis/abces) or brain abscess [22]. Oxford et al. [23] reports that 90% of complications of sinusitis in children - include periorbital/orbital cellulitis and subperiosteal/orbital abscess, Lerner et al. [24] 3% report intracranial complications and S.Hultman Denniso et al.[34], 4,2% needed surgery due to their orbital complications.

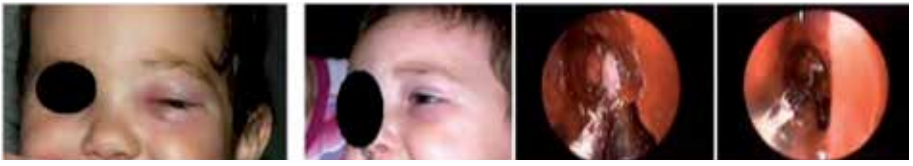
Cases 1 and 2. Orbital cellulitis. Conservative treatment



Case 3. 3 years old, female.

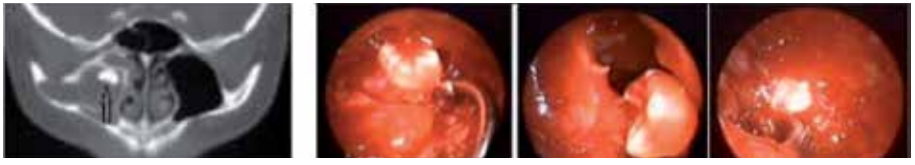


Preoperative – Clinical examination and CT scan.



5 hours postop. 19 hours postop. Orbital decompression with drainage of orbital abscess

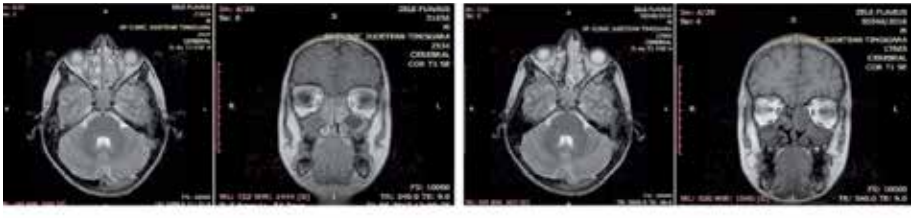
Case 4. Odontogenic sinusitis. Maxillary sinus ectopic tooth. 15 years old, female.
Preoperative CT scan and intraoperative view.



Cystic fibrosis and endoscopic sinus surgery

Cystic fibrosis occurs primarily in the white population in 1 in 2000 to 6000 births and is caused by autosomal recessive inheritance of mutations in the CFTR chloride transport gene, and exocrine gland dysfunction. Secretions become viscous and stagnant in CF patients and contributing to frequent bouts of CRS in the upper airway, and bronchopulmonary disease in the lower airway [24,25]. Indications for surgery are controversial, but center on symptom improvement and decreasing overall burden of bacterial disease. ESS in the CF population often has high rates of revision surgery and persistent radiographic abnormalities. Surgery is directed towards debriding affected tissue and creating large confluent cavities that will able to drain appropriately, as well to improve irrigation potential. Limited endoscopic medial maxillectomy - mega-antrostomy with takedown of the midportion of the inferior turbinate might to be effective tehnique to treat refractory cases [26].

Case 5. 9 years old, male.



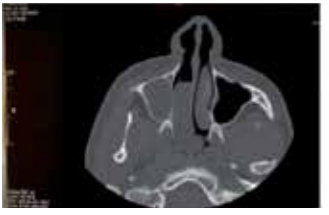
Preoperative CT scan CT scan after 4 years

Preoperative view – Revision surgery after 4 years

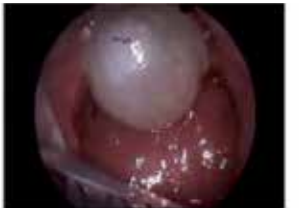
Antrochoanal polyp and endoscopic sinus surgery

Antrochoanal polyp constitute approximately 4-6% of all nasal polyps in the general population [27], while Cook et al. [28] found a higher incidence of antrochoanal polyp, approximately 10.4%. The etiopathogenesis of antrochoanal polyp has not been clarified. Chronic sinusitis and allergy have been implicated. Cook et al.[29] considers that approximately 70% of their patients with antrochoanal polyp had allergic rhinitis, while Lee and Huang [30] reports that 65% of the patients with antrochoanal polyp had chronic sinusitis. Treatment is always surgical, simple polypectomy and a Caldwell Luc procedure were the previously preferred methods; in recent years, endoscopic sinus surgery became the more preferred surgical technique. Anyway, endoscopic sinus surgery is a safe and effective method for treating antrochoanal polyp and consists of resection of the nasal part of the polyp and the cystic antral part with attachment to the maxillary wall via the middle meatus. Some authors used a mini-Caldwell approach with endoscopic sinus surgery or recommended powered instrumentation during endoscopic sinus surgery [31,32].

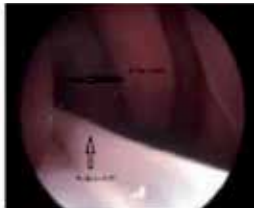
Case 6. Left antrochoanal polyp, 12 years old, female.



Preoperative CT Scan



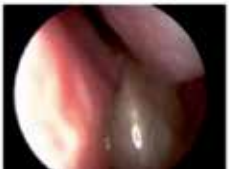
Antrochoanal polyp pluging



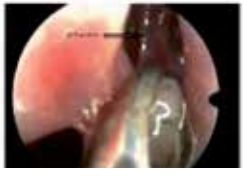
Intraoperative view from rhinopharynx

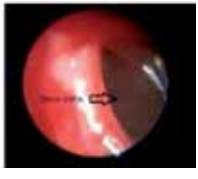
Case 7. Left antrochoanal polyp, 10 years old, female.

Preoperative CT scan



Preoperative view





Intraoperative view

Complications of endoscopic sinus surgery

Major complications after endoscopic sinus surgery include CSF leak, orbital injury and hemorrhage. Ramakrishnan et al.[33] reported an overall rate of major complications across all age groups was 1%, including CSF leak - 0.17%, orbital injuries - 0.07%, significant hemorrhage that required blood transfusion - 0.76%.

Conclusions

FESS - safe and effective method of treatment with minimum morbidity and complication rates. Preoperative imaging is necessary prior to surgical intervention in order to to allow the evaluation of the sinus anatomy and investigation into the extent of disease, CT scan being the golden standard. Pediatric sinus surgery is still progressing and it's role continues to be defined.

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Endoscopic closures of anterior cerebrospinal fluid leaks in children

Andreza Mariane de Azeredo, Bruna Machado Kobe, Camila Degen Meotti, MCh and **Otávio Bejzman Piltcher**, Prof DM.

Cerebrospinal fluid (CSF) rhinorrhea results from abnormal communication between subarachnoid and nasal / sinuses cavities, due to a defect in the skull bone, dura and arachnoid. CSF leaks are divided into spontaneous or traumatic and iatrogenic or non iatrogenic.

Etiologie of the anterior skull base defects in children are usually congenital, whereas most adult lesions are posttraumatic or iatrogenic [(1)]. On the other hand, with the increase of endoscopic surgeries to treat lesions of the ventral skull base, an increasing number of postoperative fistulas has been observed, with estimated rates in approximately 3.5–23% [(2-4)].

The diagnosis and management of pediatric CSF leak and encephalocele are challenging due to its rarity in pediatric population and difficulties in identifying main symptoms. Therefore, although these congenital defects are present at birth, it is likely that they are not diagnosed as early. High index of suspicion is required to diagnose these cases.

Congenital defects of the anterior skull base represent a rare group of craniofacial pathologies. The most common congenital defects include dermoid cyst, encephalocele, glioma, infantile hemangiomas and teratoma (5). Congenital meningoencephaloceles are rare, occurring in 1 of every 3000–5000 live births (10% present in the nose) [(6)].

Appropriate evaluation and early treatment are required to decrease the risk of meningitis [(5)].

A safe and efficient management of pediatric endoscopic skull base surgery requires a multidisciplinary team [(1)]. The optimal outcome relies on a detailed understanding of the pathology, of the sinonasal and skull base anatomy, of the location and extent of disease, and of the maintenance of sinonasal and neurologic structure and function [(7)].

Pediatric sinus anatomy

The main challenges about performing a pediatric endoscopic skull base surgery are their immature anatomy (small nares, sinus size and pneumatization, growth of the skull and midface), smaller blood volume, maintaining the function of the involved structures and olfaction preservation [(8)]. Since pediatric skull base is still developing and the anterior skull base grows at a faster rate than the posterior skull base, extensive surgery on this region may have an impact on the normal facial development [(9)], as well as an increased risk of neurovascular injury [(10)].

In order to foresee or to reduce risks, we must understand the development of the main skull base structures involved in this type of surgery: The ethmoid sinus is present at birth. Its pneumatization begins at approximately 1 year of age and continues until around the age of 12 years old, becoming patent around the age of 4 years old. Along with the ethmoid sinus, the sphenoid sinus pneumatization also proceeds well into adolescence - beginning at the anterior inferior sphenoid face and proceeding posteriorly - to reach its adult size around the age of 16 [(9)].

Studies show that around the age 6 to 7 years old the sphenoid face is fully pneumatized and the planum sphenoidale is nearly 90% pneumatized - the sellar type pneu-

matization pattern is the most characteristic one at this age. The complete pneumatization to the planum is generally considered sufficient to allow access to the anterior fossa without implying a significant risk to the surrounding structures. The clival recess pneumatization occurs at age of 10 [10].

In younger children, the nasal aperture, the intercarotid distances, and the transsphenoidal angle are also smaller, restricting endonasal approaches [9]. The mean nasal aperture in children between 2 to 4 yo is reported as 6.7 mm, increasing to 9.3 mm by adolescence. A similar distance growth occurs with the intercarotid distance, which increases minimally from 11.3 to 14 mm in the mentioned age groups. The transsphenoidal angle corridor is reported as 14.9 degrees in the youngest group, increasing nearly 40% by adolescence, depending on pneumatization pattern and the nares-sellar distance, which also increases with age [8].

The use of navigation system can help, especially in cases where there is a greater amount of bone to be drilled.

Diagnosis

CSF leak can be detected through a detailed history combined with nasal endoscopy, biochemical and cytological analysis and image exams.

Symptoms vary depending on the etiology of the leak, which can be displayed as nasal obstruction, recurrent meningitis, midline facial changes, and/or rhinorrhea (mostly unilateral and watery) [11]. Given that intranasal encephaloceles have less evident external manifestations, their presentation can be more insidious, varying from nasal airway obstruction to frank meningitis at a wide range of ages [12].

After a accurately collected medical history, if the complaints give us grounds to suspect CSF rhinorrhea, a visual examination involving nasal vasoconstriction and forward flexion of the head may be performed: any leaking of clear and colorless fluid may be indicative of overt CSF rhinorrhea. Differential diagnosis of CSF rhinorrhea must be made considering allergic or vasomotor rhinitis as well as a postoperative condition following rhinosurgery.

Flexible endoscopy is cost-effective and much useful to diagnose an upper airway malformation that can appear as an intranasal mass. Anterior (or ethmoidal) malformations are the most common and appear as a translucent sac along the cribriform plate adjacent to the middle turbinate vertical attachment, and usually its content does not involve vital structures [13].

In order to confirm a CSF leak, testing clear rhinorrhea for beta-2 transferrin or beta trace protein is the initial method of choice, because they are both present in the CSF at high concentrations [14]. However, even in cases of active leakage, it is difficult to collect a sample, especially in children.

Mixed with blood, CSF drops appear as a typical light-yellow halo sign around the central blood spot on either gauze, tissue or bed linens. This is known as the "halo sign" or "double ring sign". It used to be considered the earliest symptom of traumatic CSF rhinorrhea [15]. This sign appears if the CSF mixed with blood is at a concentration of 30 to 90%. Nevertheless, it has been proven that this sign is not specific for cerebrospinal fluids - if mixed with other clear fluids (as tap water or saline solution, for instance) blood drops will also appear with a halo sign around it [16]. Therefore, current recommendation is to avoid the ring sign in diagnosing a CSF leak [14].

Glucose testing of the fluid was also traditionally considered an option for CSF leak confirmation. Yet, due to its low specificity and sensitivity, one should avoid this test [14].

Preoperative imaging, including computed tomography (CT) and magnetic resonance imaging (MRI), are of paramount importance in the detection of the defect site along with the choice of the best operative approach and the proper reconstructive graft material for it. A thin slice CT appears to be the best method for this purpose. Furthermore, the CT exam can be performed with intrathecal administration of contrast (cisternography) to confirm and identify the leak site [17].

MRI is a noninvasive study and is able to confirm and localize the leak. T2-weighted images are the most important, showing an inherent bright signal of CSF passing from intracranial into paranasal sinuses, as well as identifying the herniated soft tissue through the skull-base defects [14].

Intrathecal administration of sodium fluorescein solution through a lumbar puncture can allow the visualization of the solution in the nose during an endoscopy, which may also confirm the diagnosis and the localization of the CSF leak. The use of intrathecal fluorescein for this purpose is still off- label, in spite of being considered a legitimate diagnose option [14]. However, such as the CT cisternography, these are invasive tests and should have a limited use in children. Thereby, its recommendation must be individualized for each case [18].

Conservative treatment

Conservative treatment consists in measures as bed rest, head elevation, lumbar drainage, diuretics, antiemetics and antitussives drugs, strict blood pressure management and avoidance of Valsalva maneuvers. The goal of these measures is to reduce the active flow through the leak and the CSF pressure, allowing the defect to heal by sealing the leak without surgical intervention and skull base reconstruction techniques.

Traumatic (non iatrogenic) leaks usually resolve themselves spontaneously with conservative measures. Nevertheless, its repair should be considered if the leak does not heal within 1 to 2 weeks of the trauma, in order to prevent meningitis. Iatrogenic CSF leaks generally occur under skull base resections or sinus dissection surgeries. For these particularly leaks, immediate closure is required [7, 17].

Surgery

The surgical approaches and techniques are dependent on the location of the lesion, the pathology, the extent of the disease, and the surgical goals [19].

In order to decide the best approach, one must consider the surgeon's expertise and comfort level with each technique.

Endonasal or open surgery

Traditionally, anterior skull base encephaloceles were managed with open craniofacial approaches, which often combined craniotomy with intranasal techniques [20]. Craniotomy provides direct access to the defect and allows not only the repair of multiple sites of leak as well as the repair of large bone defects [18,21]. Complications associated with open approaches to the anterior skull base, including cerebrospinal fluid leak, meningitis, intracranial hemorrhage, and pneumocephalus may occur in more than 20% of the cases [22].

Following the first report by Wigand in 1981, pediatric endoscopic endonasal surgery has become a prevalent method for treatment of multiple malignant and benign lesions [7; 19]. In the last several years, the endonasal endoscopic approach in children

has experienced a significant progress [7] due to the variety of technologic and surgical advances, multidisciplinary team approaches, and continued innovation [19].

The main advantages of endoscopic surgery are less blood loss, less possibility to hinder normal growth of the skull and midface [8], avoidance of craniotomies, external incisions, brain retraction and neurovascular manipulation. Atop of that, it provides visualization of transcribiform, transtubercular, transsellar, and transclival areas [8]. Which all together has decreased complication rate and hospital stay in endoscopic skull base surgeries [17].

The major concern for isolated transnasal approach is the compact anatomy that may hinder endoscopic repair, especially in very young children. However, several studies suggest that endoscopic approaches remain a safe and effective intervention for managing these lesions. Thompson et al., in a multi-institutional retrospective study, showed that congenital encephaloceles in children as young as 2 months old were successfully repaired using endoscopic techniques [12]. Nation et al. have shown that this kind of approach is safe even in the youngest patients (less than 6 years) [23].

The endonasal endoscopic approach has become the gold standard for treating CSF leakage in the anterior floor of the skull base. This technique provides a less invasive and less morbid therapy option [5].

Finally, although recognizing the advantages of endoscopic transnasal skull base surgery, when chosen this technique one must also be prepared to switch to an open procedure if necessary.

Considerations in endoscopic approaches

It is essential that nasal cavities are decongested properly, so that the operative field is as large as possible. Adrenaline-soaked patties can be used in children. In addition to that, great care must be taken to avoid mucosal trauma (mainly septal) and blood loss.

A combination of miniaturized instruments and an adequate nasal endoscope gives an excellent visual field and an adequate working space [24]. Due to the lack of space, many surgeons use a 2.7 mm pediatric endoscope, but most cases can be safely performed with 4-mm, depending on the patient's age and nasal cavity size. If specific delicate endonasal instruments are not available, ear instruments can assist.

The treatment of congenital defects involves specific surgical difficulties. In fact, in such cases the intraoperative localization of the defect might be difficult. However, in most patients, the defect can be correctly localized by direct endoscopic view [1]. In addition to identifying the exact location of the fistula, the defect must be circumferentially visualized.

In cases of encephalocele, in which herniated brain tissue is typically nonfunctional, steps are basically removal (reduction) of the intranasal mass (sac and contents) with bipolar coagulation and micro instruments, exposure of the defect, removal of all the mucosa around and, finally, reconstruction. We must always keep in mind that removal of structures (bone or cartilage) should be as minimal as possible to prevent damage to the nasal growth.

Due to the small size of the nasal cavity in the pediatric population, special care should be taken with synechiae. Silastic sheet can be placed in the nasal cavity to sustain the graft and also prevent postoperative synechiae between the lateral and medial walls of the nasal septum [1].

The specific indications and usefulness of lumbar drainage remain to be determined. Di Rocco et al. have demonstrated that even some large defects with abundant CSF rhinorrhea can be successfully cured endoscopically without using a lumbar drain. The authors recommend its use preoperatively in cases of abundant CSF leak or postoperatively in cases of early recurrence to facilitate the sealing [1].

Reconstruction

Skull base reconstruction, either by correction of isolated CSF fistulas or after resection of benign or malignant lesions, aims mainly to interrupt the flow of CSF in the nasal cavity and to prevent contamination of the intracranial space.

There are several types of grafts available, such as bone, cartilage (septal or conchal), muscle, fascia (lata or temporalis), fat, mucosa, as well as synthetic materials. They can be positioned as underlay (between dura and skull base, in the cranial side) and/or overlay (over the nasal side of the defect) fashion. Multilayer closure strategies have been successfully used to seal skull-base defects.

The advantages of underlay grafts are that they are firmly stabilized between the bone and dura mater and they cannot obstruct the frontonasal duct. However, elevation of the dura from the underlying bone may traumatize critical structures, especially the olfactory bulb [1].

The type of graft, its over or underlay positioning, and the use of fixators (fibrin glue, Surgicel) did not influence the surgical outcome [1].

Very small defects can make it difficult to place underlay grafts. In these cases, overlay graft may be sufficient.

When using overlay grafts, it is important to carefully remove all the mucosa surrounding the edges of the defect to promote watertight adhesion between the graft and the overlying bone [1]. The major disadvantage of the overlay technique is the risk of obstruction of the frontonasal duct when sealing anterior defects.

Overlay grafting may be performed with a free mucosal graft or a vascularized pedicled mucosal flap. The most used flaps are nasoseptal, inferior turbinate and middle turbinate, all of them vascularized by branches of the sphenopalatine artery [7].

The nasoseptal flap (NSF) is the most popular vascularized pedicled flap, described by Haddad et al. in 2006 [25]. The anatomical differences seen in pediatric patients make this kind of repair more challenging, due to the reduced septal surface area and the diminished range of flap rotation [26], requiring additional preoperative planning and specific operative techniques. Despite these obstacles, the NSF is the most reliable option for repair of extensive anterior skull base defects in the youngest patients, including infants. Pediatric skull base reconstruction using the NSF has similar outcomes to adults, with overall low rates of CSF leak [27].

If nasal packing is required, it can be removed in the operating room, under anesthesia, depending on the patient's age. At this time, an appropriate endoscopic review can be performed. Dissolvable nasal packing can also be a good option in children, as they do not need to be removed.

Follow-up

The postoperative period is another peculiarity of endoscopic surgeries in children, due to the difficulty in performing endoscopic exams and frequent aspirations.

Long-term monitoring is necessary in all cases, as complications can develop months to years or even decades following the surgery. Sinus complications can develop such as sinusitis or mucocele formation due to scar tissue formation and sequestration of mucosa. Finally, facial growth can be affected by disruption of any growth centers [5].

Di Rocco et al. recommend imaging follow-up lasting at least 5 years, especially in the case of anterior defects located nearby the frontonasal duct and treated with an overlay technique [1]. CSF leak recurrence might occur especially during the first 2 years after the endoscopic repair [28].

Conclusion

We should always share concerns with the family and explain about the natural evolution of these cases and also the possible complications and complaints due to nasal anatomical modifications. ENT's (ear, nose and throat surgeons) must be part of the team from diagnosis to treatment. Generally, most cases among children may be treated isolated by an otorhinolaryngologist. Nevertheless, there should always be a neurosurgeon evaluation from the beginning, in case a combined approach becomes necessary.

Although there is still a need for better data to define if there is any difference between endoscopic techniques and materials in terms of efficacy and effectiveness, studies show that transnasal endoscopic approach for treating anterior skull base defects is minimally invasive, efficient, and safe in pediatric patients.

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Cystic fibrosis surgery

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Introduction

Cystic fibrosis (CF) is an irreversible autosomal-recessive genetic disease whose problem is located in the long arm of chromosome 7 (7q31). It affects about 70,000 children and adults worldwide and its incidence varies in different countries or regions. It is most often diagnosed in white populations of Caucasian descent, with a frequency of 1 in every 2,000 to 3,000 newborns in the European Union, and in the USA this frequency is 1 in every 3,500. In countries with a heterogeneous ethnic composition, a lower frequency of CF is observed, as in Brazil for example, where it is estimated that the incidence is 1 in 7,358 live births [(1)].

The genetic alteration causes dysfunction of the protein Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), located in the apical membrane of the epithelial cells of many organs and whose main function is to be a chlorine transport channel. Due to the defect in anionic transport on the apical surface of epithelial cells, there is an increase in the absorption of sodium and, consequently, of water in the luminal surface. As a result, exocrine secretions change their composition, changing their density and viscosity, leading to the occurrence of inflammation and recurrent infections [(2)].

About 1,872 mutations that cause CF have already been registered in a database, the Delta F508 being the most common. It results in a systemic disease, preferentially affecting the respiratory and gastrointestinal systems and, classically, it is characterized by exocrine pancreatic dysfunction, liver disease, problems in intestinal motility, male infertility, high concentrations of electrolytes in sweat due to the hyperviscosity of fluids produced by mucous glands and progressive lung disease [(3-5)]. The average life expectancy of CF patients is 48.5 years, and most CF-related mortality is due to progressive lung decline, with many patients eventually needing lung transplantation [(6)].

Despite the epidemiological importance of pulmonary failure as the main cause of death from CF, most patients invariably develop complications in the upper airways. Mucociliary clearance is compromised, making it an environment conducive to bacterial infections with neutrophilic infiltration [7,8]. Thus, almost 100% of CF patients have nasosinusal pathologies, such as chronic rhinosinusitis, in addition to marked edema of the sinus mucosa [9-11]. In addition, two thirds of patients have nasal polyposis, which makes chronic rhinosinusitis even more complicated. Despite this series of factors, only a small proportion of patients (about 20%) have the classic symptoms of chronic rhinosinusitis [12-15].

Among the anatomical changes caused by the disease, we have changes in paranasal sinuses (uni or bilateral), involvement of ethmoid and diffuse polyposis. These changes can be seen in radiological and endoscopic exams. Some of these changes, such as frontal sinus agenesis, present in 63% of CF patients, are caused by chronic infection, since the early life of these patients, causing changes in the development of these structures [16]. So we can say that this anomalous mucosa added to anatomical changes and the absence of a definitive treatment, translate into a reduction in the quality of life of these patients.

That said, it is important to note that there is more and more evidence about the relationship between the health of the upper airways and the health of the lungs, with a bacterial translocation from the upper to the lower airways. Therefore, taking care of presentations such as rhinosinusitis and polyposis, in addition to improving the quality of life, there is also an additional benefit in lung health care [17].

Clinical manifestations and diagnosis

Therefore, the major manifestations of the upper airways, as previously mentioned, present in these patients are chronic rhinosinusitis and chronic rhinosinusitis with polyposis.

Nasal polyposis in cystic fibrosis is the first manifestation described, presenting very variable incidence - from 6 to 67%, with peak incidence between 4 and 12 years and predominance of neutrophils.

In computed tomography without contrast, the following findings have been described:

- Hypoplasia or aplasia of the frontal sinus or the medial sinus;
- Medial bulging of the lateral nasal wall;
- Demineralization of the uncinated process;
- Opacification of paranasal sinuses;

Other important anatomical changes that are frequently observed are Haller cells and bullous shell rarely visible, while Onodi cells are frequently observed [20,21].

Nasal endoscopy may show the presence of nasal polyps or mucopurulent discharge, edema or mucosal obstruction, especially in the middle meatus, in addition to changes in the paranasal sinuses. [17,18].

Clinical treatment

Within the clinical management of these patients, drug actions are mainly directed towards the use of saline solutions, topical corticosteroids and antibiotics (especially in view of the high rates of airway infection), however, without a well-established level of effectiveness.

Saline solutions are widely used mainly for mechanical cleaning and reduction of mucosal edema and secretion, improving the quality of life and exacerbating pulmonary manifestations. The use of topical corticosteroids is aimed at reducing edema and inflammation of the mucosa, providing improvement of symptoms and also reduction in polyps, being the therapeutic option that presents the best level of evidence in CF. Antibiotic therapy is necessary in view of the high rates of infection, but with a low level of evidence. The main pathogens in CF are: pseudomonas aeruginosa,staphylococcus aureus,haemophilus influenzae and burkholderia cepacia. Since in children there is a predominance of staphylococcus aureus.

In addition to these general measures, it is worth mentioning the use of recombinant human Dnase, one that acts on the cleavage of extracellular DNA present in the airways, used in the form of nebulization, reducing mucus viscosity and, consequently, reducing the exacerbation of nasosinusal and pulmonary manifestations [17, 18].

However, recently, a new alternative has emerged in the treatment of cystic fibrosis. Ivacaftor is effective in those patients with type III mutation, and acts by modulating the transport of chlorine ions at the cellular level, leading to improvement in the symptoms of the disease [17,18]. More recently, in October 2019, the Food and Drugs Administration (FDA) approved the use of Trikafta in CF patients over 12 years of age, who have the Delta F508 mutation in the CFTR gene. This drug combines the mechanisms of action of ivacaftor, elexacaftor and tezacaftor, so that, while elexacaftor and tazacaftor bind to different parts of the CFTR allowing a greater amount of this protein to reach the cell surface, ivacaftor provides opening of chlorine channels of the protein on the surface, restoring its function [23].

Surgical treatment

Despite adequate clinical treatment, between 20 and 60% of patients who meet the radiological criteria will need to undergo a surgical procedure. Functional Sinus Endoscopic Surgery (FESS), in addition to alleviating the symptoms of CRS in CF, plays an important role in reducing the risk of bacterial infection in the upper airways, preventing its subsequent spread to the lower airways. In addition, it has the added benefit of creating an open system making the sinus cavity accessible for topical therapies [24].

Some retrospective studies have shown that severe CFTR and previous FESS mutations are predictive of new surgery, while the Sinonasal Outcome Test (SNOT-22) meets these results, demonstrating that the impact on the quality of life of individuals with CSR without prior surgery is worse [25]. Another study demonstrates that in patients with CF and nasal polyposis with a previous history of FESS, they had lower Forced Expiratory Volume in the first second (FEV1), higher Lund-Mackay score and higher SNOT-22 score, indicative of therapy surgery at the expense of outpatient treatment [26].

There are no current and specific guidelines for the management of patients with CF and chronic rhinosinusitis, nor are there clear criteria for the selection of those patients who should be referred for surgical treatment [25, 26]. Therefore, in view of this lack of clarity, the selection must follow the recommendations established for chronic rhinosinusitis, with the extra objective of reducing the colonization of lung pathogens, especially in CF patients who have already undergone lung transplantation [20]. However, taking into account the response of each patient to clinical treatment, evaluating each case individually.

Once the need for a surgical intervention is established, the preoperative computed tomography evaluation is extremely important to avoid surprises during the procedu-

re, and to ensure the complete removal of all bone partitions, as partial removal can generate favorable environments for the accumulation of secretions and allow new locus of infection. Recent studies demonstrate that serious radiographic findings (measured by the Lund-Mackay score) are related to high-risk CF mutations [27].

One of the techniques used in the surgical approach is the Modified Medial Endoscopic Maxillectomy (MMEM). They have been shown to be useful in CF patients, allowing the opening of cavities for severity-dependent drainage, resulting in better administration of topical medications and access for outpatient debridement.

Alternatively, maxillary sinus opening and / or total ethmoidectomy can be performed, which provides a significant reduction in sinus volume, decreasing mucus accumulation and, therefore, reducing chronic bacterial colonization of the sinus cavity [28].

A combined Caldwell-Luc approach and medial maxillectomy for CRS due to CF in patients with failure prior to FESS were effective in reducing episodes of hospitalizations and for the use of intravenous antibiotics. Interestingly, FEV1 improved significantly at 6 months [29]. It is worth mentioning that a mixed approach to endoscopic maxillary sinus surgery plus post-surgical adjuvant medical therapy represents the most ideal treatment for the control disease in CF and CRS.

EPOS 2020 cites, in general terms, 6 surgical techniques that can be used to approach CSR [33].

– Polypectomy: polyps of the nasal cavity are removed;
– Minimum Removal: most of the mucosa is maintained, removing only the damaged tissue;
– Complete as in FESS: where the sinus is completely open, added to the anterior and posterior ethmoidectomy, medium meatus antrostomies, sphenoidotomy and frontal opening;
– Extended: also similar to FESS, but extends beyond the limits of the breasts, reaching the base of the skull, orbit, pterygopalatine and infratemporal fossa;
– Radical – in addition to the sinus opening, it includes significant removal of the inflamed dysfunctional mucosa;
– Functional – usually seen in endoscopic sinus surgery; however, it must meet the following criteria: create a sinus cavity that incorporates the natural ostium to allow adequate sinus ventilation to facilitate mucociliary clearance; provide the applicability of topical therapies.

Currently, cases of CRS children have surgical treatment reserved for cases of failure to drug treatment, in which there is persistence of symptoms for a period of 12 weeks associated with changes in CT according to the criteria of Lund-Mackay. A persistence of nasosinusal symptoms in the pediatric population can also be assessed using the Sinus and Nasal Quality of Life Survey (SN-5) questionnaire, which stratifies quality of life and correlates with CT findings [29,31].

EPOS (European position paper on rhinosinusitis and nasal polyps) 2020 suggested that the surgical algorithm for CRS in children starts with adenoidectomy and that concomitant dilation of the maxillary sinus balloon can be considered. Functional endoscopic sinus surgery (FESS) would be reserved for treatment failures, patients without adenoid hypertrophy or in patients with disorders that directly affect mucociliary function. However, as with adults, there is no consensus on surgical treatment for CRS in childhood [30, 32]. FESS has shown high rates of success in the treatment of pediatric CRS, and previous concerns that it would have adverse consequences on facial development have proved unfounded [33].

Conclusion

The treatment of chronic rhinosinusitis in cystic fibrosis is complex and challenging. The high disease burden found on endoscopic and tomographic exams generally does not correlate with symptoms self-reported by the patient and the data currently available are limited. Endoscopic surgeries have been shown to decrease sinus and pulmonary bacterial colonization, as well as relieve patients' symptoms. Although there is no consensus on the best surgical approach to paranasal sinuses in children, surgical treatment has been increasingly considered and without future consequences for the development of these sinuses. Despite the lack of an established treatment algorithm, we can conclude that research suggests that a multidisciplinary clinical and surgical approach offers the best treatment strategy for patients with CRS with CF.

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HEARING

Treatment of ear deformities using molding therapy in the neonatal period

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There are two types of congenital alterations in auricular morphogenesis: deformities and malformations. Deformities have all the anatomical components of the ear but with an abnormal architecture or shape. In malformations, partial absence of skin or cartilage is observed, characterizing the different types of microtia [(1)]. The most common congenital auricular deformities are prominent ear, Stahl's ear, and cryptotia [(2)]. Treatments for auricular malformations, such as microtia, are surgical, unlike those for congenital deformities, which can be treated early with ear molding or at a later time, usually from 6 or 7 years of age [(2)].

Congenital ear deformities are common conditions and approximately 30% of cases resolve spontaneously [(8)]. Ear deformities secondary to birth trauma improve significantly at the end of the first week of life. The familial feature of prominent ears may require timely intervention. Nevertheless, in a significant number of patients spontaneous resolution will not occur. In these cases the deformities may be corrected by adequate molding therapy if started in the first weeks of life [(8)].

Therefore, prominent ears and other deformities, usually identified by the pediatrician, often in the delivery room, should be accompanied by adequate counselling of the family regarding the possibility of early treatment.

As deformations of the ears have an impact on the self-esteem of the child, affecting social inclusion and sometimes resulting in bullying, early correction is required.

Daniali et al. created a classification system for the grading of ear deformity (Figure 1) consisting of three classes of increasing severity. Each class is characterized by progressive changes in the longitudinal auricular axis, helical rim, superior crus, scapha, prominence, and degree of helical and antihelical constriction. The aim of the classification is to assess pretreatment severity and measure posttreatment outcomes.

A specially designed mold is ideally be applied in the first four weeks of life of a baby with a prominent ear or other deformities. The best results are obtained up to the first 6 to 8 weeks when there is a higher level of circulating maternal estrogen that increases proteoglycan synthesis and the amount of hyaluronic acid favoring reorganization and molding of auricular cartilaginous tissue.

The evaluation of patients who are candidates for molding treatment should be multidisciplinary, starting with primary care professionals, such as pediatricians and nurses, in the first few days of life.

Neonatal molding, therefore, reduces the need for surgical correction resulting in outcomes that are often better than those that may be achieved by surgery.

The first studies describing non-surgical correction of congenital auricular deformities were published in the 1980s.

Van Wijk et al. conducted a systematic review of studies on non-surgical treatments for auricular deformity correction published between 1984 and 2007, evaluating indications,

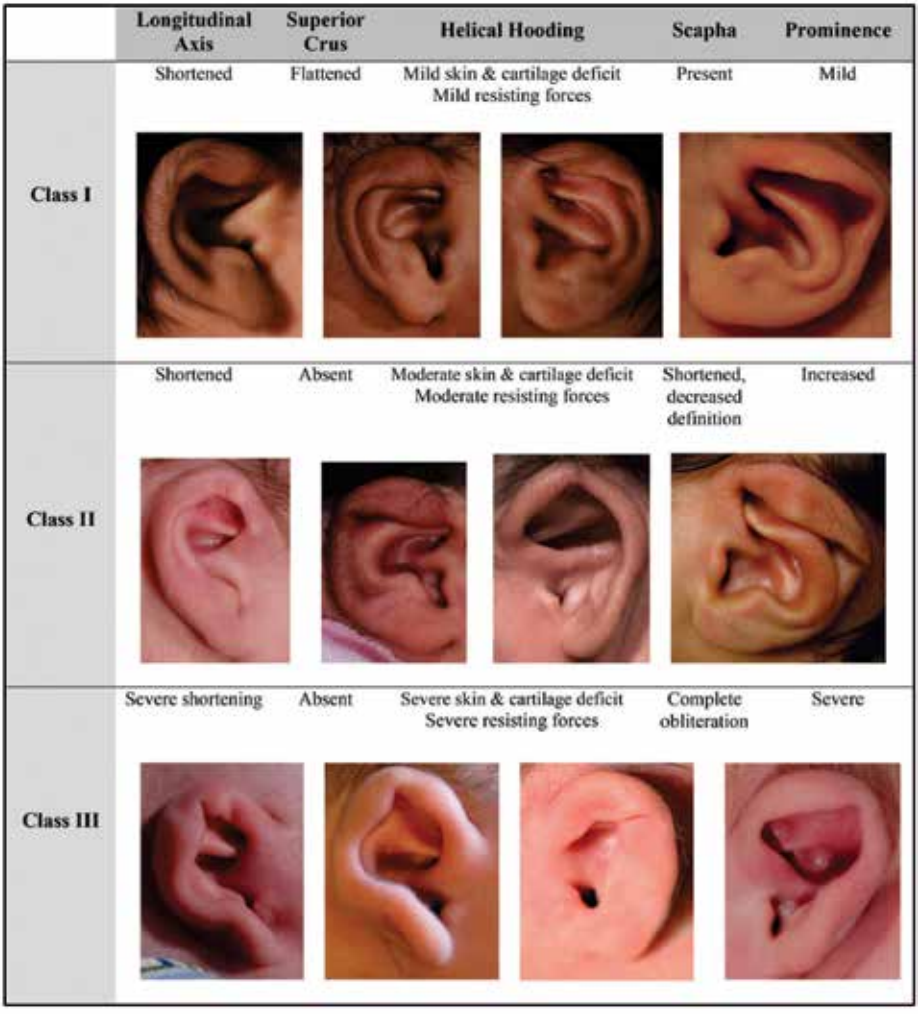

Figure 1. Classification system for the grading of ear deformity severity. (Daniali et al, 2017

duration of treatment, outcome, and possible complications. Splinting was used with or without tape (Figure 2). Time of treatment was between 1 and 6 weeks and age at treatment initiation varied widely, between the newborn period up to 3 years.

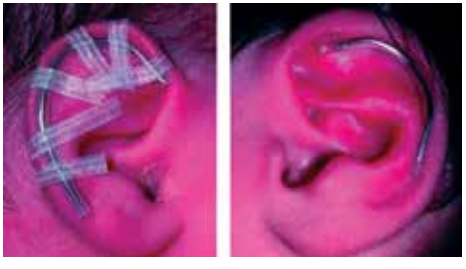

Figure 2. Splint with and without tape (Van Wijk et al., 2007).

In 2009, Schonauer et al. published a study using a thin splint (Figure 3), consisting of a wire core segment in a silastic tube, fixed with steri strips for a time of 3 to 6 weeks. The majority of ears improved significantly in the first two weeks of treatment. In 2012, Van Wijk et al. described Earbuddies@ (Figure 4), using a splint fixing the ear to the head of the child. Better results were observed in children up to 6 weeks of life.

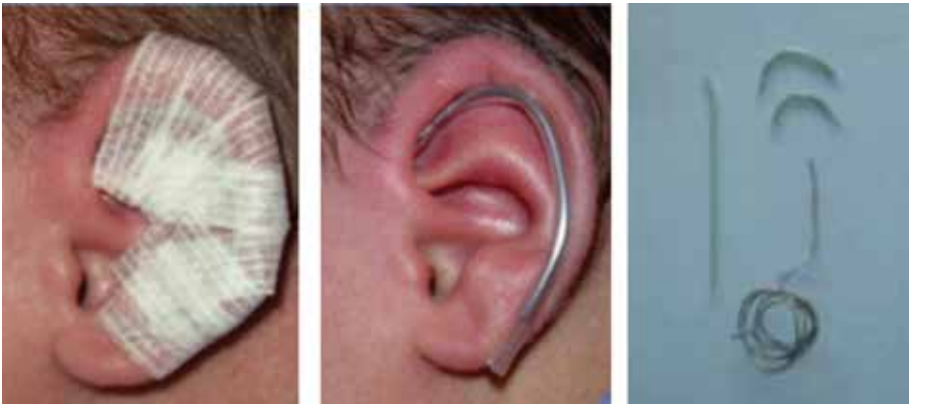

Figure 3. Ear splintage method (Schonauer et al, 2009).

Figure 4. Earbuddies Ltd (Van Wijk et al., 2012).

Mohammadi et al. obtained good results in Iranian children using stainless steel wires encased in soft and flexible silicone (Figure 5). Chang and Bartlett used a new technique with a Velcro-based splint attached to the mastoid region with Dermabond® tape, soft silicone molds in the ear, and fixation with polysiloxane gel (Figure 6). Good results were achieved in more than 90% of the cases.

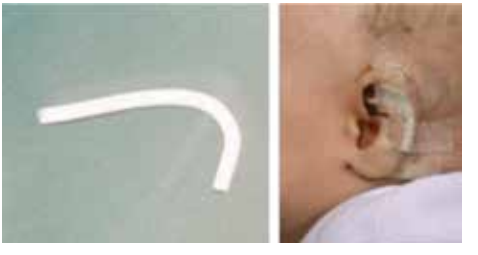

Figure 5. Splints of stainless steel and silicone. (Mohammadi et al., 2016).

Figure 6. Memosil (Chang and Barlett, 2017).

The most recently described method is the EarWell System (Daniali et al. 2017), composed of retractors anchored in cyanomethacrylate tape and a silicone mold (Figure 7). The molding of the EarWell System around the ear effectively corrected the deformities. Success rate of the EarWell System for the treatment of neonatal auricular deformations and mild malformations of the ear is high, depending on the severity of the deformities at the time of treatment initiation [7].

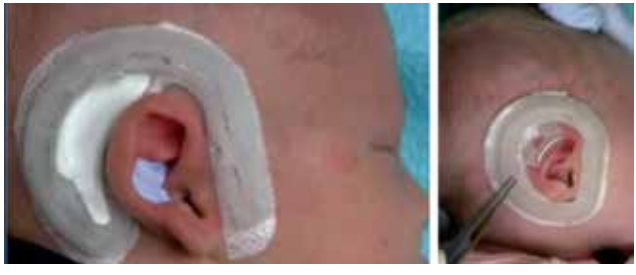

Figure 7. EarWell System (Daniali et al., 2017).

At our center, we developed a mold of the same material (silicone and a catalyst) that is placed around the ear without the need for anesthesia supported with micropore tape that is periodically changed (every 10 or 14 days) over a period of 4 to 6 weeks.

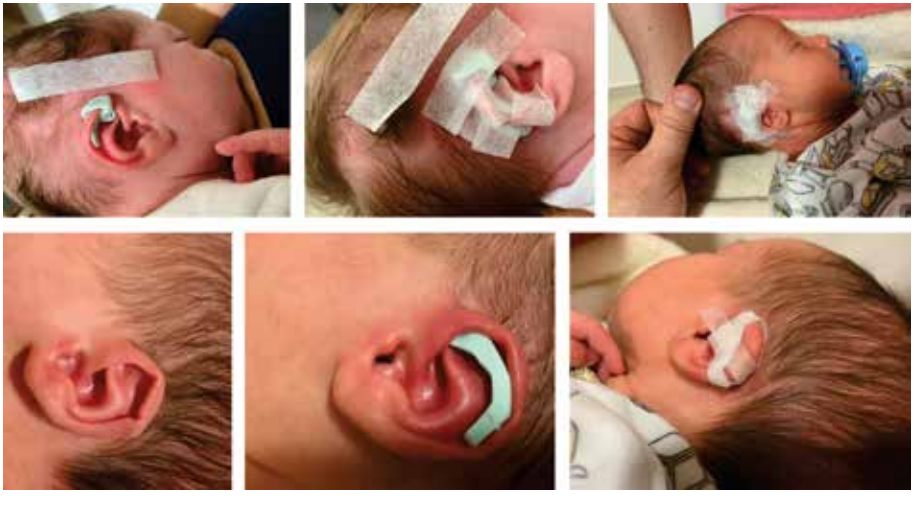

Figure 8. Silicone mold.

In conclusion, by correcting the ear deformity as early as possible after birth using a non-invasive, practical, and reliable technique, we may significantly improve the auricular shape, avoiding future surgical interventions and possible psychological trauma.

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The otoscope and beyond: New techniques for otitis media diagnosis

Tal Marom, MD, **Oded Kraus**, MD, **Nadeem Habashi**, MD and **Sharon Ovnat Tamir**, MD.

Introduction

Otitis media (OM) is a common childhood infection. The hand-held otoscope is the "traditional tool" used for OM diagnosis for many years, and it is in widespread use for the diagnosis of common tympanic membrane (TM) and middle ear pathologies in outpatient clinics, emergency rooms and medical departments. A trained examiner should accurately diagnose with the otoscope the normal aerated middle ear behind an intact TM, in order to differentiate the normal state from other pathologies: acute otitis media (AOM) and otitis media with effusion (OME). In AOM cases, otoscopy reveals TM bulging and hyperemia, loss of the TM translucency and presence of "cloudy" fluid behind it. In OME, clear fluid is present behind the TM, in the absence of acute symptoms (Figure 1).

Diagnosis with otoscopy is largely dependent on the physician's experience. It is a challenging task, with a time-dependent learning curve, and associated with various difficulties: obstructing cerumen, a non-cooperative child, anterior blunting of the external ear canal, misinterpretation of otoscopic findings and insufficient illumination. The addition of pneumatic otoscopy or tympanometry are helpful in some cases, but are not in reach in many settings.

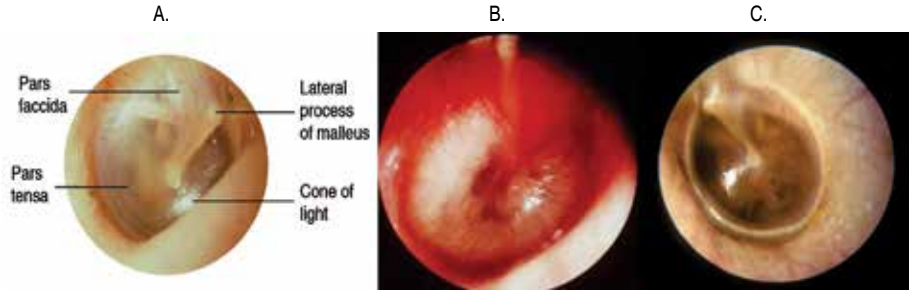

Figure 1. Otoscopic images of (A) normal aerated middle ear, (B) AOM and (C) OME.

In recent years, new technologies have been introduced to overcome the objective limitations of otoscopy. Advantages of the new tools include their ease of performance, minimal discomfort to the patient, simple interpretation, rapid acquisition time and high reliability. We present these new technologies and explain the scientific principles behind them.

Review of new technologies

A. Spectral gradient acoustic reflectometry

Principle: Measurement of the levels of sound transmitted and reflected from the middle ear in a probe tip placed against the external ear canal and directed toward the TM. It does not require an airtight fit in the external ear canal, unlike *tympanometry*, and can be successfully performed even with a struggling child.

Use: First reports in OM diagnosis were published in the 1980s, but its use has been abandoned due to its relatively high cost and its inability to clearly differentiate between AOM and MEE. Recent reports with improved devices have recently shown the applicability of this technology to detect MEE, even when the examination is performed by parents. Despite these advances, gradient acoustic spectrometry still cannot distinguish AOM from MEE, and does not correlate with the hearing loss severity associated with these conditions (Figures 2 and 3).

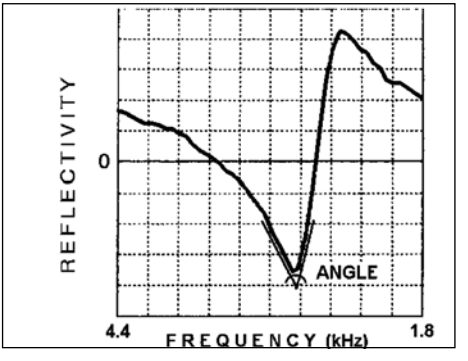

Figure 2. Spectrometer.

Figure 3. Spectral gradient acoustic reflectometry printout. Curve displays the function of sound reflectivity and frequency. The more tympanic membrane reflects sound energy (e.g., in MEE), the narrower the frequency spectrum of the reflected sound becomes, making the spectral gradient angle (marked, at the nadir of the reflectivity curve) narrow. Thus, narrow, or sharp (<90°) angle is suggestive of MEE.

B. Digital otoscopy

Principle: Digital recording of examinations of the ear, focusing on the TM, for remote viewing and assessment.

Use: Already in use in a variety of telemedicine applications including primary care, pediatrics, correctional facilities, and community clinics. Nurses, clinicians or specialty providers are able to quickly inspect the ear, easily capture quality digital images and video and then instantly share this valuable diagnostic data with remote physicians or other healthcare providers. Due to the quality and data handling issues, the average correct scores for normal TM images from digital otoscopy devices is medium-high (72%), but the overall accuracy of diagnosis for middle ear pathologies ranges from low, 48% (for TM perforation) to very high, 100% [tympanostomy tube (TT) in place]. Researchers work on improving image acquisition quality: resolution, colors and spatiality (Figures 4 and 5).

Figure 4. Hand-held digital otoscope.
Figure 5. The handle of the otoscope can be connected to tablets or smartphones via a specific application or to computers via Wi-Fi / USB connection for further analysis.

C. Tympanic membrane image analysis

Principle: automated software analysis of standard otoscopy images obtained from an inexpensive commercial video-otoscope.

Use: Hundreds of TM images were obtained from rural South African children: 80% were used to train the software system to diagnose 5 conditions: 1) obstructing cerumen or foreign body in the external ear canal; 2) normal TM; 3) AOM; 4) OME; and 5) chronic OM (perforation), and 20% were used to validate and test the system. An overall accuracy of 81% was calculated for correct diagnoses output by the software. This compares well with the average diagnostic accuracy of OM diagnosis using standard otoscopes among pediatricians (60%), general practitioners (64-75%) and otolaryngologists (73%). (Figure 6).

Figure 6. Side view of the low-cost, custom-made video-otoscope.

D. Multi-color reflectance imaging

Principle: Multi-color TM imaging to enable superior characterization of the middle ear contents, by exploiting changes in tissue absorption and light scattering of the TM brought about by pathologic changes. Such fine details cannot be assessed in standard otoscopy.

Use: When narrow-band reflectance image sequences were obtained from 1) healthy volunteers (normal TM, served as a reference for other pathologies), 2) patients scheduled for TT placement and 3) patients undergoing congenital cholesteatoma excision, the captured high definition images enabled improved outlining middle ear mucosal structures, and thus enabled demonstrating MEE and presence of keratin. Because the metabolic activity in the middle ear is different in AOM and MEE states, this technique can potentially differentiate between these 2 conditions in a more objective manner (Figures 7 and 8).

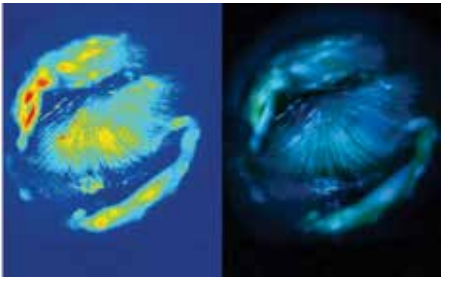

Figure 7. Image from a patient with AOM using simultaneous green and blue illumination. The green/blue-green illuminations showed increased contrast of purulent material behind the TM.

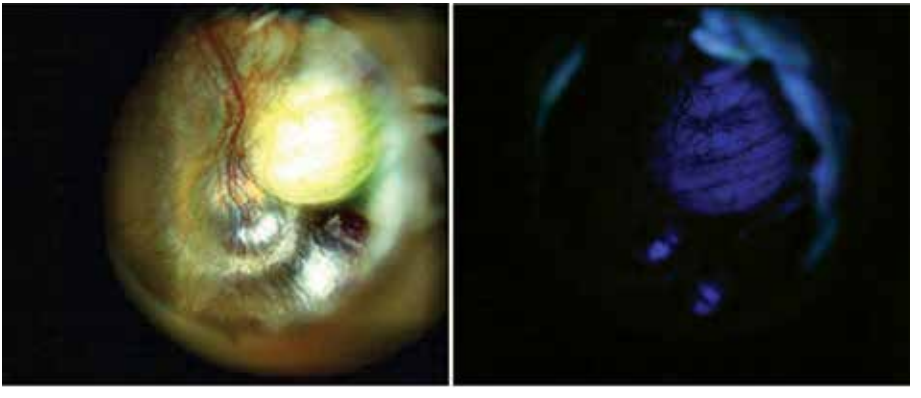

Figure 8. Congenital cholesteatoma, using multicolor reflectance imagining.

E. Anti-confocal middle ear assessment

Principle: Blood is the main absorber in mucosal tissues, such as the one in the middle ear cavity. Increased metabolism, such as seen in various OM cases, results in a higher absorption coefficient with a concomitant decreased reflection signal.

Use: Preliminary experiments showed reliable assessments of the inflammatory state within the middle ear cavity in various OM states. A remaining problem was the

influence of other parameters in the middle ear, such as color and translucency of the TM, which resulted in distortion of some measurements (Figure 9).

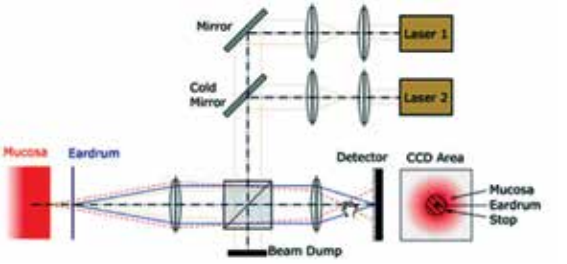

Figure 9. Optic system consisting of beam expansion and alignment of 2 lasers and the anti-confocal setup including a beam splitter, focusing lenses, and charged coupled device detector allowing filtering in post-processing. Illumination is shown in yellow, background from the tympanic membrane in blue, and signal from the mucosa in red. The expected signal distribution is shown in the right bottom.

F. Coherence tomography

Principle: using long wavelengths allows deep tissue penetration, which allows interference patterns after reflecting off the tissue of interest and enables high resolution visualization at the micrometer level. In OM, the organ of interest is the middle ear cavity.

Use: patients with chronic MEE scheduled for TTs placement were imaged with an experimental hand-held otoscope adjunct with optical coherent tomography. If present, MEEs were first imaged in vivo, and after myringotomy, the MEE was aspirated (ex vivo), observed and imaged. Such imaging technique demonstrated the content of the MEE in its different inflammatory states, such as planktonic bacteria, biofilm and MEE (Figures 10 and 11).

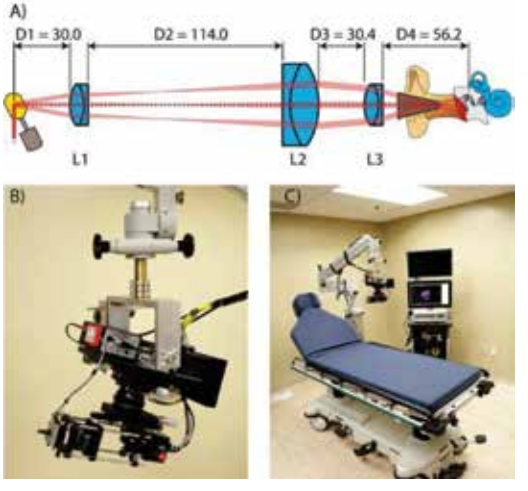

Figure 10. A) Optical layout, B) Closeup of the middle ear OCT scanning microscope used for imaging down the ear canal through a 4 mm otoscopic speculum and mounted to surgical microscope arm, C) Complete in-clinic, real-time imaging system mounted to an articulating arm. Units are in mm.

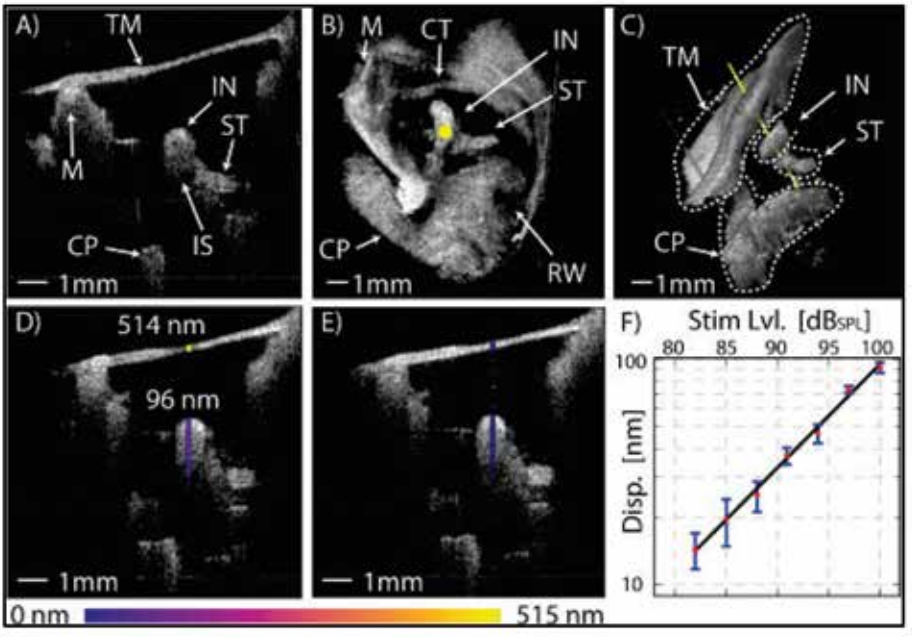

Figure 11. In vivo, real-time functional imaging of a normal left ear's response at 1030Hz.

A) Shows a 1 × 1cm2 2D cross-section of the middle ear in the transverse plane. Visualization 3 shows the macroscopic changes to the ear anatomy during a Valsalva maneuver. B) Shows a 1 × 1 × 1cm3 3D volume render of the middle ear as seen from the perspective of the ear canal with the TM digitally removed (see Visualization 4). C) From an inferior-posterior perspective with the TM in-place showing the axis of Doppler measurement along the yellow line passing through the incus at the stapedius tendon. Functional measurements of the TM and incus' peak-to-peak vibrational response at 1kHz are shown in D) with a 100dBSPL tone applied to the ear and E) without stimulus. F) A plot of displacement response versus sound pressure level showing excellent linearity from 80dBSPL to 100dBSPL. Error bars represent ± one standard deviation of the response over the pixels along the axial length of the incus. Tympanic membrane (TM), malleus (M), incus (IN), incudo-stapedial joint (IS), stapedius tendon (ST), chorda tympani nerve (CT), cochlear promontory (CP), round-window niche (RW).

G. Quantative pneumatic otoscopy

Principle: The combination of OCT and pneumatic otoscopy enables the measurement of minute TM deflections from insufflation pressure stimuli. This technique can be helpful at times when such a distinction is hard to make, and in conjunction with the clinical scenario of subjective hearing loss or delayed language acquisition, as well as with an abnormal audiometric evaluation.

Use: In a study in various TM locations from 15 otherwise healthy volunteers and patients with MEE, researchers have shown that they were able to quantitatively differentiate normal ears from ears with MEE (Figure 12).

H. Trans-mastoid ultrasound

Principle: probing the mastoid with an ultrasound transducer to characterize the fluid-filled mastoid and thus indirectly identify MEE. When air cells in the mastoid are filled with air and fluid, a wide range of intensities and amplitudes are seen. Once mastoid air cells are fluid filled this variance decreases.

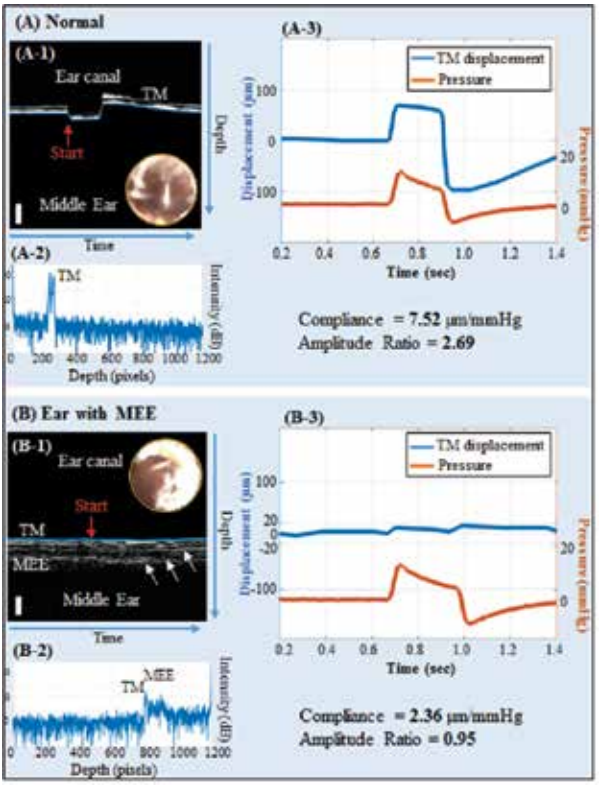

Figure 12. Comparison of (A) a normal ear and (B) an ear with a MEE.
(A-1) and (B-1) show M-scans of the TM when pressure was applied. The start of the pneumatic stimulus is indicated with a red arrow. White arrows point to scattering from the middle ear effusion (MEE). (A-1) and (B-1) show the corresponding en face surface views of the TM. Strong reflections near the edge in (B-1) are from earwax. (A-2) and (B-2) represent A-scans. (A-3) and (B-3) illustrate the plot of the TM displacement and the pressure dynamics.

Use: authors showed an increase in the Nagakami parameter, a physical parameter for density measurement in the mastoid area, when MEE was present when compared with normal ears. A receiver operating characteristic analysis revealed an 81% diagnostic accuracy for this technique (Figure 13).

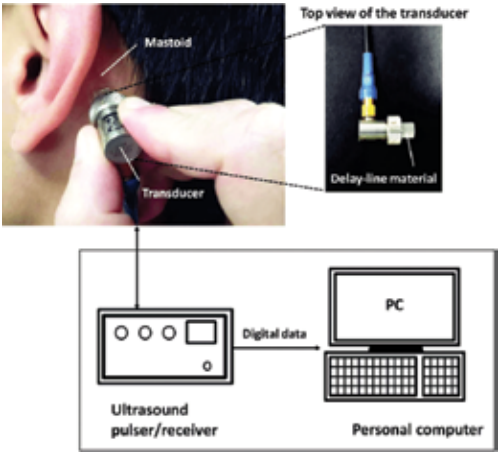

Figure 13. Trans-mastoid ultrasound system comprises a 2.25-MHz delay-line transducer, portable ultrasound pulser–receiver and computer.

Wideband measurements

Principle: wideband immittance (which includes absorbance and acoustic admittance) is measured at the external ear canal, and enables analysis of the acoustic transfer functions of the ear canal and middle ear. Wideband acoustic absorbance values range from 0 to 100, where 0 represents the whole energy being reflected back to the microphone and 100 represents the whole energy being absorbed by the middle ear cavity.

Use: complex broadband measurements were measured from 5 TMs containing biofilms, fluid or both. The acoustic properties of ears with and without confirmed bacterial biofilms enabled their comparison. Ears with a bacterial biofilm had an elevated power reflectance in the 1-3 kHz range, corresponding to an abnormally high resistance. Thus, this is a possible tool for assessing the viscosity and content of the MEE in chronic cases when other measurements are not possible (i.e. perforated TM) or convincible (tympanometry C measurements in the presence of clinical MEE) (Figure 14).

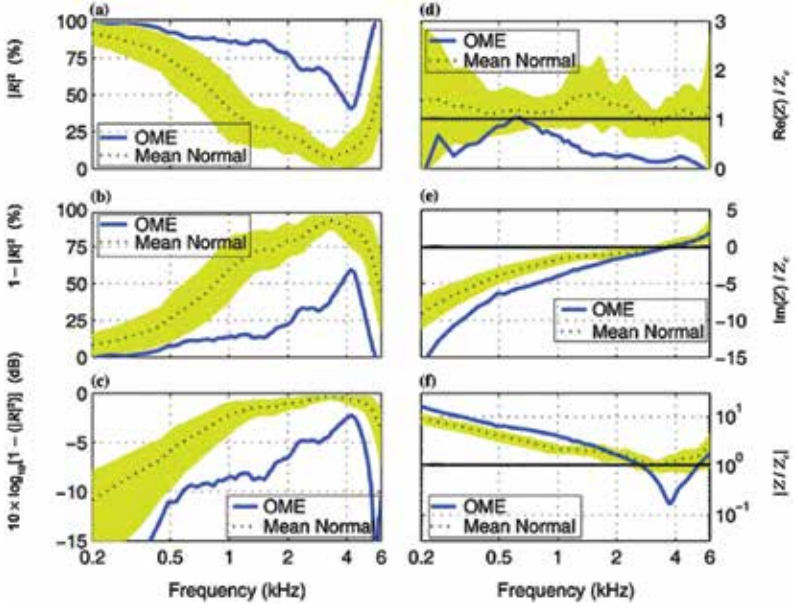

Figure 14. Recording form a child with bilateral OME. Normal range is colored in yellow.

Tympanic membrane thickness mapping

Principle: the use a low coherence light source to accurately measure multiple layer membranes at the micrometer level, such as the TM.

Use: in vivo assesmnet of 6 human TMs showed thickness distributions across different TM regions. After these TMs were scanned at 500 locations, a mosaicking algorithm was used to reconstruct the whole TM map. All the 6 TMs had similar thickness distributions at distinct TM locations, with only 10% variabililty (all four TM quadrants, pars flaccida alone and pars tensa alone were compared and analyzed). When AOM or MEE were present, the thickness of the TM was 100-200% that of a normal TM, thus giving the thickness distribution maps with mosaicking visualization a promising future in TM pathology diagnosis which may indicate pathologcial middle ear changes (Figure 15).

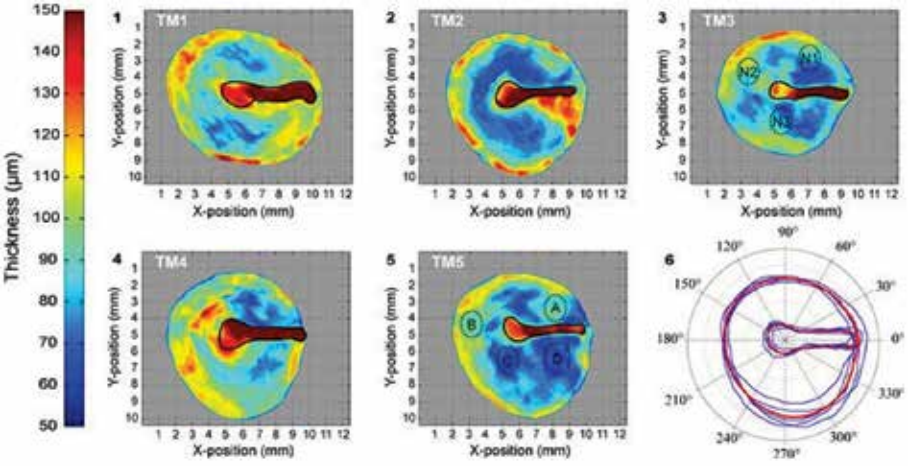

Figure 15. Thickness maps of the 5 individual membranes (TM1-5). The manubrium border of each membrane is illustrated by a solid black line, delimiting the areas in which a greater thickness uncertainty exists due to limited penetration of the imaging beam. Inset 6 includes the contours of TM1-5 in blue and the resulting averaged contour of TMA in red.

I. Shortwave Infra-red (SWIR) imaging

Princilple: use of longer wavelengths than the near infrared and visible light which show less sacttering properties giving enhanced sensitivity to chromophores (water, lipids, collagen). Imaging with this technology enhances TM transperacy and intensifies contrast when fluid is present. compared to visible light images.

Use: when 18 TMs of 10 adults and one 3-D printed middle ear model were used to test this method, the authors showed the anatomical differences between visible light otoscopy and SWIR imaging in healthy ears. The SWIR light otoscopy extended the available evaluation of middle ear pathologies to a regimen in which endogenous contrast of middle ear fluid and anatomy may be assessed more objectively given the inherent properties of these low wavelengths (Figure 16).

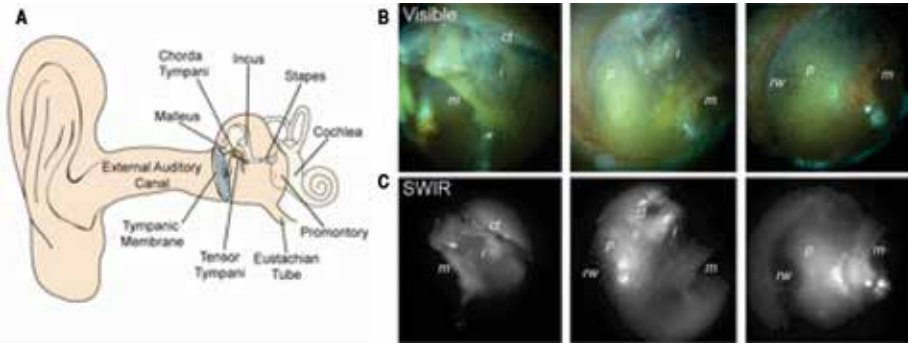

Figure 16. Schematic of the middle ear and comparison between SWIR and visible examinations in healthy adults. Under visible examination, all anatomy besides the malleus is obstructed by the tympanic membrane (B). Using the SWIR otoscope, the chorda tympani, malleus, incus, stapes, stapedial tendon, cochlear promontory, and round window niche (indicated by ct, m, i, s, st, p, and rw, respectively, and shown schematically in A) are all clearly identifiable (C).

J. Wideband acoustic transfer functions

Principle: Measurements of middle ear function across a broad frequency spectrum, 0.25-8 KHz, that provide a spectral analysis and acoustic transfer function of the external ear canal and the middle ear cleft.

Use: Researchers have shown that the absorbance was reduced in ears with MEE compared to normal ears. An index combining 3 tested physical parameters was the most accurate to predict MEE presence. Absorbance varied systematically with TM mobility based on data from pneumatic otoscopy (Figure 17).

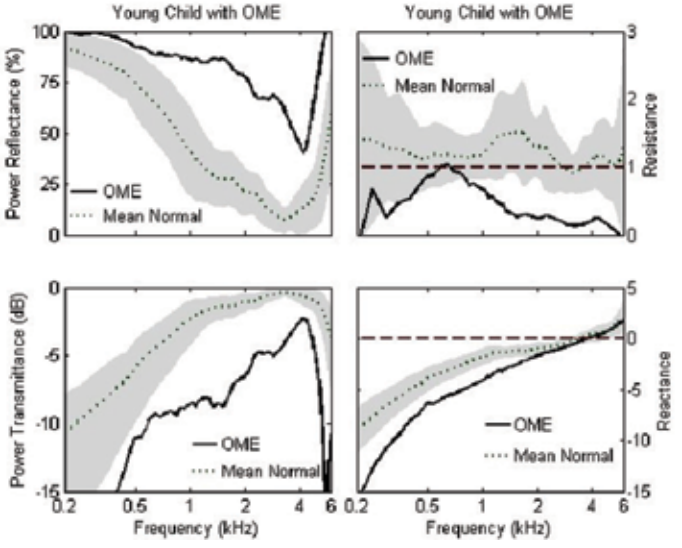

Figure 17. Young child with OME. The power reflectance, power transmittance, normalized resistance, and normalized reactance measured from the ear with OME (solid black line) are compared to those of 31 ears with normal middle-ear function (dotted mean line and ±1SD) as determined by tympanometry, otoscopic evaluation, and the children's medical history.

Future directions

Most technologies described in this review are emerging and are still under investigation, thus they are still not found in widespread use. None of them have yet been shown to be superior to standard otoscopy for the diagnosis of diagnosing OM.

To achieve common clinical and commercial use beyond the initial discoveries of these diagnostic techniques, future in vivo imaging/measuring devices should be affordable, combining to major characteristics: ease of use and easy-to-teach. They should feature low-cost probes and transducers, simple designs with fast imaging acquisition modalities that should prove to be superior to the standard otoscope. The appearance of these tools in daily practice is dependent on their success in clinical trials and their future cost.

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Complementary and alternative medicine for otitis media

Tal Marom, MD and **Sharon Ovnat Tamir**, MD.

Introduction

Alternative medicine is any practice claiming to possess the healing effects of conventional medicine, but does not originate from evidence-based scientific methods. It consists of a range of healthcare practices, products and therapies, ranging from being biologically plausible but not scientifically tested, to being directly contradicted by evidence, or even harmful or toxic. **Complementary medicine** is an alternative medicine used in conjunction with conventional medicine, in a belief that it may be synergistic.

Complementary and alternative medicine (CAM) is popular worldwide, although not always scientifically backed up. The main reasons for choosing CAM therapies in children are that CAM attempts to provide a personalized approach to the sick child, parents' previous disappointments with conventional medicine, personal or professio-

nal recommendations, and parents' previous experience. Only few have shown effectiveness, leading physicians to question their efficacy (Figure 1).

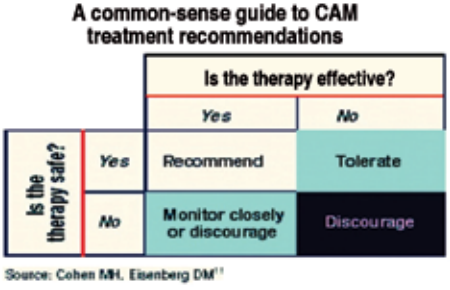

Figure 1. A common sense guide to CAM treatment recommendations.

Otitis media (OM) includes a spectrum of diseases, which range from middle ear fluid collection (otitis media with effusion, OME), to purulent fluid behind the tympanic membrane (acute otitis media, AOM) and recurrent AOM (RAOM). Many countries published local guidelines for OM treatment. To date, CAM therapies are either ignored or discouraged those guidelines, even in countries where CAM is popular, such as in Asia.

Due to the prevalence of OM in children, physicians occasionally may be asked their opinion regarding CAM therapies for pediatric OM, but they may often feel uncomfortable advising parents due to lack of knowledge of the treatment options available in the market. We review these options, and provide the proofs favoring or against CAM therapies for pediatric OM.

Treatment options

Reported complementary and alternative medicine (CAM) treatment options for otitis media (OM), according to OM type. (Table 1).

Treatment	AOM	RAOM	OME	Overall Efficacy
Acupuncture	+			Effective with concomitant antibiotic therapy.
Homeopathy	+	+	+	Mild.
Herbal Medicine/Phytotherapy	+			Mild to moderate.
Osteopathy	+	+	+	Very few benefits.
Chiropractic medicine			+	Very few benefits.
Xylitol	+	+		Conflicting results. Problematic daily dosing.
Ear candling	+			Potentially hazardous.
Vitamin D		+		Questionable. Mainly for prevention.
Probiotics (Systemic/intranasal)	+	+	+	Encouraging results.

Table 1. Complementary and alternative medicine treatment options for otitis media.

AOM: acute otitis media; CAM: complementary and alternative medicine; OME: otitis media with effusion; RAOM, recurrent otitis media.

Acupuncture

Acupuncture (needle puncturing) derives from traditional Chinese medicine, and involves inserting thin needles into the body at specific points. According to acupuncture, the body's energy force, chi, differentiates a corpse from a live human being. Acupuncture balances and enhances chi to bring the body into a healthy state.

The auricle harbors numerous locations which are punctured for the treatment of many diseases. Yet, 4 specific locations around the external canal are believed to be the primary gatekeepers of the ear's energy, and they are punctured in OM cases (Figure 2). There is little understanding why acupuncture is beneficial, but it is suggested that it has immunomodulatory properties that may play a role in clearance of middle ear fluid.

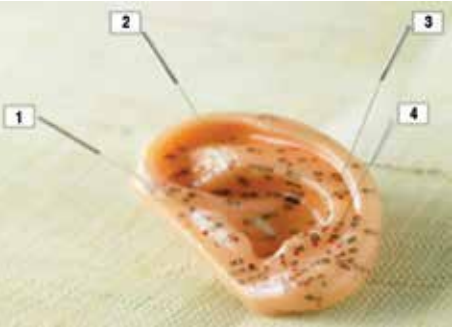

Figure 2. Areas in the auricle to be punctured in order to relieve OM.

There only a few studies concerning acupuncture for the treatment of OM in humans in Chinese. All reported on good outcomes; however, the methodology and their results were unclear.

Homeopathy

Homeopathy is based on the "like cures like" doctrine: a substance that causes the symptoms of a disease in healthy people would cure similar symptoms in sick people [(1)]. Homeopaths generally prescribe remedies that have a "symptom picture", which they consider most closely equates to the constellation of the patient's symptoms.

Most remedies combine an extract of a natural substance, combined with a synthetic compound, which enhances the therapeutic effect. A list of homeopathic remedies for OM treatment is shown in the following table (Table 2).

The first prospective cohort study comparing the use of homeopathy for RAOM with conventional treatment was reported in 1997: 71% children from the homeopathic group had fewer OM episodes, whereas 57% of the conventional group received treatment for OM. The unequal numbers between the homeopathic (103) and conventional group [(28)] and the absence of randomization considerably weakened the study's validity.

Two subsequent randomized controlled trials (RCTs) also showed promising results. The first compared homeopathic and placebo for AOM in 75 children who presented with otalgia and tympanic membrane bulging of ≤ 36h duration. A significant decrease in symptoms at 24h and 64h after treatment were observed in the homeopathy group, and there were fewer treatment failures in this group after 5 days, 2 weeks and 6 weeks, but they were not statistically significant. In another study from Jaipur, India, 81 young children with AOM were randomly assigned to conventional (antipyretics, analgesics) and homeopathy treatment groups. Nearly all children in the conventional group eventually required antibiotics, compared to none in the homeopathy group. The number of children experiencing 'cure' suggested that early homeopathic treatment could have advantages beyond a "watch and wait" policy.

Agent	Common Indications	Figure
Belladonna	1. Earache beginning suddenly with intense pain, with few prior symptoms of URTI (e.g., watery rhinorrhea) 2. Signs of uncomplicated AOM: bright red outer ear, ear canal, or eardrum without pus formation, sudden high fever 3. Ear pain extending down into the neck, or accompanied with sore throat	
Ferrum phosphate Fe3(PO4)2	1. Early stages of earaches before pus has formed; symptoms similar to Belladonna, but not as sudden or severe 2. Alternatively, if Belladonna did not improve symptoms	
Hepar sulfate	1. Sharp, severe otalgia 2. Earache with by thick rhinorrhea or otorrhea 3. Irritability 4. Chilliness and aversion to the cold or uncovering; desire for warmth 5. Earache worse in cold or open air or from cold applications better from warmth; worse at night	
Pulsatilla	1. Mild disposition; craves affection and physical contact 2. Purulent rhinorrhea/otorrhea 3. Ear pain worse at night, even in a warm room. 4. Worse in general from warmth, wants fresh air 5. Little or no thirst	
Chamomilla	1. Extreme irritability 2. Severe ear pain 3. Symptoms are worse when stooping or bending over and i mproved by warmth or being wrapped in warm covers 4. Watery rhinorrhea	
Soluble Mercurius	1. Apply when otorrhea is present 2. Earache worse from warmth and worse at night 3. Profuse, bad-smelling perspiration, head sweats 4. Increased salivation, puffiness of the tongue	
Silica	1. Later stages of an earache: physical weakness and tiredness, chilliness, desire for warm covering 2. Pain behind the ear in the region of the mastoid 3. Sweating about the head or on the hands or feet	
Colloidal Silver	1. Mild-moderate cases of OM 2. Sub-microscopic particles of mineral silver in colloidal silver adhere to the cell walls of harmful microorganisms, inhibiting enzyme production and, in effect, smothering them. 3. If the silver particles are small enough, they can even adhere to the DNA of viruses, and disrupt their ability to replicate.	

Table 2. Common homeopathic remedies for otitis media.

AOM: acute otitis media; OM: otitis media; URTI: upper respiratory tract infection.

In a RCT which compared homeopathic and conventional treatment in 33 children diagnosed with OME, 75% in the homeopathic group had a normal tympanogram after 12 months, compared to 31% in the conventional group. A higher proportion

of children receiving homeopathic treatment had a hearing loss <20dB at follow-up, though the difference was not statistically significant. In another prospective observational study of 230 children receiving homeopathic treatment for AOM, pain control was achieved in ~40% of patients after 6h, and in further 33% of patients after 12h. The rate of AOM resolution in the homeopathic group was 2.4 times faster, without complications.

Herbal medicine / phytotherapy

Herbal medicine and homeopathy are interchangeable practiced together and sometimes confused. Herbal medicine is the use of plants for medicinal purposes [1]. Herbal products are generally considered as safe, though efficacy is unclear and side effects may vary. **Phytotherapy** is the study of the use of extracts of natural origin as medicines or health-promoting agents. While standard pharmacology isolates an active compound from a given plant, phytotherapy aims to preserve the complexity of substances from a given plant. Phytotherapy avoids mixing plant ingredients with synthetic substances.

Phytotherapy has been reported to be effective in the management of ear pain in OM. Otic solutions, such as Otikon (Healthy-On, Israel), which contains extracts of garlic bulb, mullein flower, calendula flower and St. John's wort herb in olive oil, or Mullein Garlic (Equinox Botanicals, USA), which contains extract of mullein flowers, garlic, yarrow, calendula flowers and vitamin E, were shown to be as effective as oral amoxicillin and topical anesthetics due to their presumed antimicrobial, anti-inflammatory, immunostimulating effects and good penetration through the tympanic membrane [2,3]. Yet, phytotherapy has been heavily criticized by others, since the alleged anti-inflammatory properties could not be tested or confirmed in vitro.

Osteopathy

Osteopathy is a non-invasive manual medicine that focuses on total body health by treating and strengthening the musculoskeletal framework. Its aim is to positively affect the body's nervous, circulatory and lymphatic systems, leading to "balance" and providing overall good health and well-being.

The 2 most common OMTs for OM include: 1) ***"Galbreath"*** maneuver, a movement of the mandible aimed to indirectly generate a pumping action on the Eustachian tube (ET), and 2) ***"Muncie"*** and ***"modified Muncie"*** techniques, the placement of a fingertip on the Rosenmuller's fossa to open the ET (Figure 3).

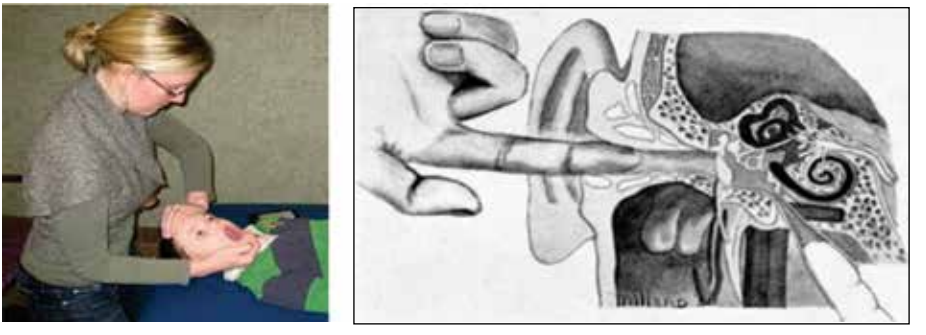

Figure 3. OMTs for pediatric OM.

In the largest study so far, combinations of OMTs with antibiotics decreased the frequency of AOM episodes and the insertion of tympanostomy tubes in otitis-prone children, when compared to antibiotics without OMTs. Children who received weekly treatments had fewer episodes of AOM (P =0.04), and fewer required tympanostomy tubes (p=0.03). Yet, there were no differences in the overall antibiotic use, tympanometry measurements, behavioral parameters and hearing results between both groups. When considering the large drop-out rate (~25%), these conclusions are questionable. Other studies have shown that OMTs administered adjunctively with standard care for children with AOM resulted in faster resolution of MEE following AOM, there are no serious adverse effects, and that OMTs may change the progression of recurrent OM cases. The methodology of these studies is lacking; the study groups were small with high drop-out rates and lacked a control group.

Chiropractic

Chiropractic medicine focuses on the diagnosis and treatment of mechanical disorders of the musculoskeletal system, especially the spine. Chiropractic medicine believes that disorders of the musculoskeletal system affect the general health, via the nervous system. The main techniques involve manipulations of the spine, joints, and soft tissues.

It is hypothesized that spinal manipulation therapy (SMT) mediates changes in the sympathetic and parasympathetic neural activity via the biomechanical changes produced in the spine during treatment. Another hypothesis suggests that cervical SMT reduces tension within hypertonic muscles, increasing both lymphatic drainage and ET opening. Chiropractic is thought to prevent recurrent infections by correcting 'misalignments', and allowing fluid drainage from the middle ear. A systematic report found only a limited quality of evidence for SMT use in children with OM. Although there were no serious adverse effects of SMT, there was no clear evidence to support using SMT.

Xylitol

Xylitol is a 5-carbon sugar alcohol, which is naturally found in low concentrations in the fibers of fruits and vegetables. Fair evidence found that xylitol reduced the incidence of AOM episodes in healthy children. The alleged properties of xylitol to prevent OM are summarized in the following table (Table 3).

1. Inhibition of Streptococcus pneumoniae growth.
2. Inhibition of the attachment of Streptococcus pneumoniae and Haemophilus influenzae to nasopharyngeal cells.
3. Decreases the salt concentration of human airway surface that contains antimicrobial substances, including lysozyme, lactoferrin, human □-defensins and cathelicidin.
4. Increases the efficacy of the innate immune system.
5. Exposure to xylitol lowered cpsB (pneumococcal capsular locus) gene. expression, which changes the ultrastructure of the pneumococcal capsule.
6. Decrease biofilm production by Streptococcus pneumoniae.

Table 3. Protective characteristics of xylitol.

In 1996, Uhari first published a RCT, in which xylitol reduced AOM occurrence by 41%, and fewer children receiving xylitol required antibiotics. Later, the same group showed that xylitol was effective in AOM prevention among daycare toddlers. While ≥1 AOM episode(s) was observed in 41% of the children who received control syrup,

only 29% of the children who received xylitol had AOM episode(s) (30% decrease, 95% CI 4.6-55.4). AOM incidence decreased by 40% compared with control subjects in the children who received xylitol chewing gum, and by 20% in the lozenges group.

These encouraging results encouraged additional studies. In RCTs in which different xylitol remedies were used yielded fewer convincing results. Xylitol was shown to be ineffective in children with indwelling tympanostomy tubes. When xylitol mixture, control mixture, control chewing gum, xylitol chewing gum, and xylitol lozenges were given during an active upper respiratory tract infection (URTI), there was no preventive effect for any of the xylitol mixtures. Recent Cochrane review examined the evidence gathered for the use of xylitol in preventing recurrent OM, and found 4 RCT studies that met the criteria for analysis. Overall, it demonstrated a statistically significant reduction (25%) in the risk of occurrence of OM among healthy children in the xylitol group, compared with the control placebo group (RR 0.75; 95% CI: 0.65-0.88; 95% CI: -0.12 to -0.03). Chewing gum and lozenges containing xylitol appeared to be more effective than syrup; however, it emphasized that children <2 years who are at the greatest risk of developing OM cannot safely use lozenges or chewing gum. Most studies report a 5 times-per-day dosing schedule, which lowers the compliance in most children. Concomitant increase of quantity in each dose reduced the number of xylitol doses to 3-times-per-day, but resulted in various side effects.

A recent National Institute of Health funded study examined if viscous xylitol solution at a dose of 5 g 3-times-per-day could reduce the occurrence of clinically diagnosed AOM among otitis-prone children 6 months through 5 years. Unfortunately, the results were discouraging, as there were no significant differences in the occurrence of AOM and total antibiotic use between the xylitol group vs the placebo group. Therefore, the use of xylitol was not opted by many national guidelines as a means to prevent OM.

Ear candling

E*ar candling*, also known as ear coning or thermal-auricular therapy, consists of placing a hollow candle in the ear canal and lighting the other end (Figure 4). Ear coning has its roots in the traditional healing practices of China, Greece, Egypt, Tibet and North America.

Figure 4. Ear candling.

Ear candling claims to "purify the blood" and heal children with OM through "cleaning" of the middle ear cleft by creating a "negative pressure". It was reported that that ear candling is implausible and demonstrably wrong, leading to deposit of candle residue in the ear canal with no therapeutic effect on extraction of cerumen or the middle ear. It was stated that this therapy may be harmful, causing ear injuries (burns,

occlusions of the ear canal and tympanic membrane perforation), as well as otitis externa.

Vitamin D supplement

In addition to its role in bone metabolism and calcium homeostasis, vitamin D plays a role in immunity and infection. In particular, it has been postulated that 25-hydroxyvitamin D [25(OH)D], the isoform that reflects the individual's vitamin D status, acts as an immunomodulator of both innate and adaptive immune systems, by shifting the T-helper cell pool towards Th2 status, inducing antimicrobial peptide synthesis, i.e., cathelicidin and β-defensins, and inhibiting the production of pro-inflammatory cytokines. Moreover, vitamin D is involved in the modulation of macrophages and dendritic cells activities, and in regulation of toll-like receptor mediated events in neutrophils. Therefore, vitamin D status may influence the incidence and severity of some bacterial and viral infections, as indicated by previous clinical studies performed in patients with tuberculosis, respiratory tract infections and AOM.

A longitudinal cross-sectional study was conducted in 84 children aged 1-5 years with RAOM and in 108 comparable healthy controls. A significantly reduced mean serum 25(OH)D levels was found in children with RAOM compared to controls (11.4±9.8 ng/mL vs. 29.2±13.9 ng/mL; $p<0.05$), and an increased percentage of children with serum 25(OH) D levels<20 ng/mL in the study group compared to controls (69% vs. 30%; $p<0.05$). When vitamin D was given to children with RAOM who also had vitamin D deficiency, the occurrence of AOM and RAOM significantly dropped during the 1-year follow-up period. Vitamin D quantities may play a role in the susceptibility to OM. These data were confirmed by the same group, which has recently reported in a single-blind, case-control study significantly reduced serum 25(OH)D levels in 88 children with AOM compared to 81 healthy controls (20.6±10.2 ng/mL vs. 23.8±10.3 ng/mL; $p<0.05$).

The relationship between decreased vitamin D levels and the increased risk of RAOM was also evaluated. The possible effect of vitamin D supplementation in reducing the number of AOM episodes was studied in 116 otitis-prone children (58 receiving vitamin D supplementation and 58 receiving placebo). It was found that the number of children experiencing at least one AOM episode was significantly lower in the treatment group, when compared with the placebo group (26/58 vs. 38/58; $p=0.03$), and that the mean number of global AOM episodes ($p=0.03$) and uncomplicated AOM episodes ($p<0.001$) occurring in the vitamin D group was significantly lower, when compared to the control group. The likelihood of AOM occurrence was significantly reduced in patients with serum 25(OH) D levels ≥30 ng/mL. This study concluded that vitamin D deficiency is frequent in otitis-prone children, and that blood 25(OH)D concentrations ≥30 ng/mL are protective.

Despite these data, there is not enough evidence to support a causative effect of vitamin D deficiency on the etiology and pathogenesis of AOM, and to suggest a protective effect of vitamin D supplementation in children with RAOM; further controlled clinical trials are needed to solve these questions.

Probiotics

Oral probiotics

Probiotics are live microorganisms that offer health benefits by modulating the microbial community and enhancing host immunity. These effects can be obtained through inhibition of pathogen colonization, production of bacteriocins and enhancement of both mucosal and systemic immunity.

Commercial probiotics preparations are based on single or multiple bacteria. Most of the data regarding preventive efficacy of probiotics against infections have been obtained in patients with gastrointestinal diseases, in whom it was demonstrated that administration of probiotics can significantly reduce the risk of development of antibiotic-associated diarrhea.

Data regarding the use of probiotics on OM have gathered in the last few years, showing variable efficacy. In general, the reduction in OM incidence in treated children was limited. The possibility that probiotics could reduce the occurrence and duration of AOM episodes or the nasopharyngeal carriage of otopathogens in otitis-prone children was assessed in a study involving 309 children, aged 10 months to 6 years, who were randomized to consume for 24 weeks a probiotic daily or a placebo capsule. The probiotic treatment did not reduce the occurrence (probiotic versus placebo 72% vs 65%) or the recurrence(≥3 episodes) of AOM (probiotic versus placebo 18% vs 17%), while a reduction in the occurrence of recurrent URTIs was noticed in the probiotic group (OR for ≥ 4 URTIs = 0.56, OR for ≥ 6 URTIs = 0.59). The administration of probiotics did not modify the nasopharyngeal carriage of Streptococcus pneumoniae or Haemophilus influenzae, but increased the carriage of Moraxella catarrhalis (OR = 1.79), confirming from a microbiological point of view the basis for the negative results in prevention of AOM.

81 infants requiring formula feeding were recruited in another study, and were randomized to receive either infant formula supplemented with the probiotics Lactobacillus rhamnosus GG and Bifidobacterium lactis Bb-12 or placebo until the age of 12 months. During the first 7 months of life, the proportion of AOM episodes was significantly lower (treated: 22% vs placebo: 50%, p=0.01), and antibiotics were significantly less prescribed (treated: 31% versus placebo: 60%, p=0.01). However, when considering the whole first year of life, the prevalence of AOM was not statistically different (treated: 13% vs 25%).

In a double-blind, placebo-controlled trial, follow-up formula supplemented with probiotics and prebiotics was tested if it could reduce the risk of AOM. Two hundred twenty-four healthy infants aged 7 to 13 months were randomly assigned to follow-up formula supplemented with probiotics and prebiotics (Raftilose/Raftiline), or follow-up formula alone. During the 12 months study period, the treatment and the control groups did not differ in the incidence of AOM (incidence rate ratio, 1.0, 95% CI: 0.8-1.2), lower URIs incidence (IRR 0.9, 95% CI: 0.7-1.2) or number of antibiotic treatment courses (RR 1.0, 95% CI: 0.8-1.2), which were mainly prescribed for AOM (82%). The nasopharyngeal flora composition did not differ in the two groups at any time during the follow-up.

Topical probiotics

Topical administration of probiotics has been considered as a method to reduce the risk of recurrent AOM in children when administered by nasal spray. The most largely studied microorganism has been -hemolytic Streptococcus (AHS), taking into account that the presence in the nasopharynx could interfere with survival and multiplication of pathogens more frequently associated with AOM development.

108 otitis-prone children were enrolled and after a 10-day antibiotic course, they were randomized to receive a nasal spray containing 5 AHS strains (selected among those colonizing the Eustachian tubes opening, because of their superior inhibitory activities against otopathogens) or a placebo solution. Both streptococcal and placebo solutions were sprayed for a first 10-day period and then resumed for 10 days starting

from day 60 of the study. During the 3-months follow-up, children who were given AHS-supplemented spray experienced significantly more cure from AOM (42% versus 22%, p=0.02) and less recurrences (40% versus 51%, p=0.04). The author's conclusions favoured the use of AHS to protect against RAOM.

Subsequently, 43 children were randomized to receive with a nasal spray daily for 4 months a suspension of 10% skim milk and 0.9% NaCl containing 5 selected AHS strains with very good in vitro inhibitory activity on otopathogens, or skim milk with 0.9% NaCl[4]. The proportion of children with recurrences was similar in the two groups (treatment group: 44%; placebo group: 40%) and no significant changes in the nasopharyngeal colonization of otopathogens was detected.

The negative results, in association with the potential risk of infections directly due to the bacteria used for topical treatment, have led to halting of research with these strains. More recently, *Streptococcus salivarius*, an AHS isolated from the pharynx of healthy subjects, has received attention. It is a potential nasopharyngeal probiotic, thanks to its immunomodulatory and anti-inflammatory skills, its production of plasmin-encoded bacteriocins and its good safety profile. The role of S. salivarius K12 in preventing recurrent streptococcal pharyngitis and AOM was evaluated in 82 children aged 3 to 12 years with a recent history of recurrent oral streptococcal pathology, who were randomized to be administered an oral slow-release tablet containing five billion colony-forming units of S. salivarius K12 and to a control group. The 41 children who completed the 90-days treatment had significantly fewer episodes of streptococcal pharyngeal infections (- 92.2%) and/or of reported AOM (- 40%) during the 90-day probiotic intake compared to the previous 12 months (but the difference was not significant for AOM if adjusted for the time period). A reduction in the reported incidence of pharyngeal and middle ear infections by 65.9% was also registered in the treatment group in the 6 months follow-up after the treatment.

The results of the first study in which Streptococcus salivarius 24SMB, with significant activity against AOM pathogens, was intranasally administered in otitis-prone children were also reported. Children aged 1-5 years with RAOM history were randomized 1:1 to receive an intranasal S. salivarius 24SMB or placebo twice daily for 5 days each month for 3 consecutive months and followed up for 6 months. The number of children who did not experience any AOM was higher among the children treated with the S. salivarius 24SMB preparation than among those in the placebo group (30.0 vs 14.9 %; p=0.076) and among children colonized by S. salivarius 24SMB after treatment compared to the non- colonized (42.8 vs 13.6 %; p=0.03). Similar results were observed when the children treated with antibiotics for AOM were analysed (67.8 vs 95.5 %; p=0.029).

Probiotics indeed seem a promising method in the prevention of AOM and URI but, because of the contrasting results of the available studies, further clinical evaluation is needed in order to assess their true potential.

Conclusion

Despite the conservative therapeutic nature of CAM therapies for OM, which do not include drugs or surgery, CAM is currently not considered a treatment option for OM in the medical community, due to the limited and confusing supporting scientific evidence. In our opinion, there may be some benefits using homeopathy, phytotherapy, xylitol, vitamin D and probiotics for the prevention, and treatment of AOM. For RAOM, we have noticed scant benefit for the use of probiotics and vitamin D. For OME, a mild-moderate benefit was demonstrated for the use of probiotics and xylitol.

At this time, we recommend that further studies should be conducted in order to establish the additive value of the of CAM therapies for OM. We propose RCTs in pediatric mild-moderate AOM cases, in which antibiotics can be deferred or withheld, so the tested CAM therapy will be evaluated vs. placebo/no treatment. We further suggest that trials should be conducted in which infants fed with probiotic-enriched formulas will be evaluated against others fed with standard formula, in terms of age of first AOM episode and RAOM prevalence.

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Subannular tube: A treatment option to chronic Eustachian tube dysfunction

Pedro Alexandre, MD, **Sónia Pires Martins**, MD, **Margarida Santos**, MD and **Carla Pinto Moura**, MD, PhD.

History and procedure

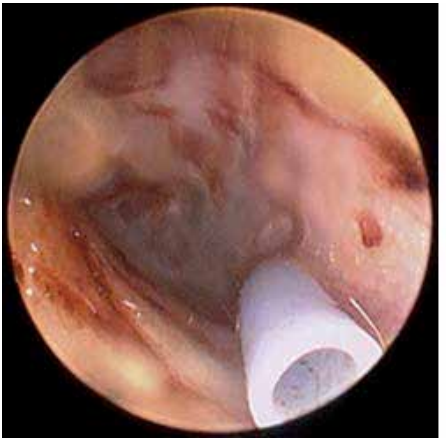
The subannular tube placement is a procedure in which a ventilation tube is inserted beneath the tympanic annulus, firstly illustrated by M. S. Ersner and Alexander, and first described by Simonton in 1968 [1]. This technique was developed in order to avoid the placement of transtympanic ventilation tubes in weakened and atrophic tympanic membranes, providing long-term ventilation of the middle ear without interfering with the tympanic membrane.

The original procedure, as described by Simonton, uses a miringotomy knife to make a 5 mm long incision in the skin of the ear canal, 3 mm from the tympanic membrane. A tunnel is created by elevating the skin and the fibrocartilaginous ring, in order to gain access to the middle ear. A stapedectomy pick is then inserted through the incision, the miringotomy knife withdrawn, and a suction tip introduced to remove fluid from the middle ear. The technique is completed after the placement of a tube, flanged at the medial end, into the tunnel created under the skin and fibrocartilaginous ring.

In our practice the procedure is performed in the operating room under general anethesia with the use of a microscope. A classic Rosen incision is done in the skin of the ear canal, about 4 to 5 mm from the annulus. A tympanomeatal flap is created to allow for an exploratory tympanotomy. This modification is proven to be advantageous since there are often middle ear adhesions and inflammatory tissue between the ossicular chain and the tympanic membrane or promontory. These are removed, and retractions pockets are elevated, if present. Any effusion encountered is removed with a suction catheter and the status and mobility of the ossicular chain are inspected. Care must be taken to preserve the chorda tympani and ossicular chain's integrity while removing the middle ear effusion and adhesions.

Depending on the inflammation state of the middle ear, a silastic sheet is laid on the promontory of the tympanic cavity. The silastic was shown to promote mucosal regeneration and help preventing the recurrence or formation middle-ear adhesions, thus contributing to an improved post-operative hearing [2]. It was also proved that the long-term placement of silastic in the middle ear does not cause foreign body reaction, rejection, or chronic inflammation [3].

The flanges of a T-tube are trimmed, one longer than the other, and the tube is placed in the posterior-inferior quadrant of the tympanic membrane, under the elevated border of the tympanic sulcus. The shorter flange is fitted into the hypotympanum and facial recess, and the longer one is accommodated in the mesotympanum. The tympanomeatal flap is then repositioned over the tube. Careful attention is paid not to interfere with the ossicular chain during the tube placement. As Saliba et al. described, the subannular tube extrusion rates without bony groove were similar to the extrusion rates of Carr and Robinson, that performed a groove in the bony canal posterior wall to hold the shaft of the tube in place [4,5]. Although we do not drill a bony groove in the external auditory canal, we have similar results of extrusion rates with reduced risk to damage the facial or corda tympani nerves. After the tube insertion and repositioning of the flap, a silastic sheet is laid between the tube and the wall of the canal, in order to reduce the risk of post-operative tube lumen occlusion with granulation tissue. The last step involves packing of the external auditory canal with silastic sheets and merocel® soaked in antibiotic (ofloxacin) drops. The ear packing is removed after 2 weeks. During the procedure a tympanoplasty or ossicular chain reconstruction can also be performed if indicated. (Figures 1 and 2).



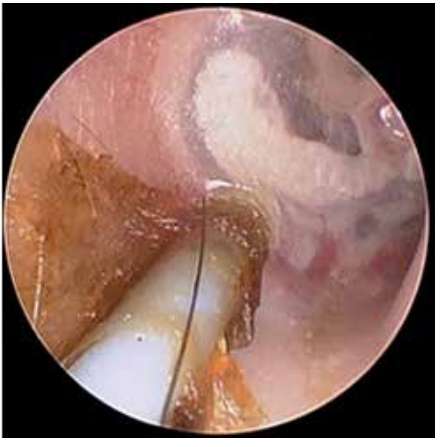


Figure 1. Tympanic membrane with central retraction pocket (right ear).
Figure 2. Tympanic membrane with a Tube of Good in subannular position (right ear).

Surgical indications

Chronic Eustachian tube dysfunction and/or effusion of the middle ear often induce tympanic membrane changes that include retraction pockets, incudostapediopexy, atrophy, and atelectasis. Such tympanic membranes present a challenge to the ventilation of the middle ear with tympanostomy tubes because of their rapid extrusion due to the lack of fibrous tissue to support it, or because of the impact of potential complications (miringosclerosis, focal atrophy, perforation) on an already weakened membrane. Therefore, long term subannular tubes have been primarily aimed to treat recurrent/refractory otitis media with effusion and chronic Eustachian tube dysfunction with significant tympanic membrane changes [6,7].

Special attention is paid to certain populations at risk. Cleft palate is among the most common congenital defects, and otitis media with effusion is nearly universal in this population [8,9]. The anatomical changes of the palatal muscles that occur in cleft

palate predispose to chronic Eustachian tube dysfunction [10,11]. Surgical correction of the palate doesn't reduce the risk of otitis media with effusion [12]. As a result, children with cleft palate are often submitted to multiple sets of transtympanic tubes - with the intrinsic complications - until they "outgrow" the Eustachian tube dysfunction. Repeated transtympanic ventilation tube insertion is associated with tympanosclerosis, retraction pockets, cholesteatoma, perforation and otorrhea [13,14]. While long-term transtympanic tubes (T-tubes) could remain in place for a reasonable period of time, they are associated with a non-neglectable impact on the integrity of the membrane, with higher rates of perforation [15]. The insertion of a long-term tube beneath the tympanic annulus could provide a solution to the middle ear pathology in this specific population while minimizing adverse outcomes. At our department the subannular tube technique has been used in children with cleft palate who present long term ear pathology and then extended to non-cleft palate patients who presented chronic severe middle ear pathology that were faced with the same therapeutic dilemma.

Complications associated with the technique

Subannular tube complications are similar to those resulting from the placement of conventional transtympanic tubes and include otorrhea, lumen blockage, granulation tissue, perforation and early tube extrusion. The majority of studies with the subannular technique reported relatively low rates for each complication, excepting Jassar et al. [16]. Saliba et al. reported otorrhea in 21.4% of the patients [5], Daudia et al. reported a 16% rate of lumen blockage and a 5% rate of granulation tissue around the tube [6], and Elluru et al. reported a 2% rate of perforation after tube removal or extrusion [7]. Follow-up at the outpatient clinic is of the uppermost importance in the post-surgical period to identify and manage these complications. Obstruction of the tube by cerumen or secretion is not rare and requires cleaning with suction in the outpatient visit. Hence, patient cooperation is paramount and a prerequisite to surgical success.

The perforation after tube removal or extrusion is reported to be lower in subannular than in transtympanic tubes [6]. Nevertheless, perforation of the membrane can occur during the surgical procedure, since it is performed a tympanotomy. A rupture of the membrane can occur specially if adhesions between the membrane and the ossicular chain or promontory are present. If it happens, it can be managed with a tympanoplasty procedure. Extrusion may occur earlier than expected, especially during processes of otorrhea, or accidentally in the cleaning process.

Conclusion

Subannular tube placement is a simple and safe procedure that appears to be a viable alternative to ventilate the middle ear with chronic Eustachian tube dysfunction, especially if tympanic membrane trophic changes are present. In our clinical practice they offer a more interesting alternative to multiple short-term tubes or long term transtympanic tubes.

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Cartilage in middle ear surgery in children

Marc Pellicer, Prof., MD. and **Anubis Contreras**, MD.

Introduction

For several decades now cartilage has been the material of choice for middle ear surgery. It is mainly used for reconstructing the tympanic membrane or the external auditory canal. Fascia temporalis has been progressively replaced by cartilage as reconstruction material for bony and tympanic substance losses in middle ear pathology, specially in Cholesteatoma surgery.

Since cartilage is far more resistant to depression of middle ear cavities than fascia (Duckert) [(1)], it is even becoming popular for ossiculoplasty as an alternative to partial ossicular replacement prosthesis (PORP).

Tos [(2)] published in 2008 a classification of cartilage tympanoplasty methods that shows a wide range of techniques in the use of cartilage in otology both in adults and children.

Techniques chosen in Cholesteatoma surgery must be decided by the surgeon and must be adapted to the field and to the history of the disease in any given case, disregarding all ideological or school considerations [(3)].

Tympanic reconstruction and canal wall reinforcement is mandatory in cases of extended cholesteatoma in pediatric population given the high risk of retractive pathology in this group. (Lazard) [(4)].

Regarding to the material used for reconstruction, autologous cartilage, whether obtained from tragus, cymba or conchae, has a greater resistance than fascia or perichondrium to negative pressure in the middle ear, because of its rigidity and convexity, therefore avoiding retractions, adhesions and atelectasis. Hence, it is an excellent alternative material for tympanic membrane reconstruction in cases of poor middle ear ventilation from Eustachian tube dysfunction.

Cartilage nourishes by diffusion, and unlike fascia and perichondrium does not need new vascular support, being therefore more resistant to insufficient blood suply and infections.

Nevertheless, rigidity and thickness of tympanic membrane and its possible impact in hearing outcomes is controversial (Zahnert) [5].

Historically, use of cartilage in middle ear surgery, was pioneered by Jansen [6] in 1963. Goodhill [7] introduced the perichondral-cartilage grafts in 1967, revisited by Dornhoffer [8] in 2003. The Palisade cartilage technique, firstly reported by Heerman [9] (1970), has been modified by reducing the number of cartilage trips from six to three by Bernal in 2003 [10]. Sound transmission seems to be improved by this latter modification because of a better contact with the ossicular chain, ossiculoplasty or prosthesis material. The double cartilage block ossiculoplasty for partial ossicular reconstruction in the presence of an intact stapes was described in 1987 by Luetje and Denninghoff [11] Roulleau and Roger [12] sistematically introduced its use in routine surgical treatment of Retraction pockets, Dornhoffer [13] (2003) gathered even more insight in its use. Tos [2] published his "Cartilage tympanoplasty methods: Proposal of a classification" in 2008 and Nevoux [13] and Gaillardin [14] published, in 2011, large series on the use of "Shield cartilage" and "Modeling cartilage" respectively for reconstruction in Canal Wall Up (CWU) Tympanoplasties for Cholesteatoma.

Following their lead, this chapter highlights our ideas on cartilage use in timpanoplasties and some of our series results.

We use cartilage in different techniques adapting to the conditions encountered during surgeries.

We use cartilage grafts for: 1) Tympanic membrane reconstruction in special circumstances, 2) In Sade's grade IV and III Retraction pockets surgery, 3) In type III CWU tympanoplasties (Shield cartilage for tympanic membrane and Double cartilage block for ossiculoplasty if stapes present), 4) In CWD type III tympanoplasties (Shield and Palisade techniques); and 5) To create a Neoplatina after cholesteatoma excision with the "Cartilage shoe technique" (Figure 1).

These techniques offer two major advantages: they use well tolerated autologous material and they offer no additional cost.

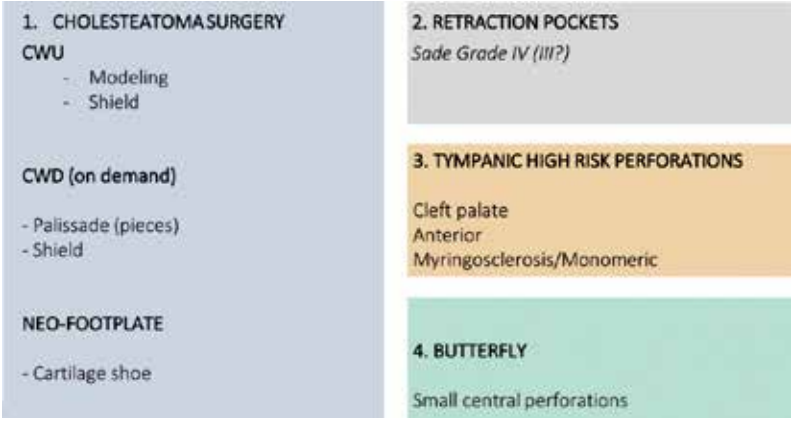

Figure 1. Cartilage graft uses.

Tympanic membrane reconstruction

As far as tympanic perforations is concerned, we use the butterfly technique for small and central perforations and the shield technique for high risk perforations (those anterior, in cleft palate patients or with large tympanosclerosis), as well as for cases of failure of previous surgery where fascia was used.

We would like to underscore some technical hints in the use of cartilage to repair large tympanic perforations when performing shield technique: 1) Cartilage can be harvested from tragus or cimba; 2) Cartilage must be thinned centrifugally. In case of using a chondro-perichondrium graft, it also has to be thinned, on the perichondrium-free side, and conserving a 1 to 2 mm peripheral perichondral border; 3) Cartilage must be placed under the malleus handle and it must lean on the External auditory canal (EAC), 4) In some cases, a second piece of cartilage can be used to reinforce the pars flaccida; 5) There should be no spaces left between the bone and the cartilage or between pieces of cartilage. We recommend, especially for junior specialists, to keep in mind the basis of ear surgery, such as staying parallel to structures when separating/dissecting them, or keeping your instruments inferiorly when clamping the cartilage or reconstruction material of choice, in order to avoid injuries to ossicular chain when present.

Surgery can be scheduled from age 7 yo provided there has been not otorrhea in the previous 6 months. The goals are: a) To close the perforation to avoid infections from outer origin; b) To improve the child's quality of life so aquatic activities can be enjoyed; c) To improve hearing if impaired; d) To prevent epidermic migration through the perforation; e) To make use of hearing aids easier if needed. We will also use cartilage (or cartilage-perichondrium) in some special circumstances such as: 1) Craneofacial malformations (i.e. Cleft palate), 2) Down syndrome (oto-endoscopic surgery might have a place as it offers several advantadges, in our hands, in those cases of narrow EAC and atlanto-axial instability), 3) Allergy, Eustachian tube dysfunction or Primary ciliary dyskinesia – Kartagener syndrome-, 4) Failure of previous surgery with other material (Bernal, Koch) [10,15].

In a series from our team, 40 Cleft palate patients with a subtotal tympanic perforation (ages 7-14 yo) who underwent type I endoaural tympanoplasty were randomized in two groups. In the first group (20 patients) m. temporalis fascia graft was used, and in the second group tragal cartilage was used, in both cases by underlay technique. Otoscopic and audiometric follow-up (14-21 months) showed the following results (Table 1, Table 2): a) No lateralization or blunting occurred; b) Success –closing of perforation- was achieved in 95% of cartilage cases –only one retraction- and a 100% closing of the Air-Bone Gap (ABG) at<20 db – (Ozbeck)(16); c) Only 70% of success was achieved in the fascia temporalis group - 3 reperforations and 3 atelectasis – with temporarily good results on ABG closing with a tendency towards Rinne worsening in later audiometry tests during follow up – (Harterink) [17].

Rate of success	(Closing of perforation)		Total
	Yes	No	
Cartilage	19 (95%)	1 (5%)	20
Fascia	14 (70%)	6 (30%)	20
Total	33 (82%)	7 (18%)	40

p = 0.091; Fisher's exact test.

Table 1. Anatomic results: perforation closure.

		Media	SD	P Value
Cartilage		*Db*		
	Rinne before surgery	24.75	3.43	<0.001
	Rinne after surgery	14	3.84	
Fascia				
	Rinne before surgery	25	3.63	<0.001
	Rinne after surgery	14.25	4.38	

Table 2. Functional results: Air-bone gap.
Paired T-Test.

Retraction pockets and cholesteatoma surgery in children

Sade's Type IV Retraction pockets and some cases of type III that relapse after ventilation tube placement can be treated by means of Canal wall up (CWU) tympanoplasty and cartilage graft reinforcement (Roger) [12].

In cholesteatoma in children, our team endeavours to perform CWU tympanoplasty with double cartilage block ossiculoplasy and tympanic membrane reconstruction with "cartilage shield" (Nevoux) [13] to achieve better hearing outcomes as well as improve quality of life, and ability to enjoy aquatic activities.

Because cartilage grafts are opaque, follow up must be done with Eco-plannar wheighted diffusion MRI at 12 months (Lecler) [18] to rule out cholesteatoma relapse and/or with CT scan to evaluate osiculoplasty in case of ABG worsening.

Surgical technique

A majority of patients undergo one stage surgery by retroauricular incision, while small external epitympanum cholesteatomas are operated endoaurally. In most cases we perform a canal wall-up technique (CWU). In the few cases we need to do a CWD technique it is usually because a large extension of cholesteatoma precludes a good exeresis by means of a more conservative technique. Minor aticottomies and antrostomies are closed with cartilage grafts in contact with the preserved EAC. Cartilage is usually obtained from the cimba and seldom from the tragus when a retroauricular incision is performed.

There are nuances regarding Cartilage plate techniques within literature, with authors differing on whether the perichondrium has to be removed from one or both sides of the cartilage fragments, as well as the size of the grafts, especially that in contact with the tympanic membrane.

In our practice, the cartilaginous tympanic membrane repair is made with a cartilage island graft wide enough to cover every perforation border and surpass them by 1-2 mm of tympanic membrane, with its perichondrium cover on the superficial side, which has to have a greater diameter. We seek to preserve a part of the native tympanic membrane free of reinforcement to facilitate postoperative otoscopic control. Some authors also support preserving a part of the native tympanic membrane free of reinforcement in case a tympanic tube insertion is needed for persistent ventilation problems.

The ossiculoplasty must not modify the quality of the tympanic membrane reinforcement and must take into account that oftentimes distances are reduced in the middle ear cavity of these patients. If stapes is present, we use a double block cartilage ossiculoplasty (Luetje and Denningnhoff) [11] - without perichondrium (Nevoux) [13] – between stapes and the cartilage tympanic graft (Figure 2). The absence of perichondrium between the fragments, provide a more rigid assembly and, thus, less energy loss in sound transmission. In some cases, just one fragment is enough. If stapes is absent, we use a tytanium TORP (Total Ossicular Reconstruction Prosthesis) between the oval window and the cartilage tympanic graft (severing the malleus muscle tendon previously). In those rare cases where platina is absent because eroded by the cholesteatoma, a new cartilage "neoplatina" can be built (Cartilage shoe neoplatina) and ossiculoplasty can be completed with a TORP in a second stage, Bremke) [19,20].

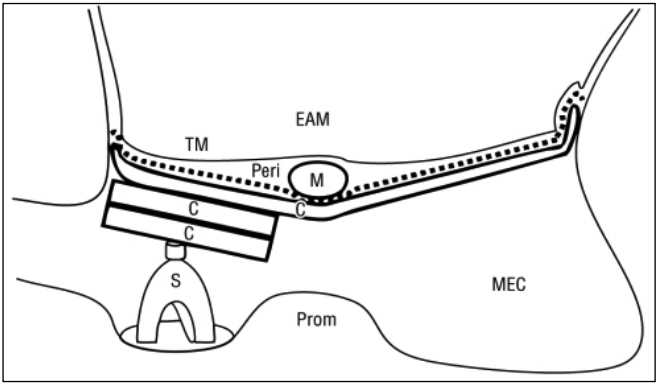

Figure 2. Cartilage shield tympanoplasty associated with double cartilage plate ossiculoplasty. C indicates cartilage; EAM, external acoustic meatus; M, malleus; MEC, middle ear cleft; Peri, perichondrium; Prom, promontory; S, stapes; and TM, tympanic membrane. (From Nevoux J et al, 2011).

In one of our series, comprising 120 tympanoplasties type III (64 right and 56 left), average age 14 yo, follow up 3 to 8 years, with stable results, tympanic closure was achieved in 98,5% of cases, reperforation ocurred in 1,5%, retraction in 2,5% and residual cholesteatoma in 2,0%. Average ABG was 34,4 db preoperatively, average ABG was 18,1 db post-operatively (>80% of patients with 0-20 db ABG at 3 years of follow-up).

Canal wall down (CWD) tympanoplasty with a radical cavity must be spared (reserved) for those rare cases with large destruction of the EAC posterior wall, anatomical modifications, or in relapse cases. In those cases, open cavities are obliterated partially with cavum conchae cartilage, using little pieces of cartilage to fill the anterior epitympanum, antrum and to cover posterior semicirculat canal (psc). Meatoconchoplasty was done in all CWD cases, using the obtained cartilage for reconstruction.

For CWD tympanoplasty, we use palisade technique instead of shields since small cartilage fragments adapt easily to anatomical variants of middle ear. Well placed side by side are as resistant as shields are. Separation (gap) between cartilage strips must be avoided by all means as retrations between them with epidermic epithelium may lead to relapse of cholesteatoma (Bernal) [10]. Complete obliteration of anterior epitympanum, supratubal fossae and atticum is strongly recommended. In cases with poor

ventilation of the middle ear a partial retraction might occur. Revision surgery after palisade reconstruction technique is more difficult because the modification of cartilage consistency and fibrous adhesions to the promontory.

In summary, albeit its rigidity has risen some controversies, the resistance of cartilage has provided a wide range of uses in ear surgery. When properly modeled, chopped, and thinned -if needed- the cartilage can be used for closing tympanic membrane perforations, from small ones by butterfly technique, to larger perforations and cholesteatoma surgery reconstructions by modeling, shield or palisade technique, as well as in ossiculoplasty, with great functional and anatomic results. This versatile, autologous material can be harvested from different anatomical sites according to the type of surgery planned. Due to all the aforementioned it seems suitable to assure it is worthwhile learning to manage cartilage in ear surgery.

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Long-time outcome of tympanoplasties in children

Sergio Sanhueza Cubillos, MD.

Summary

The anatomical and functional outcome of 257 primary tympanoplasties performed in a pediatric population between January 1991 and December 2017, as well as the results obtained in secondary and tertiary surgeries in this same population were prospectively analyzed. The processes that were standardized to make outcomes comparable are discussed. Mean follow-up was 13.5 years. Outcomes were are analyzed according to age of the patients divided into the following groups: < 10 years, < 13 years, and < 15 years. Among different variables that were analyzed as predictive factors, size and site of tympanic membrane perforation were found to be statistically significant. No significant differences were observed in surgical technique, graft type, or status of the contralateral ear. Closure of the perforation was obtained with an adequate graft position in 85.99% of the interventions (N 221), closure of the perforation but with lateralized graft in relation to its annulus in 6.61% (N 17), and perforation of the graft occurred in 7.39 % (N 19).

Outcome of reinterventions was poor as closure of the perforation with a properly positioned graft was achieved in only 42.10% of this population (N 8), while a second perforation of the graft was observed in 21.05% sample (N 4), lateralization of the tympanic graft in 26.31% (N 5), and secondary cholesteatomas in 10.52% of these 19 cases (N 2).

None of the patients with graft lateralization required revision surgery and none of the six patients who underwent reintervention presented with anatomical or functional complications. Secondary cholesteatomas were approached via posterior tympanotomy without recurrences after a follow-up of 8.3 to 9.5 years.

Hearing results may considered to be satisfactory as an air-bone ga < 10 decibels or closure of the gap was achieved in 58.75% of interventions (N 151), with an overall reduction in the thresholds of 13.72 dB; in secondary interventions these results were achieved in only 36.84% of the sample (N 7).

No complications were observed in tertiary surgeries.

Key words: Tympanoplasty, follow-up, secondary tympanoplasty, tertiary tympanoplasty, posterior tympanotomy, hearing, graft.

Problem analysis

In children, as in adults, studies on tympanoplasty report large differences in the rates of graft loss and hearing results achieved [(1)] (Table 1). Nevertheless, comparison of different studies is complex, as in addition to differences in and number of variables, there are large differences in follow-up times, techniques used, biological settings in which the intervention was performed, age at intervention, and conditions of the upper respiratory tract at the time of surgery.

As a result, controversy exists regarding the factors that may affect final anatomical and functional outcomes of pediatric tympanoplasty. Nevertheless, these data are essential to define which patients may have a better outcomes and to identify factors for a poor prognosis.

AUTHORS	SAMPLE SIZE	YEAR	GRAFT LOSS		FOLLOW-UP
RIBEIRO	91	2010	14.3 %	TEMPORAL FASCIA	> 36 MONTHS
CABRA & MONOUX	117	2010	17.78%	CARTILAGE - PERICHONDRIUM	
			34.40 %	FASCIA	> 24 MONTHS
DUVAL & GRIMMER	285	2014	27.5 %	PERICHONDRIUM CARTILAGE – PERICHONDRIUM	> 7 MONTHS
SABORNIN	94	2017	13.1 %	TRAGAL PERICHONDRIUM	> 60 MONTHS
YEGIN & CELIK	108	2017	7.90 %	CARTILAGE – PERICHONDRIUM	
			35.0 %	FASCIA	> 12 MONTHS

Table 1. Variability in outcomes published on graft preservation in timpanoplasty in children.

Objective

To identify variables that, independently or in combination, have an impact on the anatomical and functional outcome of tympanoplasties performed in children, assessing the anatomical and functional results achieved in children that underwent primary, secondary, or tertiary tympanoplasty. Furthermore it was evaluated if these variables could be validated as predictors of functional and/or anatomical success of this surgical procedure.

Definitions

Good anatomical outcome was considered complete closure of the tympanic membrane defined as intact at least 12 months after the surgery. To compare hearing results, pre- and postoperative auditory thresholds of frequencies of 250 cycles per second (cps), 500 cps, 1000 cps, and 2000 cps were considered.

Material and methods

A prospective study was conducted evaluating the anatomical and functional outcomes of 257 tympanoplasties performed in 236 children, of which sequential tympanoplasties were performed in both ears in 21, between January 1991 and December 2017. Age of the patients ranged from 6 years 3 months to 14 years 11 months at the time of surgery. Patients were divided into three groups: younger than 10 years (N 33), younger than 13 years (N 177), and younger than 15 years (N 47).

General inclusion criteria

- Pediatric population with chronic otitis media without cholesteatoma.
- Primary, secondary or tertiary surgical intervention performed at Hospital Naval of Viña del Mar.
- At least one preoperative pure-tone audiometry.
- At least one audiometry in the immediate postoperative period (third month postop).
- Last audiometric recording in the last half of 2015 or later.

Specific criteria of the simple

- Uniform and consensual criteria were established in order to correctly identify the indications and procedures carried out: indications, approach, type of grafts used, surgical technique, and follow-up were standardized for the entire sample at the different Navy Hospitals.
- All surgeries were evaluated in terms of anatomical and functional results obtained and complications, according to age group, with a special focus on hearing outcome assessed by pre- and postoperative pure-tone audiometry.
- Surgical procedures were performed by surgeons trained in otolaryngology surgery or under their supervision.

Selection variables as prognostic factors of tympanoplasty:

1. **Age**: A lower age limit of 6 years was established, mainly because it allowed reliable pure-tonal audiometry; children over 6 years of age are more likely to follow directions. Different reports support this age as the threshold to achieve satisfactory results [(2)], although other studies reported satisfactory results at all ages [(3)].

2. **Biological behavior**: There is consensus on the hypothesis that recurrent bacterial inflammatory activity in chronic otitis media affects final outcome, resulting in a poor prognosis for anatomical graft survival. In this study, only patients in whom symptoms of bacterial infection were resolved with short-term local therapy or those who required oral antibiotics occasionally for short periods achieving a dry ear were included. The time of absence of otorrhea in the ear was arbitrarily set at 60 days.

3. **Approach**: The surgical approach was mainly defined by visual observation of the perforation margins:

Endaural: full view, through the canal, of the perforation margins. This was the approach of choice, as it is possible to perform these procedures satisfactorily through the external auditory canal, with or without endaural incisions; outcome is similar to the traditional retroauricular (postaural) technique [(4)], with well-known advantages over retroauricular approach including a shorter surgical time, less postoperative discomfort, and a lower risk of surgical-wound infection [(5-8)].

Retroauricular: incomplete view, through the canal, of the perforation margins.

However, **posterior tympanotomy** was selected as the approach of choice in mastoid cavities with cholesteatoma [(9)].

In the majority of cases, a surgical microscope was used (96% of the interventions), while an endoscopic approach was only used in 2015, 2016, and 2017 and only in cases with central perforations with good perimetral margins after removal of the fibrous margin [(10-12)].

4. **Surgical techniques**: Protocolized criteria were used to decide for either a medial or lateral technique, graft position, and indications for partial (PORP) or total ossicular replacement prosthesis (TORP).

- **Medial technique:** central perforations posterior or inferior marginal perforations
- **Lateral technique**: anterior marginal perforations

Concept of medial and lateral techniques:

- Medial or underlay technique: graft is placed ***medial*** to the remaining drum and ossicles.
- Lateral or overlay technique: graft is placed ***lateral*** to the remaining drum and ossicles.

5. **Feasible technical solutions**:
- **Type I:** Normal ossicular chain: MYRINGOPLASTY.
- **Type II**: Present stapes with mobile footplate + missing incus: TYMPANOPLASTY + PORP.
- **Type III**: Missing stapes suprastructure with mobile footplate + missing incus: TYMPANOPLASTY + TORP.
- **Type IV**: Fixed footplate. Missing incus.

6. **Perforation repair material:** In this series, similar biological grafts were used in primary, secondary, and tertiary surgeries. Tragal and perichondrial cartilage was used in endaural techniques and tragal cartilage and temporal fascia in retro-auricular techniques.
7. **General conditions of via aerea**: Previous adenoidectomy and/or tonsillectomy was required in case of hypertrophy and/or associated recurrent suppurative otitis, as these factors are commonly identified to affect success of tympanoplasty [13].
8. **Status of the contralateral ear**: Eustachian tube function has been considered an important prognostic factor in tympanoplasties in children. Therefore, many authors consider the surgical prognosis to be uncertain in case of bilateral chronic otitis media, a contralateral retraction pocket, or contralateral suppurative otitis media or otitis media with effusion [14-16]. Nevertheless, other authors have found no correlation between status of the contralateral ear and surgical results [17]. In agreement with these latter authors, we observed no differences between the condition of the contralateral ear and surgical results achieved.
9. **Size of the perforation**: This is one of the predictive factors often mentioned in the literature. In our study, diameter of the perforation was measured after surgical removal of the fibrous margins. A considerable difference was found in this variable pre- and intraoperatively. In addition, perforation size was used as an initial indicator for the recommended surgical approach.
10. **Follow up**: Anatomical and functional results were evaluated over a follow-up between 1991 and 2017 (mean, 13.5 years).
- 3-monthly follow-up during the first year.
- Indefinite yearly follo-up visits as long as the patient was affiliated to the Navy Health Care System.

11. **Audit of surgical failures in the routine follow up protocol:** All patients who had complications in terms of graft loss, lateralization of the graft, or development of cholesteatomas were analyzed at ENT Committee meetings to discuss the complication. In primary tympanoplasties, the most relevant cause of graft loss (19/14, 73.68%) occurred because of adherence to the initially proposed approach while the trimming of the fibrous edges of the perforation changed its margins and consequently required modification of the initial surgical approach. In one case the likely cause was the use of tragal cartilage and perichondrium of poor biological quality. In a second case the likely cause was inadequate anterior graft stabilization. No probable cause could be established in three cases.

Unused selection variables

1. **Cause of the perforation**: Cause of perforation could not be established in the majority of cases. Nevertheless, in children with traumatic perforations without ossicular chain involvement, as well as those with chronic otitis media associated with craniofacial syndromes were excluded from this study, considering that they constitute entirely different conditions [17]. Cases with perforations secondary to transtympanic tube placement were included in the study.

2. **Suppurative otitis:** Suppurative otitis in the intervened ear was not considered to be a surgical complication in this population (N 14 patients, 5.44 %). In none of the patients this led to perforation of the drum and the use of transtympanic tubes was not required.

Results

PRIMARY TYMPANOPLASTIES IN CHILDREN 1991 – 2017 (N 257): GRAFT PERFORATION

POPULATION ACCORDING TO AGE GROUP < 15 AÑOS N 236 AND N SURGERIES 257 BILATERAL 21

PRIMARY SURGERIES	257 TOTAL	PERFORATION	LATERALIZATION
6 YEARS – 9 YEARS:	33	5	8
10 YEARS – 12 YEARS:	177	12	6
13 YEARS – 14 YEARS:	47	2	3

Overall, 257 tympanoplasties were performed in 236 children between 6 years 3 months and 14 years 11 months of age. In general terms, closure of the perforation and adequate graft position was achieved in 85.99% (221/257), with a mean follow-up of 13.7 years (range, 14 months-18.3 years). In addition, in 17 interventions (6.61%), lateralization of the graft occurred, not requiring an additional surgical procedure in any of the cases. Similarly, perforation of the graft occurred in 19 interventions (7.39%); a second surgery was performed in all.

Analysis according to age groups, showed an intact membrane and adequate graft position in 60.60% of the patients younger than 10 years (13/33); in 5 (15.15%) perforation of the graft and in 8 (24.24%) lateralization of the graft was observed.

The graft was preserved and considered to be adequately placed in 93.22% of the children younger than 13 years (159/177); however, in 6 (6/177) graft lateralization (3.38%) and in 12 (12/177) graft perforation occurred (6.77%).

Similarly, preservation and adequate position of the graft was possible in 89.36% (42/47) of the children younger than 15 years; however, in 3 (3/47) graft lateralization (6.38%) and in 2 graft perforation (4.25%) occurred.

RESULTS OF SECONDARY TYMPANOPLASTIES IN CHILDREN ACCORDING TO AGE GROUP (N 257/19) (7.39%)

SECONDARY SURGERIES: N19

GRAFT PERFORATION 4
GRAFT LATERALIZATION 5
SECONDARY CHOLESTEATOMA 2

	TOTAL	PERFORATION	LATERALIZATION	SECONDARY CHOLESTEATOMA
6 YEARS – 9 YEARS:	6	2	1	1
10 YEARS – 12 YEARS:	11	2	3	1
13 YEARS – 15 YEARS:	2	0	1	0

In patients that presented with tympanic membrane perforation (19/257), a second reconstructive surgery was performed (7.39%).

In this group, the tympanic membrane remained intact and in a functional position in only 8 patients (42.10%) (8/19). In 5 cases the graft was considered to be inadequately positioned (26.31%), although hearing outcome was good and none required additional surgical procedures. Perforation of the tympanic membrane occurred in 4 patients (21.05%). Two other cases developed secondary cholesteatoma (N 2/19; 10.52%), which was resolved by posterior tympanotomy, preserving the posterior wall.

Of these patients, 3 were younger than 10 and 3 others younger than 13 years. No perforations occurred in reinterventions in patients under 15 years of age.

RESULTS OF TERTIARY TYMPANOPLASTIES IN CHILDREN ACCORDING TO AGE GROUP N 257/6 (2.33 % OF PRIMARY SURGERIES 6/257) (31.58 % OF SECONDARY SURGERIES 6/19)		
	TYPE 3 TYMPANOPLASTY	MASTOIDECTOMY VIA POSTERIOR TYMPANOTOMY
6 YEARS – 9 YEARS	2	1
10 YEARS – 12 YEARS	2	1

Six ears required a third surgery (6/257; 2.33 %), either because of graft perforation (4/257) or development of secondary cholesteatoma (2/19). Three occurred in children under 10 and 3 in children under 13 years of age.

In the 4 cases of simple perforations of the tympanic membrane, type 3 functional tympanoplasties were performed because of ossicular chain disruption. Tragal cartilage was placed directly on the stapedial structure. The tympanic membrane remained intact in all these interventions and in none of them the graft lateralized.

The 2 cases of secondary cholesteatoma were approached via posterior tympanotomy with mastoid and epitympanic obliteration ("canal wall up" technique), preserving the back wall. This technique allows for better control of these patients, avoids laborious aural toilets in the pediatric population, and facilitates placement of conventional hearing aids when required.

Neither of the patients presented with cholesteatoma recurrence during a follow-up of 8.3 and 9.5 years, respectively, assessed with Flair MRI over the last 5 years. This was considered as a satisfactory result, as recurrence has been reported in between 2.9 and 5.8% and 2.9% over a 5-year follow-up, although obviously our results are not statistically significant due to the small sample size [18-23]. (Tables 2, 3, 4 and 5).

	PRESERVED AND WELL POTITIONED GRAFT	LATERALIZATION	PERFORATION	CHOLESTEATOMA
PRIMARY N 257	N 221/257 (85.99%)	N 17/257 (6.61%)	N 19/257 (7.39%)	N 0/257 (0.0%)
SECONDARY N 19/257 (7.39%)	N 8/19 (42.10%)	N 5/19 (26.31%)	N 4/19 (21.05%)	N 2/19 (10.52%)
TERTIARY N 6/257 (2.33%)	N 4/6 (66.66%)	N 0/6 (0.0%)	N 0/6 (0.0%)	N 0/6 (0.0%)

Table 2. Summary of results and overall complications after primary, secondary and tertiary tympanoplasty in children.

	LATERALIZATION	PERFORATION	CHOLESTEATOMA	Chronic otitis media with holesteatoma
TYPE 1	14	20	2	**1**
TYPE 2	6	2	0	**1**
TYPE 3	2	1	0	**0**
MASTOIDECTOMY VIA POSTERIOR TYMPANOTOMY	0	0	0	**0**

Table 3. Overall complications after tympanoplasty and mastoidectomy in children according to surgical procedure.

	LATERALIZATION		PERFORATION		Chronic otitis media with cholesteatoma
LATERAL GRAFT N 41	2	(4.87%)	4	(9.75%)	1
MEDIAL GRAFT N 216	15	(6.94%)	15	(6.94%)	1

Table 4. Final anatomical outcome after primary tympanoplasty according to graft position.

	LATERALIZATION		PERFORATION	
CONTRALATERAL CONTRACTION POCKETS N27	3	(11.11%)	2	(7.40%)
CONTRALATERAL CHRONIC OTITIS MEDIA N 21	1	(4.76%)	0	(0.0%)
CONTRALATERAL SUPPURATIVE OTITIS MEDIA N 4	1	(25%)	0	(0.0%)

Table 5. Final anatomical outcome after primary tympanoplasty according to status of the contralateral ear.

Hearing outcome in primary tympanoplasty in children

Diseases affecting the middle ear are one of the leading causes of hearing loss in children and, at ages of increased cortical vulnerability, have a significant impact on language development and early academic outcomes. In our series, 8.17% (21/257) had hearing level (HL) thresholds of 25 dB or less at frequencies of 250 cps, 500 cps, 1000 cps, and 2000 cps, even though they had air-bone gaps ranging from 5 to 12 dB HL dB; 74.31% of the series (191/257) had conductive hearing loss and 17.51% (45/257) had mixed hearing loss with conductive hearing loss predominance.

Postoperative hearing results showed a decrease of < 10 dB or closure of the air-bone gap in 151 of the interventions (58.75%), while in the remaining 101 interventions (41.24%) an air-bone gap of > 10 dB or an increase of the gap compared to the preoperative value was observed.

When specific frequencies were considered, the greatest degree of gap closure was observed between the frequencies of 250 cps and 1000 cps, while a moderate decrease was seen at a frequency of 2000 cps.

Nevertheless, functional hearing gain, measured as the pre- and postoperative difference in the air-bone gap, decreased 13.72 HL dB at the last audiometry at a mean of 10.7 years postoperatively in patients who underwent primary tympanoplasty.

No difference was found between patients who underwent an overlay and those wo underwent underlay tympanoplasty.

There were no changes in word discrimination comparing pre- and postoperative results. (Table 6) (Figure 1).

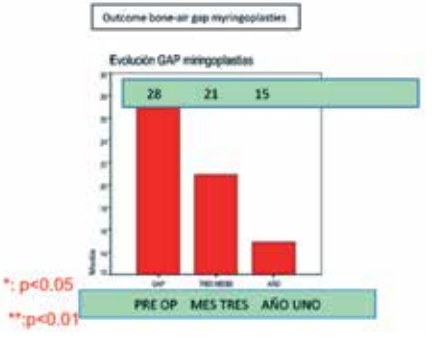

Figure 1. Hearing outcome after type 1 tympanoplasty. Air- bone gap changes.

CHANGES IN THE BONE-AIR GAP	N PRE-OPERATIVE	N POST-OPERATIVE
NO BONE-AIR GAP	14	3
BONE-AIR GAP < 5 Db	32	53
BONE-AIR GAP < 10 dB	48	95
BONE-AIR GAP < 15 dB	86	58
BONE-AIR GAP < 20 dB	22	24
BONE-AIR GAP < 25 d B	36	17
BONE-AIR GAP < 30 dB	19	7

Table 6. Hearing outcome after primary tympanoplasty in children (N 257).

Hearing outcome in secondary tympanoplasty in children

Of those who underwent secondary interventions, 19 initially presented with predominantly conductive hearing loss at frequencies of 250 cps, 500 cps, 1000 cps, and 2000 cps, with pure-tone means of 36 dB HL, and air-bone gaps between 18 and 42 dB HL.

Post-operative auditory results showed a decrease of the gap of < 10 dB in only 7 patients (36.84%) while the gap was unchanged or worsened in the remaining 12 patients (61.15%). Overall hearing deterioration was 42 dB HL at the above-mentioned frequencies after one year of follow-up (24).

There were no changes in word discrimination comparing pre- and postoperative results. (Table 7). (Figure 2).

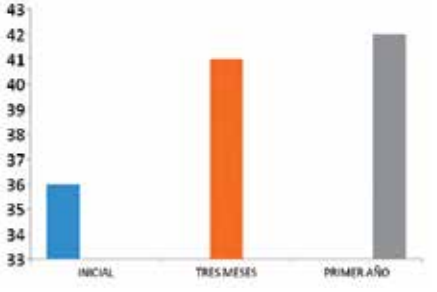

Figure 2. Change in pure-tone average of the sample: Air-bone gap pre- and 12 months postoperatively.

CHANGES IN THE BONE-AIR GAP	N PRE OPERATIVE	N POST OPERATIVE
NO BONE-AIR GAP	0	0
BONE-AIR GAP < 10 Db	5	7
BONE-AIR GAP < 20 Db	1	2
BONE-AIR GAP < 30 Db	6	4
BONE-AIR GAP < 40 dB	3	3
BONE-AIR GAP < 50 dB	4	3

Table 7. Hearing outcome after secondary tympanoplasty.

Discussion

Protocolization of the selection criteria for route of approach, surgical technique, and graft type is essential for comparative analysis. Likewise, periodic functional and anatomical follow-up after tympanoplasty is of utmost importance.

We present a series of 257 tympanoplasties performed in 236 children between 6 years 3 months and 14 years 11 months of age. Overall, closure of the perforation and

adequate graft positioning was achieved in 85.99% of the patients (221/257), with a mean follow-up of 13.7 years (range, 14 months - 18.3 years). Perforation of the graft occurred in 19 cases (7.39%), requiring a second surgery in all.

Analysis according to age group showed an intact and well-positioned tympanic membrane in 60.60% of the children younger than 10 years (13/33), in 93.22% of those younger than 13 years (159/177), and in 89.36% (42/47) of those younger than 15 years, which was statistically significant ($p < 0.05$).

Similarly, perforation of the graft occurred in 5 patients of the group of children younger than 10 years (15.15%), in 12 of those younger than 13 years (6.77%), and in 2 of those younger than 15 years (4.25%). These numbers were also statistically significant ($p < 0.05$) showing that age is a significant variable, while there were no statistically significant differences related to the surgical technique used, i.e. placement of the graft in the medial or lateral position.

Similar to age, size and location of the perforation were found to be significant variables for outcome of the perforation. Of the 19 cases in which tympanic membrane perforation occurred, 13 had a diameter greater than 50% at the time of surgical reconstruction and in 14 the location was mainly anterior.

Pre-tympanoplasty adenoidectomy may be a factor for a better functional and anatomical prognosis. None of these patients had graft perforation, but this outcome was confirmed in only 28 patients (10.89%).

The patients with a new tympanic membrane perforation (18/257), underwent a second reconstructive surgery (7.39%). This procedure, although representing a smaller number compared to the total number of surgeries, had a very high complication rate. In only 8 of these interventions (42.10%) (8/19), the tympanic membrane remained intact and in a functional position. In 5 other cases, the graft was considered to be inadequately positioned (26.31%). In 4 interventions, perforation of the tympanic membrane occurred for the third time (21.05%) and two additional surgeries resulted in secondary cholesteatoma (N 2/19; 10.52%). This suggests that in the pediatric population reintervention is associated with a relatively poor prognosis, possibly due to the difficulty of vascularization of a more fibrous and smaller remnant.

Type 3 functional tympanoplasties were performed in the 4 cases with simple membrane perforations. The tragal cartilage was directly placed on the stapedial structure. The tympanic membrane remained intact in all patients.

In the cases of secondary cholesteatoma the presence of skin inside the middle ear was strictly considered. In both cases the amount was small; therefore, posterior tympanotomy with mastoid and epitympanic space obliteration ("canal wall up" technique) was performed, resulting in satisfactory preservation of the back wall. No evidence of cholesteatoma recurrence was observed after 8.3 and 9.5 years, respectively, assessed with Flair MRI studies in the last 5 years of follow-up.

Satisfactory hearing results were obtained. Overall, 8.71% (21/257) had an HL of 25 dB or less at frequencies of 250 cps, 500 cps, 1000 cps, and 2000 cps, even though they had air-bone gaps ranging from 5 to 12 dB HL dB; 74.31% of this series (191/257) had conductive hearing loss and 17.51% (45/257) had mixed hearing loss with conductive hearing loss predominance.

Postoperatively, air-bone gaps were found to have decreased or closed in 219 interventions (85.21%), while the gap remained unchanged in only 38 interventions.

Gap closure was the greatest between the frequencies of 250 cps and 1000 cps, while a moderate decrease was seen at a frequency of 2000 cps. Functional hearing gain, measured as the pre- and postoperative difference in the air-bone gap, decreased 13.72 HL dB at the last audiometry at a mean of 10.7 years postoperatively in patients who underwent primary tympanoplasty.

Of 19 who underwent secondary interventions, decrease or closure of the gap was seen in 10 (52.63 %), while the gap remained unchanged in 3 (15.78%) and worsened in the remaining 6 (31.57%). Hearing deterioration was 42 dB HL at the above-mentioned frequencies after one year of follow-up.

In this study, status of the contralateral ear was not found to be statistically significant.

Conclusions

- Tympanoplasty is valid therapeutic option for the treatment of chronic otitis media in children older than 6 years.
- Size and location of the perforation were found to be significant variables affecting outcome of primary tympanoplasty.
- The surgical technique was not found to be a relevant factor for outcome of primary tympanoplasty in this study.
- Our results are similar as those published in the literature. No significant differences were observed when comparing the status of the contralateral ear and surgical outcome of secondary tympanoplasty.
- Statistically significant high rates of graft lateralization (26.31%), graft perforation (21.05%), and development of secondary cholesteatoma (10.52%) were observed in secondary surgeries compared to primary interventions.
- None of the patients with graft lateralization required surgical correction.
- Posterior tympanotomy with mastoid and epitympanic space obliteration ("canal wall up" technique) allowed for satisfactory preservation of the posterior wall in patients with secondary cholesteatoma.
- In primary tympanoplasties, postoperative hearing results may considered to be good as the air-bone gap closed or decreased to < 10 dB in 151 of the interventions (58.75%), while a gap of > 10 dB or an increase in the gap compared to preoperative results was observed in the remaining 101 interventions (41.24%).
- In primary tympanoplasties, overall functional hearing, measured by the pre- and postoperative change in the air-bone gap which decreased by 13.72 dB HL, improved.
- In only 7 of the 19 secondary interventions (36.84%), the air-bone gap decreased < 10 dB compared to pre-operative results, which may be considered as satisfactory. In the remaining 12 interventions (61.15%), postoperative hearing thresholds remained the same or worsened.
- At one year of follow-up, mean hearing was 42 dB HL.
- No complications were observed in tertiary surgeries.

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Transcutaneous bone conduction devices in very young children

Javier Cervera, MD.

Introduction

In children early and continuous stimulation of the cochlea is critical for normal language development. Therefore, in patients with conductive hearing loss early diagnosis is important for adequate treatment.

Vibration-based bone-conduction hearing devices applied with an elastic band (Figure 1) have been recommended as an option for patients with conductive or mixed hearing loss who do not benefit from a conventional hearing aid.

Nevertheless, the usefulness of these devices is limited by different physical factors.

Bone conduction implants can effectively rehabilitate good quality hearing for individuals who have conductive hearing loss that cannot be surgically corrected and is not amenable to the use of conventional air conduction hearing aids.

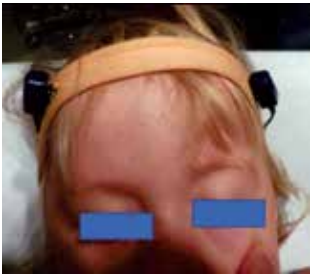


Figure 1. Elastic band with two prosthetic vibratory bone-conduction devices.

– Indications for osseointegrated hearing implants
– Microtia: Unilateral. Bilateral (Figure 2).
– Bilateral cholesteatoma.
– Acquired stenosis of the external auditory conduct.
– Unilateral deafness.

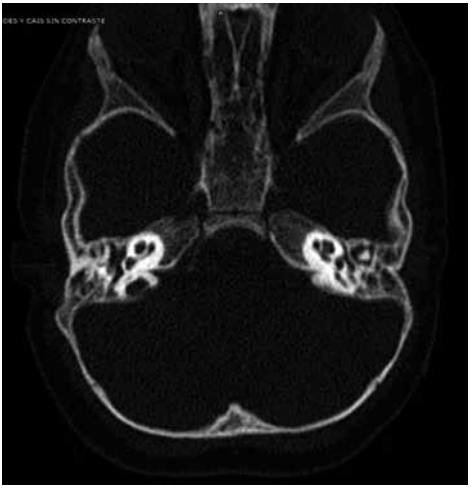


Figure 2. CT scan of mastoids with bilateral atresia of the external ears and malformation of the middle ear.

According to Tjellstrom, the earliest age for percutaneous titanium fixation in the skull is around 3 years [1].

The United States Food and Drug Administration (FDA) limits implantation of the bone-anchored hearing aid (BAHA) to children older than 5 years [2].

Currently, three devices that use bone conduction as a means of sound perception are available.

Percutaneous implants

– Baha®, by Cochlear Bone Anchored Solutions.
– Ponto, by Oticon Medical (Figure 3).

A titanium screw is implanted in the skull as part of a semi-implantable bone conduction hearing device, based on Branemark's concept of osseointegration [3]. These first bone-anchored percutaneous hearing solutions provide uninterrupted coupling of the external and the implanted components, thus enabling optimal hearing gain for both adult and pediatric patients. However, there are some drawbacks associated with percutaneous implants, including a high rate of soft tissue complications (local infection or excessive skin growth), poor esthetic results, or loss or failure of the implant [4].

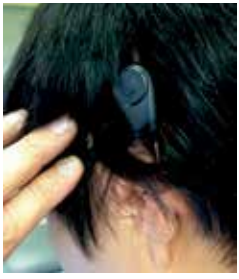


Figure 3. Ponto-type percutaneous implant.

Transcutaneous implants

– Bonebridge™ by Medel.

The BonebridgeTM transcutaneous implant is an active transcutaneous bone conduction device. In 2014 the device obtained European approval for clinical use in children over five years of age [5]. It is a semi-implantable system consisting of two parts: the internal part (Bone Conduction Implant (BCI)) contains a magnet that keeps the external audio processor in place which sends the information through the coil to the transcutaneous system. The signals that the implant sends to the audio processor are converted to mechanical vibrations that are transferred to the bone which sends sound waves to the internal ear (Figure 4).

Figure 4. Bonebridge™ transcutaneous implant by Medel.

Surgical technique: A retroauricular incision is made. The location of the coil is marked. Once the bone is exposed, a bed is drilled for the BCI and the coil and the demodulator are placed on the bone under the periosteum. Once the BCI is in position, a 2-mm screw is inserted in each anchor hole of the BCI-FM. (Figure 5).

Figure 5. View of the external part of the BonebridgeTM implant.

Audiological results: mean hearing threshold is 22.5 ± 1.5 dB HL. Mean percentage of speech recognition at 65 dB SPL is 94.4 ± 9.4% [6].

– Baha® Attract (Cochlear Bone Anchored Solutions)

The Baha® Attract has been available since 2013. It is a transcutaneous system, using a single magnet that is attached to the skull with a titanium fixture connecting the Baha sound processor to the implant. The sound processor is connected to an external magnet with a soft pad used to distribute pressure over the contact area to decrease skin sensitivity (Figure 6).

Figure 6. Baha® Attract transcutaneous implant.

Surgical technique: The implant site is identified and a C-shaped incision is marked. The implant site is marked and drilled at an angle perpendicular to the bone surface. The implant is placed by attaching the magnet with a screwdriver. Finally the flap is replaced over the implanted magnet and sutured (Figures 7 and 8).

One month postoperatively, when osseointegration is completed, the external processor is connected.

Audiological results: mean threshold is 25 ± 1.5 dB.

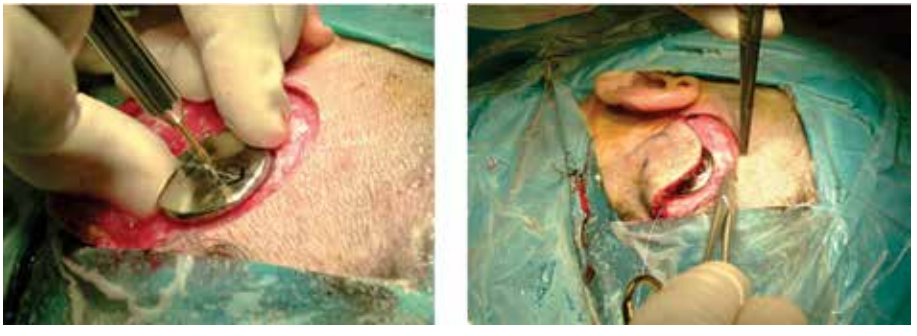


Figure 7. Fixation of the implant plate with a screwdriver.
Figure 8. Repositioning of the flap over the magnet plate and sutures

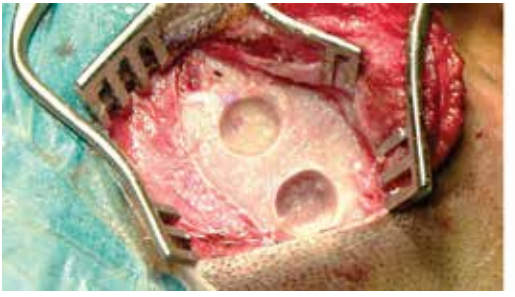
– Sophono™

Sophono, Inc, available since 2015 subsidiary of Medtronic plc.

Developed by Sieger [7], this system has a surgically implanted plate containing two magnets attached to the skull and an external sound processor that houses a bone oscillator and a metal disc. This arrangement allows for magnetic coupling of the internal and external components through intact skin.

Classic surgery: A retroauricular incision is made and a bone area of around 30x15 mm is exposed. Two beds are drilled into the bone to accommodate the magnets (Figura 9). The implant, with a thickness of 2.6 mm, is fixed to the bone with 1.5-mm screws (Figure 10). The device can be used once the incision has healed, one month after surgery (Figure 11).

According to the manufacturer, SophonoTM is designed for patients of 5 years and older with conductive or mixed hearing loss if thresholds are higher than 45 dB HL [8]



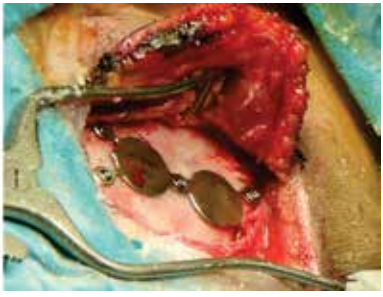


Figure 9. Sophono™ implant: beds drilled in the bone to house the magnets.
Figure 10. Implant screwed to the bone with 1.5-mm screws.

Figure 11. Sophono™ 1 implant connected one month after surgery.

To assess thickness of the temporal bone, 42 computed tomography (CT) scans were performed in children with ages ranging from 20 days to 3 years (Figure 12). At 20 days of life, thickness of the temporal bone was 1.7 mm, at 5 months 1.9 mm, at 12 months 2.0 mm, and at 3 years 3.2 mm (Table 1).

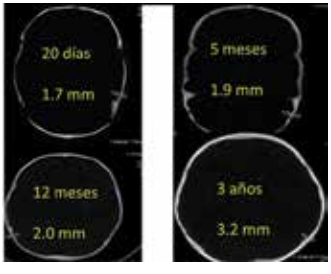


Figure 12. CT scan with the measures of temporal bone thickness according to age.

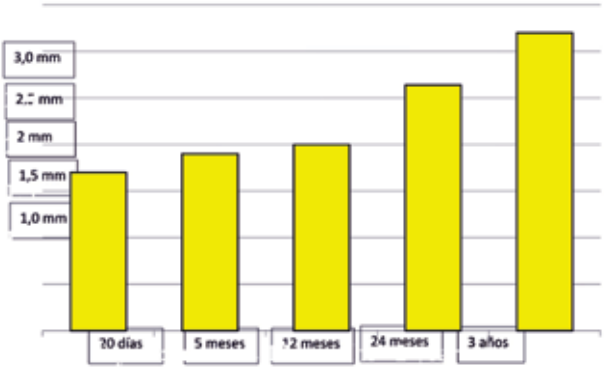


Table 1. Mean temporal bone thickness.

Based on these measures, we developed a simplified surgical technique in order to be able to perform the surgery in infants younger than 2 years. As the thickness of the implant is 2 mm, surgery would be feasible after the age of 12 months.

Two parallel incisions are made to create a subperiosteal tunnel (Figure 13). The difference is that the magnet is placed in an opposite fashion compared to the classic technique (Figure 14).

The aim is not to perforate the bone bed as the reduced bone thickness does not allow for drilling. With a micro-screwdriver, 4 screws are used to fix the titanium plate.

Subsequently, the implant is completely covered by skin, far from the incision (Figure 15). After one month, the alpha-2 processor is connected (Figure 16).

Figure 13. Two incisions are made to create a subperiosteal tunnel.
Figure 14. The magnet is placed in an opposite fashion compared to the classic technique, so as not to drill the beds.

Figure 15. With a micro-screwdriver the titanium plate is fixed with 4 screws while the implant is covered with skin.

Figure 16. One month after surgery the Alpha 2 processor is connected.

In patients with bilateral microtia, two devices may be placed in the same surgery, obtaining better sound localization, speech recognition, and sound discrimination in a noisy environment (Figure 17).

Figure 17. Bilateral alpha-2 SophonoTM.

Sophono™: Audiological results: Free-field PTA: 26.43 dB. Speech recognition: URV 30 dB, discrimination 100%.

Complications: One patient developed skin erythema that resolved with topical treatment. Another patient had skin irritation that resolved after reduction in magnet strength. No major complications were observed.

Conclusions

In very young children, the BAHA® may be placed when bone thickness is greater than 2.5 mm. This is achieved at around 2 years of age.

Bone thickness should be assessed by CT scan to confirm bone thickness is at least 2.5 mm.

The most common complication of percutaneous implants with abutment is the soft tissue reaction around the abutment, consisting of soft-tissue overgrowth or abutment site infection, rejection of the abutment, and trauma.

The Sophono™ may be adapted even after less than two years using a simplified surgery.

Surgery with Baha® Attract may be performed in children 3 years or older.

In Europe, the Bonebridge™ was approved for clinical use in children 5 years and older.

The advantages of transcutaneous devices are evident, as complication rates are lower than in percutaneous devices. Infections, excess skin growth, and loss of osseointegration are not observed using transcutaneous devices.

Transcutaneous implants may cause local skin irritation at the magnet site and erythema caused by pressure of the external magnet which is resolved by reducing this pressure.

Given that surgery for the placement of new transcutaneous bone conduction implants is feasible in children after 2 years of age, these devices may facilitate adequate language development.

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Hearing screening and follow up programs

Luisa Monteiro, MD, **Carla Moreira**, MD and **Marta Mariano**, MD.

Introduction

Hearing Loss (HL) is one of the more prevalent conditions that affects children. It includes congenital HL (present at birth) or acquired HL (perinatal or late onset HL). It is estimated to occur in 1-2 in 1000 births. Early identification and appropriate intervention is recommended to allow children to fully develop their communication, social and academic skills [(1)].

Epidemiology

Based in universal hearing screening programs data, the estimated prevalence of permanent hearing loss is 1,33 per 1000 live births [(2)]. At primary school age, the prevalence is 2.82 per 1000 children [(3,4)] and increases in adolescents to 3,5 per 1000 [(5)].

Classification of hearing loss

HL may be classified according to the site(s) of the lesion (Anna M. H. Korver, Richard J. H. Smith, Guy Van Camp, Mark R. Schleiss et al. Congenital Hearing Loss. Nat Rev Dis Primers, 2016.94).

– Conductive HL if the external or the middle ear (or both) are affected.
– Sensorial HL if the inner ear, the auditory nerve or the central auditory pathway are affected.
– Mixed HL is defined as an association of conductive and sensorineural HL.

Definition of case

Screening programs aim to identify babies and children with significant hearing loss, defined as mean hearing thresholds worst than 40 dB in the best ear. However, the great majority of screening programs also identify unilateral deafness cases as increasing evidence suggest that those cases should also be followed and treated.

Screening programs

Although early identification of deaf and hard of hearing babies has been a longstanding objective of the medical community, it was only in the eighties of the last century that the emerging technology allowed that large percentage of newborns were screened using a fast physiological test with low false negatives percentage (sensitive) and acceptable false positive rates (specific), that could be deal with retesting during a second stage. That elegant technology was the detection on the ear canal of the Otoacustic Emissions produced in the normal cochlea and transmitted backwards through a normal middle and external ear. Algorithms were designed to allow automatic decision between ***pass*** and ***refer*** and the test was widely disseminated and used to implement progressive numbers of Universal Hearing Screenings programs all over the world, especially in the developed countries. Electric Evoked Potentials were clinically available since the seventies, but were mostly used for diagnosis and for screening of high risk babies. The conditions that allowed implementing universal screening, early diagnosis and early interventions were met, and increasing scientific evidence was produced to support the recommendations that were adopted everywhere. Along the decades a decision tree was built, starting at the screening, through the audiological and etiological diagnosis and the rehabilitation pathway.

Neonatal hearing screening programs

Over 50% of cases of permanent childhood hearing impairment can be detected shortly after birth through a program of neonatal hearing screening. However, passing the neonatal screening does not guarantee normal hearing in childhood and is not a valid reason to disregard parental suspicion of hearing impairment. Progressive or late-onset hearing impairment, as seen with congenital CMV infection or in some genetic conditions, is undetected by neonatal screening programs. Thus, postnatal identification of childhood hearing loss will remain dependent upon the interaction between parents and professionals. All individuals working with children (for example, teachers and health care providers) should monitor the child's general development and especially language development [6].

Other limitations of neonatal hearing screenings are related to the sensitivity and specificity of the screening method, coverage and follow-up after a referral from screening. For example, although universal neonatal hearing screening in Flanders, Belgium, has high sensitivity (94.02%) and specificity (99.96%) [7], false positive test results might cause unnecessary anxiety in parents during the vulnerable first weeks of their newborn infant.

Coverage might be a concern in low-income countries where hearing screening programs are not available or access to them is limited. In many universal neonatal hearing screening programs, the progress from screening to intervention is the weakest point of the health care pathway, with the proportion of children lost to follow-up (and treatment) as high as 52% of those referred [8].

An increasing body of evidence shows that universal neonatal hearing screening is not only beneficial for the child's development and quality of life, but is also cost-

effective. The costs of neonatal hearing screenings are comparable with other newborn screening programs and the benefits are expected to outweigh the costs [9,10].

A - Children who refer in both ears at screening

After Otorhinolaryngology consultation and a thorough physical examination an audiological diagnosis should be completed consisting of click Auditory Brainstem Response (ABR), frequency specific ABR or Auditory Steady State Response (ASSR), Tympanometry (1000 HZ and 246 Hz) and Otoacustic emissions, before 3 months of age.

Audiological tests can confirm the presence of hearing loss and determine its type (conductive, sensorineural or auditory neuropathy spectrum disorder), laterality and severity [6].

Joint Committee recommendations on Audiologic work up:

Audiometry—Visual re-enforcement audiometry can be used to test hearing in children between 6–24 months of age. In children with adequate hearing, a new sound source will provoke an orientation reflex towards the sound. Skilled audiologists can obtain reliable results.

Play audiometry is used in children 2–4 years of age, by means of conditioning them to respond to an auditory stimulus through play activities. After 4 years of age, standard audiometry is typically used, with an air-conduction transducer (for example, an earphone) or a bone-conduction transducer (or both). The former tests the integrity of the complete auditory system, whereas the latter vibrates the skull, which stimulates the cochlea directly, bypassing the external and middle ear. Air conduction and bone conduction thresholds, mostly obtained at octave frequencies of 250–8,000 Hz, differentiate sensorineural hearing loss and conductive hearing loss

After the confirmation of hearing impairment, ideally until 3 months age, etiology of the hearing loss should be investigated.

Depending on the audiologic profile, associated conditions and family informed decisions, a habilitation plan must be established. When the best ear has hearing thresholds that equal or are worst than 40 dB, hearing aids should be fitted and language development should be monitored. A multi professional team must be involved in the planning and the development of the habilitation plan and coordinated by the otorhinolaryngologist, including, as needed, speech therapists, audiologists, pediatricians, pediatric neurologists, geneticists, psychologists, specialized teachers, social workers and others.

B – Children who pass screening but are considered at high risk for hearing loss, should be tested every 6 months until 3 years of age [7], using objective measures as recommended by the American Academy of Pediatrics Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. This paper presents the guidelines of the American Academy of Pediatrics on the importance of universal neonatal hearing screening, risk factors for congenital hearing loss and management strategies for those who fail the screening test.

Risk factors for permanent congenital, delayed or progressive hearing loss in childhood [7]:

– Hearing, speech, language or developmental delay.
– Family history of hearing loss.
– Neonatal intensive care unit stay >5 days or receiving any of the following

treatments: extra corporal membrane oxygenation, assisted ventilation, ototoxic drugs (for example, gentamycin and tobramycin), loop diuretics or exchange transfusion for hyperbilirubinaemia.
– In utero infections (toxoplasmosis, rubella, cytomegalovirus, herpes simplex or syphilis).
– Craniofacial anomalies, including ear tags (small flaps of skin in front of the ear), ear pits (A tiny opening in the skin usually in front of the ear and above the ear canal, connected to a sinus tract travelling under the skin) and anomalies that involve the outer ear, external auditory canal and temporal bone
– Physical findings associated with a syndrome known to cause permanent hearing loss (for example, white forelock, a patch of white hair above the forehead).
– Syndromes associated with congenital hearing loss or progressive or late onset hearing loss.
– Neurodegenerative disorders or sensorimotor neuropathies
– Confirmed bacterial or viral meningitis (in particular if caused by mump, herpes viruses or virus).
– Head trauma, especially of the basal skull, or temporal bone fractures, that require hospitalization.
– Chemotherapy.

A positive family history of permanent congenital hearing loss is suggested as a risk factor, but the body of evidence for its relevance is low, as only 1.43% of children with a positive family history have hearing loss [11]. Admission to a neonatal intensive care unit is a relevant risk factor; with the prevalence of hearing loss increasing as gestational age and birth weight decrease (1.2–7.5% in premature babies born at 24–31 weeks and 1.4%–4.8% in babies weighing 750–1500 g) [12]. Necessary medical interventions (such as assisted ventilation, venous access and aminoglycoside use) while in the neonatal intensive care unit increase the likelihood of hearing loss. Duration of hospitalization of ≥12 days and a history of treatment by high-frequency ventilation have also been identified as independent risk factors for hearing loss in this population [13] In addition, delayed maturation of the auditory system is has been postulated as a concern in infants hospitalized in this setting [14]. An economic analysis has confirmed that both universal and targeted screenings for congenital CMV infection are cost effective, an observation that should help drive the expansion of screening programs for this infectious cause of hearing loss in infants [15].

C – Children who refer in one ear and pass the other, should also be followed to establish the etiology of HL, and to monitor the hearing condition of the healthy ear. Growing clinical evidence recommends that a hearing aid and eventually a cochlear implant should be considered early in life, with especial emphasis whenever a progressive nature of the hearing loss, that my affect the best ear, is suspected. Unilateral HL may be caused by middle or inner ear malformations in as high as 50% of cases making hearing aids or CI not a feasible option. CMV can also be the cause of unilateral HL and the best ear has a higher chance of being involved later in life [15,16].

Whenever indicated by audiological diagnosis the habilitation program must be established by the multi professional team, according to the family wishes. Hearing aids should be adapted and audio-verbal stimulation (involving the family) should be started, before 6 months of age.

At the same time the etiology of HL should be investigated. Sometimes families are overwhelmed trying to cope with a newborn that needs special attention and a lot of tests and medical visits. Priority should be given to the habilitation tasks (Figure 1).

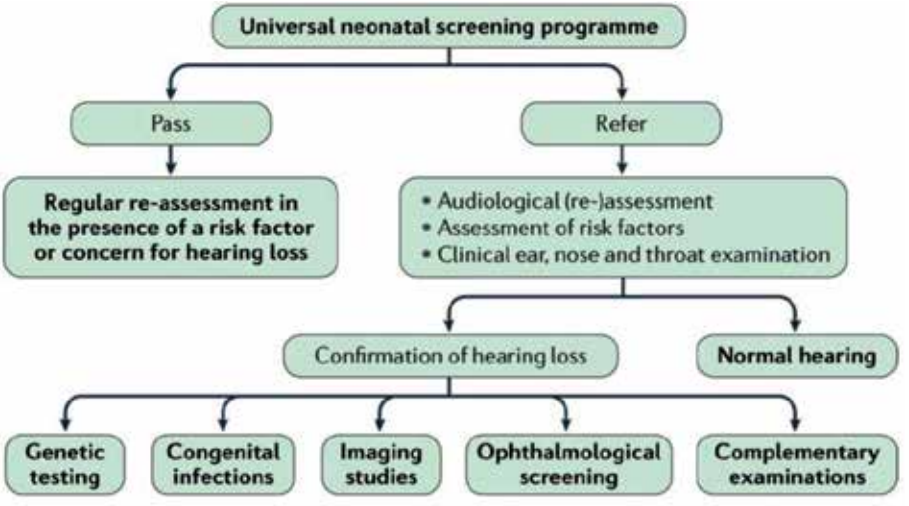

Figure 1. Multidisciplinary algorithm for the assessment of hearing function in infants [6].

Etiology

The emphasis on etiology of every HL case is based on:

- The need to provide answers (whenever possible) and closure to parents and family's anxiety and grief .
- Add information to family planning and future siblings.
- Support the audiological diagnosis.
- Find out if the hearing loss is an isolated feature or if it is a part of a syndromic case not yet identified.
- Help planning the treatment (for example early cochlear implantation) and planning habilitation.
- Enable to establish a short and a long term functional prognosis.

(Figures 2 and 3).

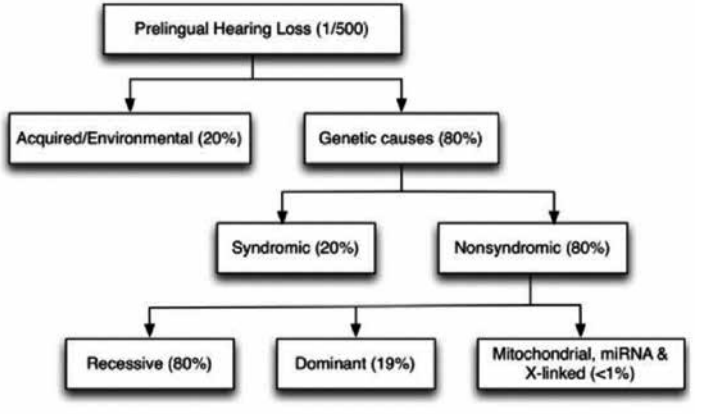

Figure 2. Etiology of hearing loss.

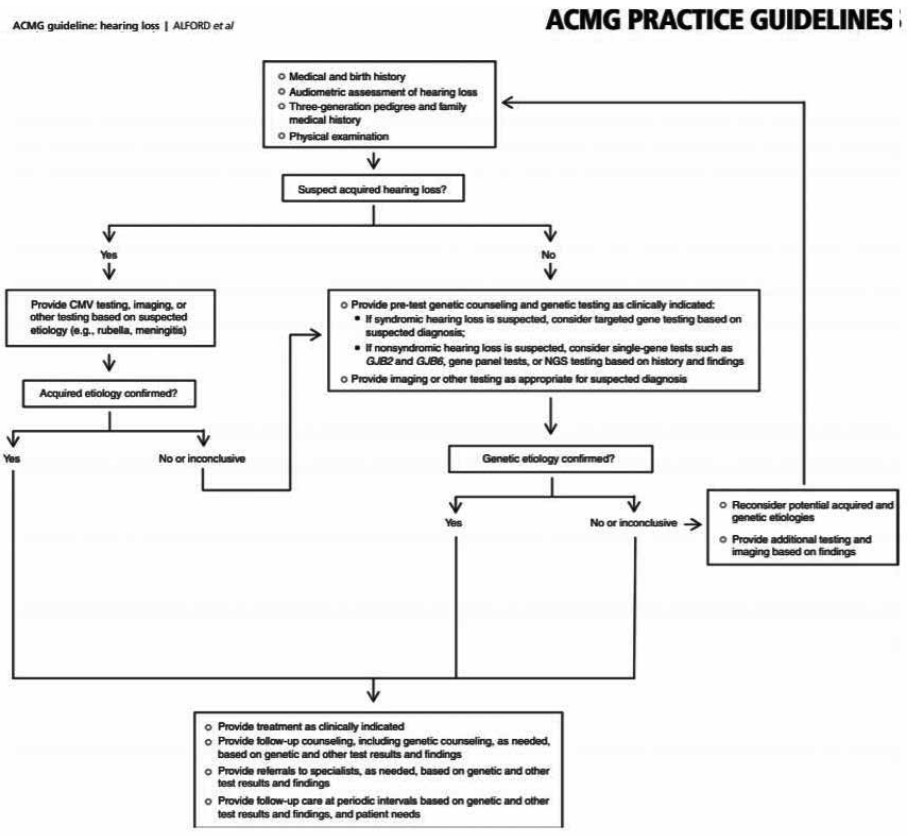

Figure 3. ACMG Practice Guidelines: hearing loss.

It is well known that congenital HL may be due to genetic causes and infectious diseases that are vertically transmitted during pregnancy (TORCH group: Toxoplasmosis, Rubella, Cytomegalovirus and Herpes virus). In both conditions, infectious or genetic the newborn may be normal hearing at birth and present later with hearing loss. For that reason pediatricians, family doctors, otorhinolaryngologists, families, teachers and pediatric development teams must be aware that a pass at newborn screening is no guarantee that a late onset hearing loss will not develop during childhood or even during early adulthood. Some genetic causes may manifest themselves later in life or have a progressive nature. Among all the late onset or progressive causes, congenital infection by Cytomegalovirus (CMV) seems to be the most relevant and demands a thorough and prolonged monitoring of every congenitally infected newborn that presents with or without hearing loss at screening.

Patient history and physical exam
– Family pedigree (3 generations) + audiological data.
– Consider non paternity, adoption, non biological children.
– Consanguinity, geography, ethnical background

Family history and pedigree: enquiring for the occurrence of HL, at least in 3 past generations and for features that may be associated with syndromic HL (ex. Waardenburg syndrome, Braquio-oto-renal syndrome) is very important.

Pregnancy history: it is very important to search for serum conversion during pregnancy, specially: toxoplasmosis, rubella, Cytomegalovirus (CMV), syphilis, herpes virus; in developed countries, most young girls are nowadays vaccinated against rubella and that congenital cause has lost importance. CMV congenital infection is now considered the more prevalent cause of nongenetic congenital or early acquired HL. Testing pregnant women to monitor IgG and IGM against CMV are not universally performed and there are still misinformation considering the "protection" that a previous infection would provide. Reactivation of a previous infecting virus that caused existing high levels of IgG or a secondary infection with a different strain of CMV can happen during pregnancy and the fetus can be infected. Only periodic monitoring of IgG and IgM titers can assure that a congenital infection did not occur during pregnancy. History of drugs intake during pregnancy is also important.

Perinatal period: prematurity, very low birth weight (< 1500 gr), low Apgar that requires reanimation and prolonged ventilation, hypoxic-ischemic syndrome, very high levels of bilirrubinaemia demanding transfusion, use of ototoxic drugs (aminoglycosides, loop diuretics) separated or in conjunction to treat serious life threatening conditions such as sepsis, meningitis, pneumonia, are the most commonly found risk factors associated with extreme prematurity and high risk labor conditions. Usually multiple risk factors have been present during the perinatal period. Some of the premature babies may also be infected with CMV which can also be the cause of stillbirths and prematurity.

Physical exam: examination must include head and neck and entire body examination looking for face and cranial anomalies, eyes, auricles, tips, neck malformations. Skin and hair alterations and other anomalies (orthopedic, neurologic) should be thoroughly search for and documented. At birth HL can be considered non syndromic and as time goes by, other alterations can be discovered and the HL will switch to a syndromic category.

Complementary analysis

Varying with hearing loss type and age, imagiology of the ear and Central Nervous System (RMN, CT), renal echography, serology, blood and urine, electrocardiogram (search for a long QT and torsades de points specially if faints occur), ophthalmic examination (fundoscopy, electroretinography) may be considered, accordingly to the suspected etiology.

Genetic investigation

Genetic Hearing Loss (congenital or late acquired)

Genetics is the study of single genes and their role in the way traits or conditions are passed from one generation to the next.

Most genetic HL is an isolated feature, nonsyndromic hearing loss, but sometimes at the time of HL diagnosis, not all extra ear manifestations of the syndrome haven yet been searched for (ex: cardiac, ophthalmic). Most authors consider that 70% percent of genetic HL cases are nonsyndromic and 80% of them are autossomic recessive, followed by 18-20% of autossomic dominant, rarely are X-linked (1-2%) or have mitochondrial inheritance (1-2%) [19]. More than 60 genes have been identified in autosomal recessive HL and 30 in autosomal dominant transmission, and growing [20]. Usually genetic etiology is suspected when external "environmental" causes described above (pre-natal and perinatal), namely CMV infections have been excluded.

Traditionally the Sanger method is used to diagnose the more frequently involved genes (candidate gene approach) accordingly to the frequency of the syndromic or nonsyndromic HL. It is an expensive and time consumer method; usually more frequent genes that are searched for are:

1 - Nonsyndromic HL, the first genes to be looked for are GJB2 and GJB6 and their mutations
2 - Syndromic HL, a candidate gene is identified accordingly to the alterations found during family history or during examination, Pendred Syndrome being the most frequent nonsyndromic HL (Figure 4).

Figure 4. Syndromic hearing loss. (Van Camp G, Smith RJH. Hereditary Hearing Loss Homepage. https://hereditaryhearingloss.org.).

Genomics is a term that describes the study of more than a gene at once.

Molecular genomics: Next Generation Sequencing (NGS) advantages:
– Interrogating >100 genes at a time cost effectively .
– Finding novel variants in no so candidate genes.
– Low input DNA.
– Sequencing microbial genomes for pathogen subtyping to enable research of critical outbreak situations.

With the development of the technology used in Human Reference Genome, several panels have been developed using panels to test several genes implicated in Hl with one test sample. This is an evolving technology and it allows to identify mutations in the genes already known to be implicated in HL; the genomic analysis report must be clinically interpreted by an experienced clinician, results may presented as **benign, likely benign, VUS** (Variant of Uncertain Significance), **likely pathogenic** or **pathogenic**.

Presently genetic screening for HL is not recommended although some trials are starting genetic investigation as soon as a child refers at second stage hearing screening even before audiologic diagnosis is complete or soon after confirmation of hearing loss, while other etiology tests (CMV, biochemistry, imagiology) are still in course. Screening large number of normal hearing and hearing loss children (concurrent hearing and genetic screening using "hotspots") will improve the knowledge of genetic causes of HL [21] but are not currently recommended.

Alternative screening programs that incorporate genetic and CMV screening at the time of hearing (physiologic) screening are emerging [18]. Although that would be the most clinically efficient option, many countries worldwide cannot afford implementing this kind of comprehensive approach to all newborns (Figure 5).

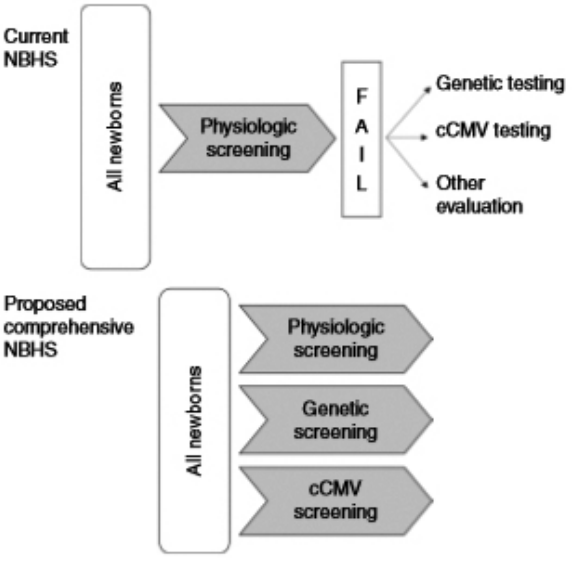

Figure 5. Comparison schematic of current and proposed newborn hearing screening (NBHS). cCMV: congenital cytomegalovirus (18).

Infectious agents

- Toxoplasma *gondii*: the inflammatory response to the tachyzoite form of T. gondii induces CNS necrosis [22,23]. The effect of treatment with pyrimethamine and sulfadiazine on hearing loss is unknown [24].
- Rubella virus: direct damage and cell death can occur in the organ of Corti and stria vascularis [25] HL can be unilateral or bilateral and mild or severe. There is no specific treatment available.
- Herpes simplex virus: HL can occur in association with microcephaly, intracranial calcifications, skin and ocular findings. The prevalence is unknown, HL can be unilateral or bilateral and severity can be mild or severe and the effect of acyclovir on HL is unknown [26].
- Treponema *pallidum*: produces an Obliterative endarteritis [27]. The prevalence and the usual severity is unknown. The effect of intravenous penicillin on hearing loss is also unknown.
- Cytomegalovirus: induces a viral labyrinthitis and inflammatory injury. The prevalence is 15% in industrialized countries, and 33% in developing countries. It can produce unilateral or bilateral HL, from mild to profound in severity. Ganciclovir or valganciclovir slow the progression and stabilize hearing loss when early detected and treated [27,28]. Established hearing loss is generally irreversible even with antiviral therapy.

Nowadays cytomegalovirus congenitally infected babies, symptomatic or asymptomatic at birth are considered a special group and should be monitored otherwise.

CMV congenital infection prevalence is 4.5 per 1000 births in the United States, with an estimated number of 20 000 newborns infected each year. Other geographic locations around the world may have different prevalence rates, but in developed countries it is an important cause of non-genetic HL. About 10 to 15% of infected newborns are symptomatic at birth, 0.5% die in the neonatal period and 20% develop permanent disabilities, of which HL is the most common [29] (Figure 6).

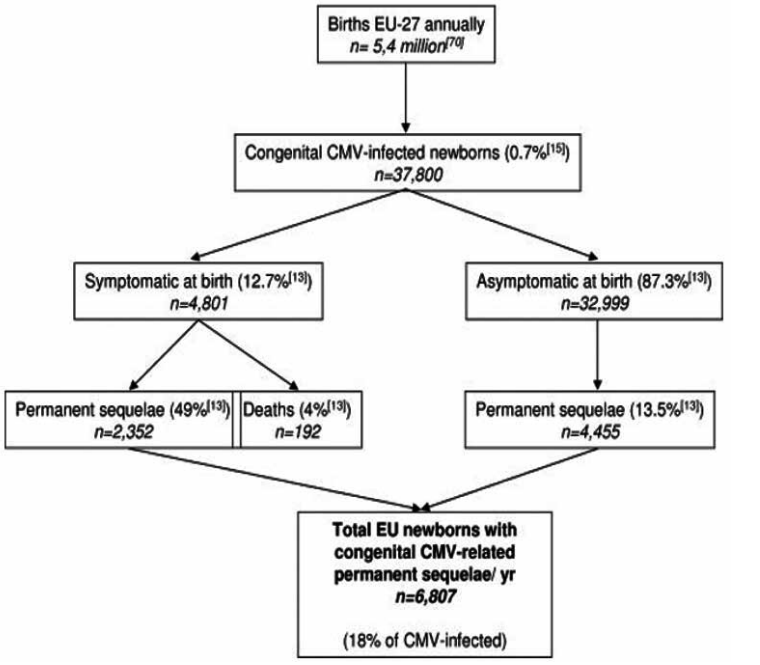

Figure 6. Estimated incidence of Congenital CMV infection and outcomes in EU [30]

Symptomatic children may present central nervous system anomalies (microcephaly, ventriculomegaly, intracerebral calcifications, cortical or cerebellar malformation), chorioretinitis, thrombocytopenia, petechiae, hepatomegaly, splenomegaly, intrauterine growth restriction or hepatitis. Isolated sensorineural hearing loss may be present at birth or develop later. It can be fluctuating but generally has a progressive nature.

As CMV infection is much prevalent worldwide, whenever considering that etiology in pediatric sensorineural hearing loss evaluation, biological samples (saliva, mouth swab, blood or urine) must be collected until the 21th day of life (incubation period); if the HL diagnosis is made later in life, Dried Blood Spot used for metabolic screening, collected at birth and that is normally stored until at least 6 years of age can be retrieved and tested using PCR analysis.

Around 10% of asymptomatic children infected with CMV will develop HL later in life [31,32] and will be missed by Universal Hearing Screening. CMV infection may produce unilateral or bilateral Hl, and progression may occur during life, being suggested that monitoring of both ears is important trough long periods of time. In 2015 a panel of experts, the International Congenital Cytomegalovirus Recommendations Group, recommended audiological testing at 6 months interval for the first 3 years and annually thereafter through adolescence (until 19 years) [33] Symptomatic babies can be treated with oral Valganciclovir and improvement in hearing levels have been reported [34]. Universal screening for CMV at birth is not yet a common practice, but can be cost-effective [35] Cannon and al (36) demonstrated that detecting early infected asymptomatic newborns trough a systematic CMV screening of all newborns can significantly improve outcomes of those that develop delayed hearing loss.

Targeted screening of all newborns that fail the hearing screening (using swab or urine samples before 3 weeks of age) can be implemented and is cost-effective [37] but children who pass the hearing screening will not be identified in that screening).

Systematic antiviral therapy is not routinely recommended for congenital cytomegalovirus infection with isolated sensorineural hearing loss and otherwise asymptomatic, based on insufficient data [33] Nevertheless if those children are treated, their data should be tracked, to contribute to the overall understanding of the safety and efficacy of such an approach [33].

Imaging

Imaging studies are recommended in all cases of bilateral hearing loss ≥60 dB or with craniofacial malformations (38). Imaging exams can rule out the presence of structural inner ear anomalies, which might occur as an independent entity, be part of a syndrome, or have therapeutic implications. Certain inner ear anomalies might place the child at increased risk for sudden hearing loss (for example, enlarged vestibular aqueducts) or meningitis and require appropriate counselling. Imaging studies are also a prerequisite before cochlear implantation to assess cochlear anatomy and confirm the presence of a cochlear nerve and its execution can be delayed until Cochlear Implantation is considered.

A frequent questions concerning the evaluation of sensorineural HL is whether and when imaging studies should be performed.

In general, imaging is recommended, besides Cochlear Implant candidacy, for unilateral sensorineural hearing loss and as an adjunct assessment in bilateral sensorineural hearing loss when genetic testing has been negative [39].

Previously, high-resolution computed tomography (CT) of temporal bones was the initial imaging study of choice. However, the increased awareness of risk of radiation exposure associated with CT scans has contributed to the rise in popularity of magnetic resonance imaging (MRI) scans [40]. MRI has long been recommended as the initial diagnostic study for patients with suspected ANSD (Auditory Neuropathy Spectrum Disease) and is thought to provide improved resolution of intracranial abnormalities, cochlear nerve, and retrocochlear pathology, particularly in investigation of abnormalities of the membranous and osseous labyrinth (cochlear aplasia, common cavity deformity, incomplete partition), but also in identification of enlarged vestibular aqueduct and [41] to exclude or confirm co-existing CNS conditions. In infants and small children sedation may be necessary to obtain quality images. Although CT is very important to visualize temporal bone anatomy care must be used in small children because of the potential arm effect of radiation. In Cochlear Implant candidates that can be the last opportunity to get clean, complete visualization of cranial structures, before Cochlear Implantation occur.

Tests should be performed and interpreted by an experienced radiologist and a "road map" to cochlear implant surgery should be used. CT is excellent for external ear and middle ear observation, namely configuration of the external ear canal and tympanic membrane position, ossicles malformations, mastoid dimensions and aeration of the cells, and the presence of fluid or masses in the middle ear space or mastoid, relative position of arterial and venous vases to the posterior wall of the ear canal, position of the tegmen (especially in small children), position of the facial nerve relative to the oval window niche and possible Fallopian canal dehiscence or aberrant trajectory, round window niche rotation, malformations of the cochlea, vestibular and cochlear aqueduct dimensions and inner ear canal width.

MRI is very important to check tympanic and vestibular ramps permeability and the presence of fluid within it and possible inflammation signs. Those are very important verifications, especially after a bacterial meningitis or labyrinthitis. MRI is much useful in verifying the presence of the cochlear nerve (division of the VIII nerve) within the inner ear canal. Sometimes the internal ear canal may be very narrow, and whenever its width is less than 1.5 mm, hypoplasia or aplasia of the cochlear branch of the VIII nerve should be suspected (Figures 7, 8 and 9).

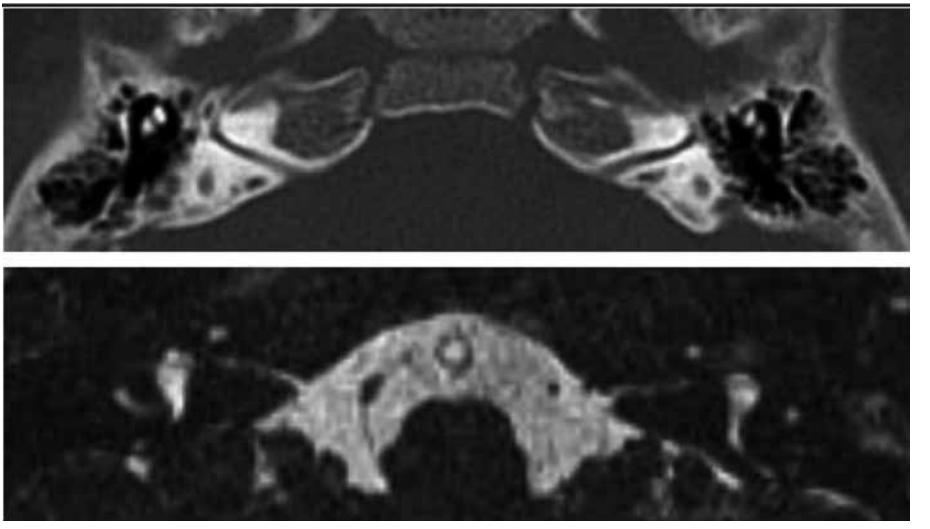

Figure 7. TC and MRI of the same patient with bilateral narrow internal auditory canal and probable VIII nerve aplasia. (Courtesy of Dr. Heredio de Sousa. H Estefania).

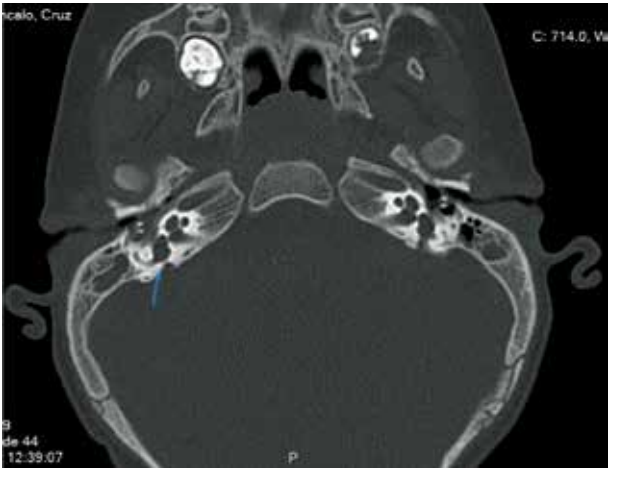

Figure 8. TC showing IP2 Cochlear Malformation on the right side and enlarged Vestibular aqueduct. (Courtesy of Dr Heredio de Sousa, H. Estefânia).

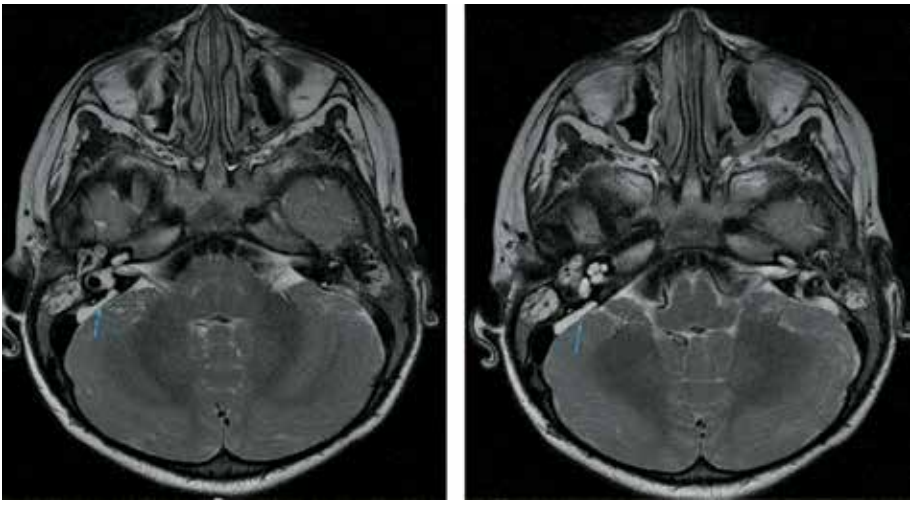

Figure 9. MRI of the same patient showing enhanced signal at the enlarged vestibular aqueduct.(Courtesy of Dr Heredio de Sousa, H. Estefânia).

Conclusion

Universal Hearing Screening Programs cannot be separated from follow up programs. The aim of the hearing screening programs is to identify HL children and early establish a habilitation program. Experience accumulated over the last decades enables us to try to establish concurrent screening programs, namely for congenital CMV infection and targeted screening to identify the genes involved in hearing loss.

Screening at the time of birth is not enough, since some conditions cause delayed hearing loss (late acquired hearing loss) and should be searched for over time to allow proper and timely intervention.

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Sudden sensorineural hearing loss in children: Treatment dilemmas

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Abstract

Pediatric sudden sensorineural hearing loss (SSNHL) is uncommon and current guidelines for its management refer to adults. Hearing is of a special importance in young children, since its loss may affect speech and language development, as well as academic and social performances. One of the dilemmas in diagnosing these children is that the youngest patients are unable to report on their hearing loss, which may go undetected during the early stage when treatment is most effective. Another issue is which treatment and for how long it should be given in children. In this review, we present our experience treating pediatric SSNHL and review the current literature.

Introduction

Unlike in adults, published data on sudden sensorineural hearing loss (SSNHL) in children is limited. Studies have shown that the annual incidence of SSNHL ranges between 10.7 and 27 per 100,000 persons [1,2]. The incidence increases with age, with 8 per 100,000 under the age of 18 years and 70 per 100,000 over 65 years [1]. Most commonly, SSNHL is defined as a unilateral or bilateral sensorineural hearing loss of ≥30 decibels (dB) affecting at least three consecutive frequencies, and occurring over a period of 72 hours [3]. It is considered to be an otologic emergency and thus, early initiation of treatment is necessary in order to avoid permanent future hearing loss. There is a special importance in children, since hearing loss at an early age may affect speech and language development, as well as academic and social performances. A major problem is that the younger patients are not always able to report on their hearing loss, which may go undetected during the early stage when treatment is most crucial and effective. The etiology of SSNHL may include infectious, anatomic, vascular, traumatic, and neoplastic causes [4]. In adults, most cases of SSNHL are idiopathic [5]. On the contrary, in children the percentage of idiopathic cases is unknown due to the small size of published series. The current treatment guidelines for SSNHL are aimed at adult patients and include systemic steroids as primary treatment and intratympanic (IT) steroids as a secondary or salvage treatment, or when systemic treatment is contraindicated [3]. There are reports on systemic treatment with steroids in children, but there is a lack of data on IT steroid administration in this age group. More data is required in order to establish specific management guidelines in children.

Our study

We performed a retrospective chart review of children with SSNHL treated at our department in order to examine the etiology, management, and outcome of this condition. We included all children ≤18 years of age that were treated the Department of Otolaryngology-Head and Neck Surgery, Shamir (Assaf Harofeh) Medical Center between 1/2003 and 9/2014. Following admission, a complete head and neck examination was performed including a micro-otoscopy. Pure tone audiometry was performed at frequencies between 0.250 and 8 kHz. Normal hearing was defined at ≤20 dB. Our treatment protocol included oral prednisone 1mg/kg/day, or intravenous (IV) hydrocortisone 1mg/kg/day divided into three doses (the latter was recently changed to methylprednisolone). Treatment was given for a minimum of 7 days. If there was no

improvement following systemic therapy, or a contraindication for systemic treatment, IT treatment was offered. Following ventilation tube insertion into the tympanic membrane, dexamethasone was instilled into the external auditory canal every 12 hours for 7 days. Following application, patients were positioned on the non-affected side for 30 minutes. Complete improvement of hearing was defined as a hearing level the same as the non-affected ear, partial hearing recovery as an improvement of more than 10 dB in at least one frequency, and no improvement when there was no change in the audiogram following treatment.

A total of 19 children were included with a mean age of 14 years (range 7-18 years). The male to female ratio was 9:10. The right ear was affected in 9 (47%), and both ears in one (5%) child. All subjects were healthy and none had a family history of hearing loss. Physical examination was normal in all except one child, who had bilateral serous otitis media. The first audiogram was done before initiation of treatment, and another one, at the end of the systemic treatment prior to discharge. Children who were treated with IT injection had another audiogram at the end of the IT treatment. The degree of hearing loss varied between mild and profound across frequencies. Sixteen patients (84%) reported other symptoms most commonly tinnitus. One patient presented with diplopia and herpetic lip lesion, but serology for the herpes simplex virus was negative. All patients reported an abrupt onset of hearing loss. The mean period between seeking medical help and initiation of treatment was 9 days (range 0-40 days). Initial treatment included oral steroids in 10 (53%) patients and IV steroids in 9 (47%). Systemic treatment lasted between 5 and 14 days (median = 7). In 2 cases, the caregivers decided to stop this treatment due to fear from side effects. Intratympanic steroids were administered in 8 (42%) children and lasted between 5 to 9 days (mean = 7). One patient refused to continue IT treatment after 5 days. Oral antibiotics were given in two. Non-contrast CT scan was performed in 3 patients and MRI in 12. None of the imaging studies demonstrated pathology. In 11/20 patients, CRP was obtained, and in only one of them it was significantly elevated (10.52, normal range: <0.06 mg/L). Serologic tests results included cytomegalovirus (CMV) IgG in 6 (32%), Epstein-Barr virus (EBV) IgM in one patient, EBV EBNA IgG in 7 (37%), and herpes simplex IgG in 3 (16%). Following treatment, tinnitus improved in 7 (37%) children, vertigo was reported in one and otalgia and fullness sensation were not reported. Hearing completely improved in 3 (16%) patients, partially improved in 9 (47%), and there was no improvement in 6 (32%). There was no worsening of hearing following treatment. One patient was lost to follow-up. Figure 1 shows the mean hearing levels before and after treatment across frequencies.

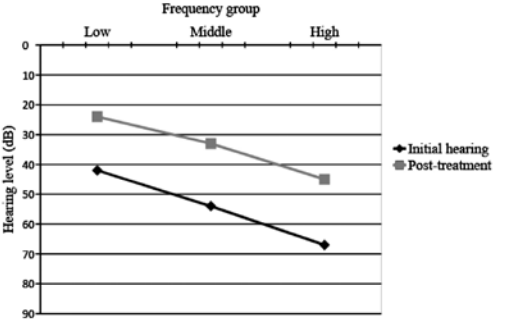

Figure 1. Mean pure-tone hearing level in the involved ears before and after treatment across mid, low, and high frequencies.

Discussion and review

A systematic review on the etiologies of SSNHL in adult patients showed that in about 70% of cases, the etiology was idiopathic [5]. Possible etiologies of SSNHL in adults include infection, Meniere's disease, autoimmune inner ear disease, trauma, vascular/hematologic event, and neoplastic disease [5]. In children, etiologies of SSNHL include congenital CMV and EBV infection, enlarged vestibular aqueduct, Mondini's dysplasia, syndrome of common cavity, ototoxicity, trauma, noise induced, meningitis and parotitis [6,7]. Cardiovascular causes associated with smoking, alcohol, hyperlipidemia, and vascular degeneration are less relevant in the pediatric population [6,8]. However, due to the scarcity of pediatric series, it is difficult to conclude the real contribution of each etiology. We found that most of the cases of pediatric SSNHL were idiopathic. Tarshish et al.. [6] reported that only 2 out of 20 pediatric patients (10%) with SSNHL were idiopathic. On the contrary, we found no etiology in most of the subjects, similar to findings in adults. Congenital CMV infection is a known etiology of hearing loss. Children with an asymptomatic CMV infection may present with acute or progressive hearing loss [9]. Fowler et al.. showed that about 18% of asymptomatic patients with congenital CMV infection can present with delayed-onset SNHL [9]. In the present study, 6 (32%) patients were found to have CMV IgG titers. However, no data was available to clarify whether these patients had a congenital CMV infection and since imaging studies were normal it was not possible to directly link the hearing loss to a viral infection. A recent EBV infection may also cause SSNHL. Shian et al. [10] presented two cases of sensorineural hearing loss following an EBV infection and reviewed the literature. They found that most cases of EBV-related SSNHL occurred during the convalescent phase. However, some even occurred without clinical symptoms of infectious mononucleosis. Only 15% of the patients with an EBV infection completely recovered their hearing. In the present study, one child had positive EBV IgM titers, pointing to a recent infection. This child had partial hearing improvement. No routine screening for viral causes is warranted in adults [5], however in children it seems that work-up for viral infection should be performed on an individual basis according to the history and clinical findings. Current guidelines for the treatment of SSNHL recommend systemic steroids as primary treatment and IT steroid administration as second line or salvage therapy [3]. Although the guidelines are aimed at patients over 18 years of age, it is also evident from the literature that children with SSNHL are treated with steroids as well. A systematic review on IT steroids for SSNHL demonstrated that salvage treatment following systemic steroid treatment failure offers a potential for some degree of additional hearing recovery. However, the age of the patients in the included studies was not specified [11]. We identified two series on IT salvage treatment for SSNHL that included children. However, there was no separation between children and adults, and therefore it was not possible to conclude on the efficacy of IT treatment specifically in children [12,13]. In our study, 8 (42%) children received IT steroids as salvage treatment. Five (62%) of these children had partial hearing improvement following the treatment and 3 did not improve. To our knowledge, this is the largest series exclusively describing children with SSNHL who received IT steroid salvage therapy. Although the numbers were small, it seems that children with SSNHL can also benefit from IT steroids. The rate of recovery from SSNHL in children varies between studies. Chen et al. [14] presented a series of 14 patients under the age of 18 years treated with IV prednisolone. The rate of complete recovery was 57%, whereas the partial recovery rate was 36%. Tarshish et al. [6] presented a series of 20 children with SSNHL. In this study, 10% had complete recovery and another 10% had some improvement. In both studies, patients

received systemic steroids and no IT treatment was given. In the present study, hearing completely improved in 16%, partially improved in 47%, and there was no improvement in 32%. Therefore, more studies are needed to elaborate on the rate of recovery from SSNHL in children. Na et al. [8] compared a group of 87 children to 707 adults with SSNHL. The rates of "complete recovery" and "no improvement" of hearing in children were 54% and 17.3% respectively. Interestingly, the "complete recovery" rate was significantly higher and the "no improvement" rate significantly lower in children than in adults. However, the overall recovery rates were similar in children and adults. In both populations, hearing recovery was significantly higher in patients with mild hearing loss compared to profound hearing loss, but in children with moderate hearing loss, the rate of recovery was lower compared to adults, whereas in children with profound hearing loss, the rate of recovery was higher compared to adults, showing that age is associated with a poorer prognosis. Interestingly, treatment in this study included oral prednisolone, a high-protein low-salt diet, peripheral vasodilators and bed rest [8]. In the present study, we found that there was an overall improvement of ~20 dB following steroid treatment, which indicates that steroid treatment is effective in children with SSNHL. The fact that there was hearing improvement in 62% of the patients in the group treated with systemic steroids as well as additional IT steroids supports the beneficial effect of IT treatment. Although our study is limited by its retrospective nature, inherent biases, and the small number of subjects, it does however, provides further data on this subject.

Conclusions

The low incidence of pediatric SSNHL is reflected in the small number of series published on this topic. It is still not clear which work-up and treatment would be most appropriate for this population. Sudden sensorineural hearing loss may be difficult to diagnose in children, especially at a young age, therefore a high index of suspicion is required. We found that the etiology of SSNHL in children is most commonly idiopathic. A careful work-up should include viral etiologies based on history and clinical findings. Most children in our study had hearing improvement. It was shown that IT steroid treatment can benefit these children and therefore should be considered as secondary treatment following systemic steroid treatment. Further research is required to establish standardization of diagnosis and management pathways in children with SSNHL.

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Advances in the clinical application of genetic screening in hereditary hearing loss

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Hearing loss (HL) is one of the most common sensory impairments worldwide. HL is common at all ages. In developed countries, it is estimated over half of HL in childhood is due to a genetic etiology [1,2]. The remaining HL occurrence can be attributed to environmental factors, such as congenital cytomegalovirus infection, meningitis, acquired conductive loss, and other causes.

Molecular analysis to diagnose HL is essentially non-invasive and may reduce the need for more extensive and expensive testing [3]. Genetic testing provides information about the etiology of hearing loss to those affected and their families in ways that were not previously possible [4]. It may predict the clinical course of the HL. Testing can be beneficial for the diagnosis of syndromic HL before additional features appear and can identify subjects with mitochondrial mutations who are at risk for iatrogenic HL when treated with aminoglycosides [5]. Another benefit of molecular analysis is the associated knowledge of the pattern of inheritance which can be useful when making reproductive choices. The surge in genetic research and testing reflects the growing role that genetics is playing in the diagnosis and characterization of congenital HL.

It has been estimated that 1.5-3 out of 1000 infants are born with congenital HL in the USA. When not identified early, prelingual HL can have long lasting negative impacts, including psychosocially, behaviorally and socioeconomically [2,6]. In the 1980s, the National Institutes of Health (NIH), the American Academy of Pediatrics (AAP) and the National Institute on Deafness and other communication disorders (NIDCD) recommended a newborn hearing screening followed by an early intervention program to prevent the potentially avoidable effects of undiagnosed HL with no intervention. This program became mainstream in 2005, when every USA state implemented a universal newborn hearing screening program (UNHS). The program requires that all hospitals test all newborns for hearing impairment prior to discharge home, as well as provide close follow up if needed. Hearing impairment is defined as HL of 30 dB or greater, "in the frequency region important for the speech recognition and comprehension in one or both ears, approximately 500 through 4,000 hertz" [7]. Testing consists of using otoacoustic emissions (OAE) and auditory brainstem response (ABR). If HL is identi-

fied, children should have confirmatory repeat testing within 3 months of age and an appropriate intervention by 6 months of age.

Despite the rise in the number of infants diagnosed with HL since the enactment of the UNHS, there are testing limitations. UNHS is a screening tool and, inherently, will miss infants with mild HL (in the range of 20-35 dB), or those infants who develop progressive or late-onset HL. Additionally, those infants that are lost to follow up after failing the UNHS will be delayed in the diagnosis of their HL and late in receiving relevant information and access to appropriate interventions [8]. It has been shown that a "passed" UNHS does not negate the possibility of HL, especially in the cases of mild, delayed onset, or progressive HL.

Wang et al. [9] showed in their study that 20% of the infants with GJB2 gene mutations passed their UNHS in China. Our institutional results showed that 5 out of 8 patients who later developed hearing loss and genetic HL variants identified initially passed the UNHS. At the present time, a risk registry of factors associated with late or delayed onset of hearing loss is used in most USA states to flag the children who will need ongoing monitoring. The more common factors include family history, known cytomegalovirus or herpes simplex infection, and perinatal anoxia. Use of the risk registry improves the ability to find late onset hearing loss but is not by itself adequate to address the totality of the issue.

The shortcomings of the UNHS can be bypassed with additional testing. For this reason, it is important that the screening test have a supplemental tool to offer more specific information and identify the positive tests that are missed by the initial screen. A review of studies that included genetic screening concurrently with UNHS found that, on average, genetic screening identified an additional 1.4% of patients with potential HL that would not otherwise be detected [10]. Furthermore, by performing genetic testing in conjunction with a confirmed failed UNHS, the etiology, characterization, and expected outcomes can be offered to the family [11]. Genetic testing can provide a better picture of the phenotype, associated co-morbidities, and the future expectations that a solitary "failed" UNHS cannot. Furthermore, genetic testing is important because more HL is linked with a genetic cause than previously thought. As more research is conducted, it is shown that much of the HL formerly identified as sporadic could be due to genetic predisposition [3,12]. Finally, concurrent genetic testing is already being performed on a large scale with results in over 180,000 infants [13], confirming the feasibility of this goal. We argue that the potential insight into the many genetic variations of HL that genetic testing offers far outweighs potential pitfalls. Genetic testing is not only useful for highlighting potential inheritance patterns but also in identifying individuals with new mutations. Many individuals affected by GJB2 associated HL have no known family history of HL.

Genetic testing is not the only effective way of detecting HL; other modalities of diagnostic testing have also been proven to be useful in identifying pediatric HL. Wendtland et al. [14] showed that when temporal bone imaging was performed among children with congenital HL, almost half (40%) demonstrated findings that explained the etiology of the SNHL and nearly the same percentage (39%) had positive genetic testing with abnormalities. While imaging can be highly effective, computed tomography does have specific drawbacks (i.e. the risks of the radiation exposure or general anesthesia required to obtain the scan). Comparatively, the unavoidable radiation and anesthesia carry more associated risks than blood or saliva collection, which is required for DNA collection and genetic testing.

Review of techniques

Direct sequencing:

Direct sequencing is used to determine the exact order of nucleotide bases in a given gene or region of interest, typically 1.000 base pairs in length [15]. The most widely used method is Sanger Sequencing. The advantage of this method is that it is able to identify almost all mutations present in a sequence, including novel mutations, and is considered the most accurate. However, this method is the most time consuming, labor intensive, and expensive. Thus, this method is now typically used to identify novel mutations or to verify results from an experimental screening technology.

Microarrays:

Microarrays, also known as mutation chips, offer a way to screen for multiple mutations at one time. Mutation chips are designed based on the mutation frequencies in a given population. They are also less expensive and faster than direct sequencing since multiple genes can be screened simultaneously. However, this method is only able to screen for the mutations included on the chip and cannot detect novel mutations in a gene. Furthermore, although several mutations can be screened at once, there is a limit as to how many mutations can be included without significantly increasing cost and time [15]. Currently, available mutation chips can identify anywhere from 15 to 300 mutations in 4 to 31 of the most common genes associated with HL [15,16]. In partnership with the company CapitalBio Technology Co. (Beijing, China), we developed the CapitalBioMiamiArray® that includes the nine most common variants present in our population of South Florida. The table shows the most common variants and their frequency. If a pathogenic variant in homozygosity or compound heterozygosity is found, the diagnosis is made and the screening stops.

Next generation sequencing (NGS):

As with Sanger sequencing, NGS, also known as massively parallel sequencing, directly sequences DNA samples. However, unlike Sanger sequencing, NGS sequences millions of DNA fragments in parallel rather than a single gene in a serial fashion. This technology is most useful for resequencing many selected parts of a genome, such as all exons from a particular set of deafness genes [17]. The critical difference between Sanger sequencing or single mutation testing and NGS is sequencing volume. While the Sanger method only sequences a single DNA fragment at a time, NGS is massively parallel, sequencing millions of fragments simultaneously per run. This high-throughput process translates into sequencing hundreds of genes at one time. NGS offers greater discovery power to detect novel or rare variants with deep sequencing. The benefits of Sanger sequencing include fast, cost-effective sequencing for low numbers of targets (1–20 targets), whereas NGS has higher sequencing depth enabling higher sensitivity (down to 1%), faster turnaround time for high sample volumes, comprehensive genomic coverage, higher throughput with sample multiplexing, higher mutation resolution and more data produced with the same amount of input DNA. It is not without its drawbacks, however. These include shorter reads, difficulty in detection certain types of variation (e.g. repeat expansions), and some areas of the genome which are resistant to NGS. Several NGS-based gene panels for comprehensive genetic testing for HL are available on the market, and many more are in development. Available panels screen for between 80 and 180 known deafness causing genes, and can take between 4 weeks and 3 months to complete [18]. At the University of Miami, we created a targeted-enriched NGS gene panel of 180 known and suspected deafness genes with a target size

of approximately 1 MB. The screened genes were identified by searching all available databases with deafness genes. To date, the design covers 2812 regions with all coding exons, 5′ and 3′ untranslated regions and 25 bases of intronic flanking sequences for each exon (MiamiOtoGenes®) [19].

Screening strategy

A cost-effective method for screening deafness genes is of paramount importance (Figure 1). At the University of Miami Ear Institute, we offer initial screening to all probands starting with the DNA microarray panel (CapitalBioMiamiArray®); this initial screening aims to simultaneously detect the most common deafness-causative mutations in our population. These mutations are including GJB2, SLC26A4 and mitochondrial RNA mutations including mt1555G>A (Table 1). In cases where a pathogenic mutation is not found with this initial screening, a customized capture/next-generation sequencing gene panel (MiamiOtoGenes®), composed of 180 known deafness genes is then performed to achieve a comprehensive interrogation of the full spectrum of variants. If a pathogenic gene is identified, studies of molecular epidemiology are then carried out to confirm the pathogenicity of the variant. If screening with MiamiOtoGenes® does not yield a pathogenic variant, consideration is given to NGS of the whole exome and/or genome.

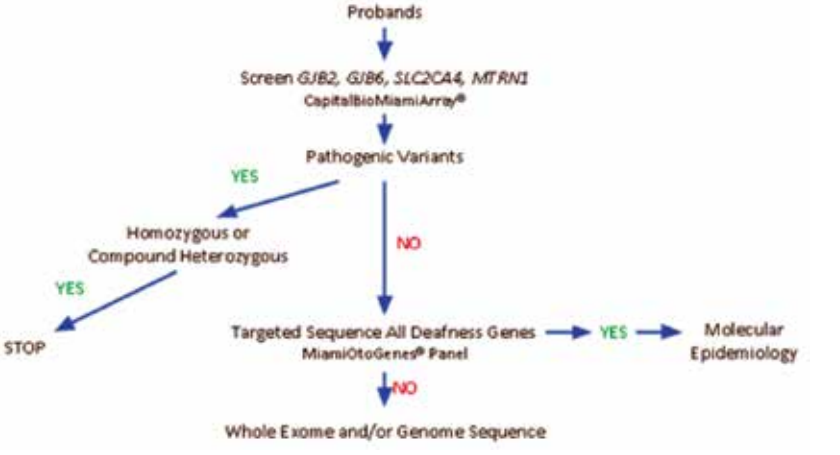

Figure 1. Sequential screening strategy to diagnose genetic deafness.

GENE	MUTATION(S)	FREQUENCY IN PATIENTS (%)	OCCURRENCE IN THE GENE (%)
GJB2	35delG W44C L90P	25.4 0.38 0.29	88 3 1
GJB6	309 kb deletion monogenic or digenic with GJB2	18	
SLC26A4	L23P T416P	5	16 15
MT-RNR1	1555A>G 7444G>A	2 1.8	38-100

Table 1. Nine common deafness mutations detection kit (CapitalBioMiamiArray®)

Limitations and genetic couseling

Despite only requiring a small blood sample or saliva swab, genetic testing has its drawbacks as well, particularly when considering the financial burden. The cost of genetic testing is expected to decrease as the modality becomes more mainstream; however, at this time, it remains a barrier to access [20]. Additionally, there is a prerequisite of an available multi-disciplinary team needed for genetic testing. All genetic testing should be done in partnership with a geneticist and genetic counselor. Lesperance, et al. [21] highlighted the barriers and challenges that some families encounter when offered genetic testing. The realization of the potential ramifications of a learned genetic deficit not only affects the patient but also extends to family members and to subsequent generations. Adequate information and proper counseling before and after genetic testing are essential. The unwanted burden of collateral information can be overwhelming for some families and may be the reason that genetic testing is declined.

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Management of pediatric unilateral hearing loss: Role of cochlear implantation

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Introduction

Hearing loss is one of the most prevalent congenital abnormalities in the United States (US), with 1-3 per 1000 infants diagnosed at birth [1]. Within the clinical diagnosis of hearing loss, unilateral sensorineural hearing loss (UHL) is the most prevalent form [2]. It is estimated that there is one congenital UHL case per 1000 births with at least one third of children born with hearing loss having UHL [3]. In the US, UHL affects approximately 3% of school age children and 10% of children born with UHL eventually develops bilateral hearing loss (BHL) [2,4].

Despite the advent of newer and more accessible technologies permitting for early identification of hearing loss, screening exams were historically equipped to screen for hearing levels worse than mild hearing loss. Depending on the screening test being employed, as many as 21-60% of children who display minimal symptoms or develop UHL after the postnatal period pass newborn hearing tests [5]. Decreased babbling or inattention are examples of earlier manifestations of UHL, subtle signs that may be easily overlooked and not identified until the child is of school age. In fact, it's been described that children with UHL do not receive intervention until the age of 5 years [6].

Importance of early intervention

Early identification of UHL is paramount for age appropriate speech, language, and social development. According to Sharma et al. (2002), the critical period of language development is between birth and 3 years of age as neuroplasticity is greatest during this period [7]. Unlike adults who use residual hearing to continue to communicate, children must rely on their residual hearing to learn how to communicate. The developing brain requires early exposure to language models in order to promote development of higher-order cognitive and psychological pathways [8]. Those without complete sensory inputs, e.g. children with UHL, have incomplete stimulation to auditory pathways and instead experience cortical reorganization, leading to downstream developmental delays [9]. The reorganization of auditory cortical pathways in children with UHL has been demonstrated in functional magnetic resonance imaging (fMRI) studies. During a speech reading task, activation of the left lateral temporal cortex, one of the major neural centers for language, was significantly reduced in congenitally unilaterally deaf children [10]. Furthermore, in children undergoing monoaural stimulation, normal-hearing participants displayed activation of the contralateral side while children with UHL displayed bilateral activation [11].

Several studies from the late 20th century documented the detrimental effects of UHL on language and speech development, particularly during the critical period of birth to 3 years of age. One of these works was Hart and Risley's landmark "30-Million-Word Gap" study in 1995 [12]. The authors revealed the importance of early exposure to auditory stimuli and its direct effect on language repertoire. They found that 86-98% of the words used by each child by the age of 3 years were derived from their parents' vocabularies [12]. In the study, the amount of words spoken by each child was directly related to socioeconomic status and the number of words spoken to them by their parents. Those who heard more words had larger vocabularies, better grades,

and greater academic achievements. Children and babies with UHL may not have access to the same language repertoire as those with binaural hearing and instead have inconsistent access to high frequency phenomes early in development, partly due to the head shadow effect and a baby's inability to control head positioning to direct their better hearing ear towards a speaker. Inconsistent access to language impacts speech perception and development.

Effects of unilateral hearing loss

One of the more obvious difficulties experienced in UHL is the loss of half of the auditory receivers available to detect sound when reducing from a binaural to a monoaural hearing system [13]. With UHL, there is also a loss of integral hearing components that allow for processing of more complex auditory signals. These include but are not limited to sound localization, binaural summation and squelch, and sound discrimination.

Children with UHL hear as little as 30-35% of intended speech due to their impaired sound localization, particularly for soft speech and sounds not directed towards the functional ear [14]. This not only presents a barrier for accurately discriminating a signal from background noise but also a safety hazard. Unfortunately, background noise is common in the classroom and failure to correctly identify speech in the presence of noise can negatively affect the learning and social environment. Children experiencing difficulties with receptive communication due to background noise and poor localization can suffer from embarrassment and feelings of social isolation [15]. Learned localization is a compensatory tool used to overcome this loss of sound localization [13]. Although the entire mechanism of how this process works is not entirely known, learned localization allows for an increased ability to identify where a sound is coming from. These compensatory methods, however, are not able to fully compensate for binaural hearing.

Binaural summation and squelch are two major binaural hearing components lost in UHL. Binaural summation is a central auditory process that allows a sound heard with both ears to be perceived as louder than the same sound heard with one ear. Increased perceptual loudness allows for increased sensitivity to differing intensities and frequencies, which are fundamental to speech comprehension in both quiet and loud settings. Binaural squelch is another central auditory process that allows a binaural listener to process stimuli received from each ear and reproduce it with higher signal-to-noise-ratio by comparing interaural time and intensity differences [14]. Both binaural summation and binaural squelch allow for better speech understanding in noise.

UHL also affects sound discrimination. The decreased ability to discrimate the signal from the noise is dependent on the combination of audiometric loss, sound shadow effects, and loss of sound localization [16]. Sound shadowing is an effect wherein the impaired ear casts a dulling effect on the functional ear, rendering it less sensitive to auditory signals [17]. To compensate for these losses, the individual with UHL must rely on the ability to visualize and focus on a specific tone or quality of the sound source in order to discriminate a signal from noise [13]. This compensatory mechanism demands a great amount of additional effort and concentration, particularly if the source of the tone and quality of the voice are similar [13]. These compensatory mechanisms can take a toll on those with UHL, particularly children, with studies reporting that children with UHL may experience significantly decreased self-esteem and increased levels of exhaustion and stress [18].

Bess and Tharpe in 1986 examined the academic and social challenges experienced by 60 children with UHL [19]. Children were matched according to age, sex, race, and socioeconomic status and their case histories were studied. They found that children with UHL were at an overall disadvantage in the classroom with 35% of them failing at least one grade, a rate ten times higher than that of the normal hearing population [19]. More recent studies have supported these early findings by showing that children with UHL exhibit lower levels of academic achievement, lower intelligence quotient scores, and greater diagnoses of behavioral problems [20].

Management of unilateral hearing loss

Modifying classroom seating and size is one way to help children with hearing loss succeed academically. Positioning the child closer to the teacher not only allows for better hearing but also better perception of visual cues [13]. This technique is primarily beneficial to those with BHL since preferential seating does not always help children with UHL. The child with UHL needs to be positioned in such a way that allows the intact ear to be facing the teacher, a challenging task in the modern classroom where teachers don't always stand in the front but instead move around the room. Smaller classrooms with fewer students can also increase the signal-to-noise ratio, which has been shown to benefit all students, particularly those with UHL [21]. Smaller classrooms, however, are often considered to be cost-ineffective, further limiting their implementation. Classroom accommodations also don't directly alter the mechanisms leading to hearing loss and are late interventions.

Hearing assistive technology (e.g. frequency modulator), bone conduction, and contralateral routing of signal (CROS) systems are currently FDA-approved treatments for UHL that can allow for early intervention, especially during a child's critical developmental period. A sound field frequency modulator (FM) system uses a microphone worn by the instructor to relay sound to a speaker near a student, providing them with a favorable signal-to-noise ratio [21]. The benefits of sound field FM devices, however, are limited by classroom acoustics and the physical and emotional burden of the child carrying a speaker. An alternative is the personal ear-level hearing aid that includes FM capabilities without the nuisance of having to carry a speaker or installing speaker systems throughout each classroom [22]. The effectiveness of FM systems is highly reliant on teachers using them properly and consistently.

Bone conduction devices work by transducing sound vibrations directly to the temporal bone and inner ear, bypassing the external and middle ear. These devices can be nonimplanted, percutaneous, or transcutaneous. Nonimplanted bone anchored devices can be held in place with a soft band and can significantly improve speech perception in UHL [23]. Nonimplanted devices, unlike percutaneous or transcutaneous bone auditory implant devices, have the advantage of avoiding surgery and often predict future success with implanted bone conduction hearing devices. The use of a nonimplanted device with a soft band is, however, limited by a child's ability to have head control and track a sound's origin. Since most children have appropriate head control by 6-7 months of age, the University of Miami Ear Institute (UMEI) protocol is to have a child with UHL in a soft band by 6 months of age.

The CROS hearing aid system takes sound from the affected ear and transmits it to the normal hearing ear by digital transmission [24]. In order to achieve this, a hearing aid must be worn on both ears so that the microphone worn on the impaired air routes the acoustic signal to the hearing aid worn on the normal ear. Despite its benefits in lifting the head shadow effect, complaints of occlusion in the normal ear, poor sound

quality, and discomfort pose limitations to these devices [25,26]. Unlike CROS systems, bone conduction devices avoid occlusion of the normal hearing ear since they don't require bilateral hearing aids [25]. CROS hearing devices are also subject to timing delays that occur when the signal is routed from the microphone to the transmitter of the better hearing ear, leading to poor sound quality and echos [25]. Amplification of extraneous noise can also reduce the intended signal in CROS hearing aids and mask hearing from the unaffected ear, leading to interference patterns [24]. To successfully use this device, the child must not only be old enough but also know how to adapt to noise, sound delays, and interference patterns. Although newer CROS devices use an open fit design to minimize obstruction, the use of this device is limited by the size of the ear canal [26]. The canal must be large enough, so the earpiece is not occluding and resulting in decreased auditory input.

Despite their limitations, bone conduction and CROS devices are early interventions that address the head shadow effect, improve sound awareness to the deaf side, and improve speech perception in noise. These devices, however, do not provide true binaural hearing since the brain only receives and processes auditory signals from one side.

Cochlear implantation in children with unilateral hearing loss

The cochlear implant (CI) is the only available treatment option able to provide binaural hearing to children with UHL. In July 2019, the U.S. Food and Drug Administration (FDA) approved one CI system for single-sided deafness and asymmetric hearing loss [27]. The MED-EL CI systems, SYNCHRONY and SYNCHRONY 2, are now indicated for individuals aged 5 years and older with UHL who have profound sensorineural hearing loss in one ear and normal hearing or mild sensorineural hearing loss in the other ear. The device is also indicated for individuals aged 5 years and older with asymmetric sensorineural hearing loss who have profound sensorineural hearing loss in one ear and mild to moderately severe sensorineural hearing loss in the other ear, with a difference of at least 15 dB in pure tone averages between ears [27].

Historically, CI has been used successfully in the treatment of severe to profound BHL. Studies performed on patients with BHL who have received bilateral CIs have shown better speech discrimination due to reacquisition of the head shadow effect, binaural summation, and binaural squelch effect after implantation [28]. Rouger at al. (2007) showed that bilaterally implanted post-lingually deaf adults were able to develop and maintain supranormal speech-reading performance, demonstrating recovery and reorganization of visual and auditory speech processing [29]. CI's effects have also been shown to span beyond better speech acquisition and address cortical auditory mapping. In patients with hearing loss, cochlear implants lead to "reversed" neuroplasticity, resulting in regression of abnormal crossmodal activations and reactivation of frontal areas normally involved in speech comprehension [30].

Fewer studies, however, have focused on the effects of CI in UHL. The use of CI in patients with UHL was originally studied for the treatment of tinnitus. The first reported study by Van de Heyning et al. in 2008 reported significant reductions in tinnitus after CI implantation [31]. Subsequent follow-up studies expanded on its therapeutic effect and investigated its impact on hearing. Arndt et al. (2010) performed a single-center trial comparing the effects of CROS, bone auditory implant devices, and CI on sound localization in adults with UHL using a multi-speaker sound field test [32]. They found that patients with CI had significantly decreased localization error and

improved speech perception when compared with controls, bone auditory implant, and CROS patients.

Hassepass et al. (2013) found similar results in a prospective study evaluating the effects of CI on speech discrimination in a group of three children with non-congenital unilateral hearing loss [33]. They found that CI improved speech discrimination in noise as well as improved localization using a similar sound field paradigm. The study's small sample size was, however, a major limitation to its experimental design and findings.

To date, there is only one randomized clinical trial investigating the effects of CI in children with UHL. Brown et al. from the University of North Carolina at Chapel Hill started this clinical trial in 2017 with an anticipated completion date in April 2021 [34]. The purpose of this trial is to demonstrate the effectiveness of CI in children with moderate to profound UHL. Outcome measures include speech perception measures, localization tasks, hearing in noise tasks, and subjective reports. Twenty participants were enrolled in this trial. Inclusion criteria included unilateral moderate to profound sensorineural hearing loss, between 3 years, 6 months and 6 years, 6 months at age of implantation, anatomically normal cochlear nerve or cochlear anatomy amenable to cochlear implantation (normal cochlear anatomy, incomplete partition type 2 with or without enlarged vestibular aqueduct or enlarged vestibular aqueduct with normal partitioning), no evidence of progressive hearing loss, willingness to undergo a 4-week hearing aid trial, aided word recognition in the ear to be implanted of 30% or less as measured with consonant-nucleus-consonant (CNC) words, and realistic parental outcome expectations. Exclusion criteria include conductive hearing loss in either ear, compromised auditory nerve, ossification of the cochlea, and inability to participate in follow-up procedures. The trial is currently still under investigation with an estimated completion date of 2021.

Although data from this randomized trial is still pending, preliminary reports suggest that implanted children with UHL not only derive measurable subjective and objective benefits in terms of binaural hearing but also with speech perception tasks in complex listening environments. Consequently, CI has emerged as a reasonable treatment option for selected children who are impacted by UHL. This is particularly important for pediatric patients who rely heavily on external stimuli for speech and language acquisition and who are not compliant or not receiving enough benefit from traditional therapies (i.e., FM-assisted system, bone auditory implants, CROS hearing aids). In addition, CI is the only one of the available therapies with the potential to prevent and revert some of the neuroplasticity changes seen in children with UHL.

Among the important factors influencing CI outcomes in children with congenital UHL are etiology of UHL, age at implantation, comorbidities, and family engagement. Some series have shown that cochlear nerve deficiency or absence can account for up to 30% of congenital UHL cases, justifying the practice of performing an MRI to exclude children with such conditions prior to consideration of CI [32]. There has also been increasing interest in the use of CI in etiologies associated with progressive hearing loss before the UHL child becomes affected by BHL. Congenital cytomegalovirus (cCMV), certain types of hereditary progressive hearing loss, and inner ear malformations are associated with progressive hearing loss in the initially unaffected ear of UHL infants. In fact, cCMV has recently been shown to be a significant cause of UHL, with one cohort study reporting cCMV as the second leading cause of early-onset UHL and asymmetrical hearing loss after cochlear nerve deficiency [35]. UHL with cCMV etiology carries significant risk for progressive deterioration of the better hearing ear, with rates

of 45-75% across studies [35]. The benefit of bone auditory implants and CROS hearing aids decreases significantly with hearing loss in the contralateral ear and early and proactive habilitation with CI in at-risk UHL cases may allow for maximal benefit from early implantation, longer duration of CI use, and avoidance of auditory deprivation.

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Vertigo and imbalance in children: Current diagnostic methods

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Introduction

When I received the invitation to participate in the First World Congress of Pediatric Otolaryngology held in Buenos Aires in April 2019 with a lecture on this extensive topic, I wondered what would be the most useful presentation. After asking the opinion of prestigious neurotologists and otologists in my country, the generalized view was that it should be a simple talk for as many professionals as possible who work with children and do not necessarily have the opportunity to update on this topic; a presentation useful for daily practice, providing tools that allow to evaluate each case individually and that, if possible, would be concise, without too many numbers, and not boring. Therefore, those who expect a presentation on physiopathology and precise data on the afferent and efferent pathways will surely be disappointed, as will those who are looking for a short synthesis, as I prefer to emphasize certain concepts.

As a result, I hope that those who are interested in a simple, useful, and clear approach to the current diagnostic options will find what they are looking for in these lines. I am not completely sure to have achieved this goal, but I sincerely tried.

Problem analysis

The assessment of patients with balance disorders is complex, especially in the case of children, in whom signs and symptoms are interpretative and provided by third parties.

It is generally believed that balance disorders in children are uncommon; however, this is not true. For example, in 1999 Russell and Abu-Arafeh reported that around 15% of more than 2100 school-aged children surveyed in Scotland mentioned an episode of vertigo in the previous year. Similarly, in 2006 Niemensivu reported that of 1000 children surveyed in schools and pediatric clinics in Helsinki (2004-2005), 8% of the

children < 12 years of age had experienced an objective episode of vertigo or recurrent imbalance over a period of 2 years. Furthermore, in 2008, Manrique Lipa found that in Madrid 2% of children younger than 16 years was referred by general physicians for ENT evaluation because of objective imbalance or vertigo.

These data show that the prevalence of this condition is higher than is often believed and the subsequent initial and therapeutic diagnostic approach is complex. Therefore, it is important to systematically assess the tools available today, considering from the outset that disorders associated with instability, vertigo, or imbalance in children may present variable manifestations, such as:

– Interruption of physical activity.
– Appearance of sudden crying.
– Sudden feelings of terror, without a clear cause (Pérez, 2002).

Underlying these manifestations, spontaneous acute non-recurrent vertigo, objective recurrent vertigo, non-vertigo instability, gait imbalance, or ataxia may be found (Casselbrandt ML, Mandel EM. 2005).

Differential diagnosis

To identify the type and etiology of the imbalance disorder in the child, a detailed clinical history, a thorough physical examination, neurological assessment, and specific instrumental tests are essential.

Firstly, the vestibular disorder is classified into peripheral or central. It should be emphasized that when symptoms include loss of consciousness neuroimaging studies should be requested (Casselbrandt ML, Mandel EM. 2005).

The following table shows the differences between central and peripheral disease (Eviatar L, 2006) (Table 1).

Signs and symptoms of peripheral vertigo	Signs and symptoms of central vertigo
1 Sudden onset without loss of consciousness	Imbalance or continuous vértigo
2 Imbalance: falls or swaying towards the affected side	Nystagmus
3 Nausea, vomiting, and autonomic dysfunction	Multidirectional
4 Nystagmus: towards the non-affected side	No changes with head movements
Induced by changes in head position	No initial latency
Maximum with the affected ear downwards	No fatigue with repetitive changes in position
Initial latency=3 to 10 sec. Duration=60 sec.	Not inhibited by eye fixation
Fatigue with repetitive changes in position	Frequent deficits of cranial nerves
Inhibited by eye fixation	Frequent pyramidal and cerebellar signs
5 Preference: Supine position with the affected ear upwards	
6 Head movements	
7 Paroxysmal torticollis in infants	

Table 1. Signs and symptoms of peripheral and central vertigo. (Modified according to Eviatar L).

Once the disorder is classified as vestibular, objective and specific instrumental evaluation is initiated.

Clinical context and diagnostic evaluation

Physical and neurotologic exploration

The aim of this presentation was to provide an easy approach to the topic. In this context, an overall analysis of this problem can be simplified as follows: balance is essentially a multifactorial process of sensory stimuli, with afferences, their processing, and efferent motor responses.

INPUT: The central aim is to understand how the patient obtains the sensory information of his or her surroundings. This information is obtained through the vestibular system, vision, the somatosensory system, hearing, and touch. These stimuli send information, which is complemented and validated to ensure that the input information to the vestibular network is real.

PROCESSING: The external sensory stimuli send their data to the brainstem, supervised by the cerebellum, and produce a mental image of the spatial position, which is compared to mentally stored sensory information.

OUTPUT: Once our position in space is known, a motor response is programmed that allows the person to adapt to a situation of movement and activity. This output consists of neural impulses in two main directions: towards the anterior horns of the spinal cord, giving rise to the vestibulospinal reflex (VSR) and towards the oculo-motor nuclei, giving rise to the vestibulo-ocular (VOR) and vestibulo-collic (VCR) reflexes.

Therefore, to understand the function of the vestibular pathway, the following reflexes are evaluated:

VOR: The vestibulo-ocular reflex serves to stabilize the gaze during head rotation; it generates rotation of the eye with the same amplitude and opposed to the direction of the head movement as a result of vestibular stimulation.

VCR: The vestibulo-collic reflex serves to maintain head stability.

VSR: The vestibulospinal reflex serves to maintain posture/gait stability.

Therefore, specific physical exams should be performed to evaluate these reflexes associated with vertigo and imbalance.

Differential diagnosis

Below an outline is shown of the different diagnostic alternatives, based on their frequency, general involvement, and their association with episodes of hearing loss. (Figure 1).

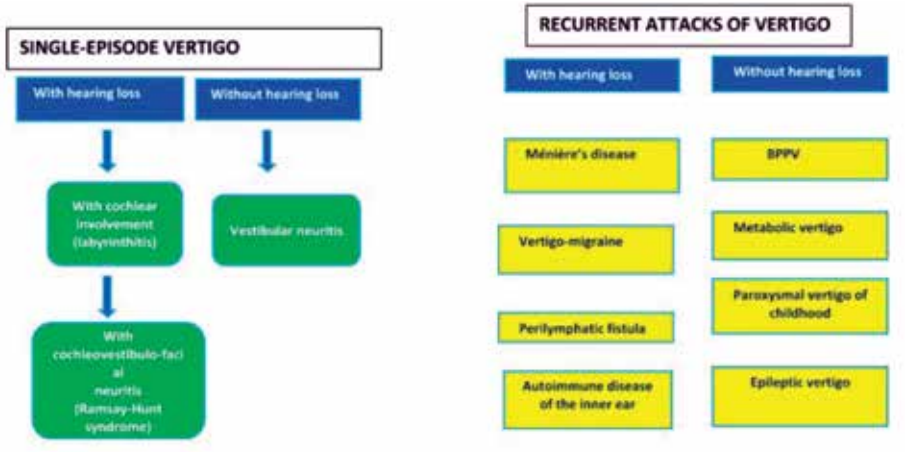

Figure 1. Classification of peripheral vertigo disorders (Morera, et al. 2008).

Common childhood vertigos

There is consensus on the five most common causes of childhood vertigo, which are:

1) Benign paroxysmal vertigo of childhood.
2) Viral infection.
3) Vestibular migraine.
4) Acute or suppurative middle-ear otitis.
5) Epileptic vertigo *(Bower y Cotton, 1995; Balatsouras y cols. 2006; Erbek y cols. 2006)*:

Pre-school children

In pre-school children, paroxysmal vertigo of childhood accounts for 70.9% of the cases and is considered to be a precursor and early manifestation of vestibular migraine. Childhood paroxysmal vertigo decreases with age while migraine increases. (Epidemiolgy Of Vertigo, Migraine And Vestibular Migraine- Headache 2009; Idiopatic BPV In Children, A Migraine Precusor - Int J. Pediatr Oto 2013; Migraine Associated A Vertigo Otolarhingol Clin N Am 2011).

The condition is typically observed in healthy children aged around 3 to 5 years, manifesting as sudden-onset episodes of vertigo, without a triggering factor, lasting from seconds to minutes, sometimes accompanied by neurovegetative symptoms and inability to maintain an upright position of the body.

The episodes usually do not occur after 12 years of age and are rarely observed in adolescence.

Consciousness is preserved, without obnubilation or drowsiness, and the children return to their activities after the episode. There are no associated hearing disturbances, or other neurotological symptoms.

Children who suffer from this disorder usually have a family history of migraine, and around 50% develops migraine later in life. Therefore, different authors consider childhood paroxysmal vertigo to be a childhood equivalent of migraine (Batuecas et al., 2006).

School-age children

In school-age children, paroxysmal vertigo of childhood (30%) and vestibular migraine (30%) are the most commonly observed causes of childhood vertigo. The latter condition is characterized by recurrent episodes of vertigo with perceptive hearing loss of unknown cause and a multiform vestibular semiology (Morera et al., 2008). It is estimated to account for 3% of the recurrent vertigos in children occurring between 6 and 12 years of age. The patients should meet the following diagnostic criteria:

1) Recurrent vestibular symptoms of at least moderate intensity.
2) Current or prior history of migraine according to the International Headache Society (IHS) criteria.
3) Presentation of at least one migraine symptom in at least two episodes of vertigo: migrainous headache, photophobia, phonophobia, or visual, auditory, or any other type of auras. (Neuhauser and Lempert, 2004).

Adolescents

In addition to the above-mentioned conditions, in adolescents the following relevant diseases are found:

– VESTIBULAR MIGRAINE 30.4%
– BPPV 12.9%
– VESTIBULAR NEURITIS 7.0%
– PSYCHOGENIC VERTIGO 6.5%
– MÉNIÈRE'S DISEASE 1.8%
– OTHER CAUSES 26.5%

Episodic Syndrome That Many Associated Whit Migraine A.K.A. "The Chilhood Periodic Syndrome", Headache 2015: 55 (10):1358 -64. Lee Jd, et al. Int J Of Pediatr. Otolaringology 2017;94: 36-9.

Epileptic vertigo

This entity may manifest both with falls and vertigo and aura preceding typical seizures.

Visceral symptoms, such as nausea and vomiting, are unusual and the EEG usually confirms the diagnosis; brain MRI is indicated to rule out tumors or other organic diseases.

Vestibulogenic seizures are extremely rare and triggered by stimuli to the temporoparietal cerebral cortex generated by complex labyrinthine disease.

Instrumental neurotologic assessment

For many years, the most commonly used examination for vestibular assessment has been the functional examination of the VIII cranial nerve, consisting of the evaluation of static and dynamic balance, cranial nerves, spontaneous and positional nystagmus, as well as alternating bithermal caloric stimulation and a hearing test. Its greatest strength is, of course, that the injured vestibular system can be defined.

The advent of **videonystagmography** (VNG) has thoroughly changed vestibular assessment, as it allows for the recording, storing, and reproduction of eye movements, essentially of spontaneous, positional, or post-caloric nystagmus through the recording with infrared cameras mounted on goggles placed on the patient's face. (Figure 2). The study has enabled objective analysis of the responses obtained, as opposed to the prior interpretation of responses to caloric stimuli by a single observer without the possibility of recording the results (Barona R., 2007).

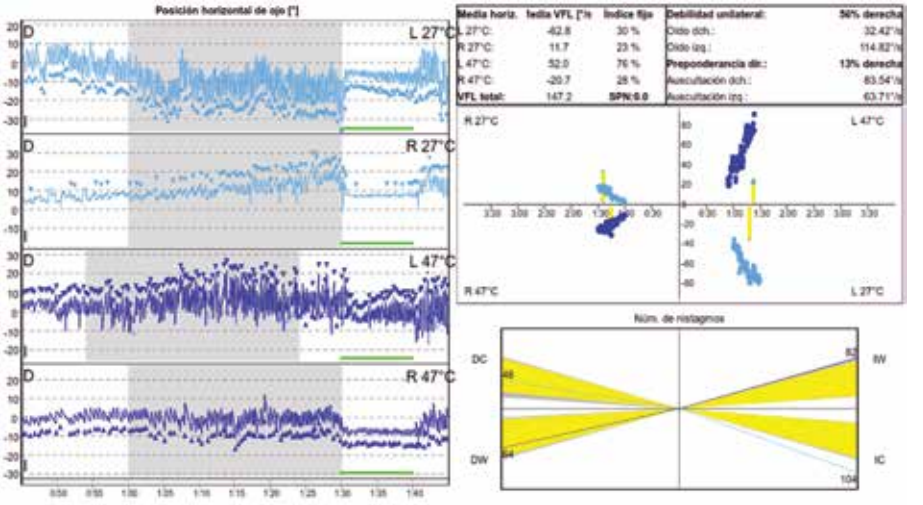

Figure 2. Videonystagmography.

Nevertheless, this traditional examination conceptually has serious limitations in terms of the objective information it provides, without considering what is usual, even in clinical settings, and may be interpreted as representative of the overall function of the vestibular pathway. And that is a serious error.

The caloric test has considerable limitations, such as the low frequency of stimulation leading to variability in the individual response to the caloric stimulus. However, its most important limitation lies in its inability to comprehensively evaluate the vestibular pathway, as it only assesses the response of the horizontal semicircular channel, resulting in uncertainty about the function of the remaining components of the vestibular system.

The different components of cranial nerve VIII testing are generally well tolerated by children, although the caloric test requires laborious preparation for adequate tolerance. Apart from this difficulty, its main problem is keeping the child with a focused gaze throughout the exam, which is particularly complex.

Consequently, this examination alone is entirely insufficient to conduct an adequate evaluation, due to both physiological and technical limitations that, in children, are particularly difficult to overcome.

In this context, it is necessary to expand our battery of tests to be able to evaluate responses from all the components of the vestibular system and thus allow an adequate topodiagnosis of the disease and the degree of injury. Therefore, we use several complementary tests; however, here I will refer only to those we routinely use:

1) Video Head Impulse Test/VHIT (VOR)
2) Cervical Vestibular Evoked Myogenic Potentials (VCR)
3) Ocular Vestibular Evoked Myogenic Potentials (VCR)
4) Posturography (VSR)

Video Head Impulse Test/VHIT

VHIT is the main tool to evaluate the vestibulo-ocular reflex (**VOR**) of the upper vestibular nerve (horizontal and anterior semicircular canal) and lower vestibular nerve (posterior semicircular canal).

The test is based on the recording of eye movements using high-speed cameras, which can capture compensatory movements during head movement and allow to separately evaluate all semicircular channels. Involvement of the semicircular canals is related to the appearance of vertigo.

A physiological stimulus is used: short head movement is much better tolerated by children than the caloric stimulus.

Rapid head impulses are made (amplitude of 15°) while the eyes remain fixed on a target; the eye should make an opposite movement of similar magnitude and should not compensate or compensation should be minimal (VOR) (Blödow A, Pannasch S, Walther E, 2012).

The head movements should be made in the same anatomical plane as the canal that is tested; i.e. to evaluate the horizontal semicircular canal, the head is rotated horizontally to the side that is tested (right or left).

To evaluate the vertical canals, oblique rotations are made: upwards oblique for the posterior semicircular canal and downwards oblique for the anterior semicircular canal.

A high-speed camera records whether there are accommodation movements in the eye and determines the ratio of the eye movement to the head rotation to identify the affected canal. This gain should yield values between 0.8 – 1.2 for horizontal semicircular canals and between 0.7 and 1.0 for vertical semicircular canals.

In addition, the presence of corrective eye movements or refixation saccades is evaluated: saccades were classified into COVERT, for those that appear 100 milliseconds after the head movement and are therefore impossible to observe with the naked eye, and OVERT, for those that appear more than 200 milliseconds after the head impulse, whose presence is also indicative of canal hypofunction (Blödow A, Pannasch S, Walther E, 2012). (Figure 3).

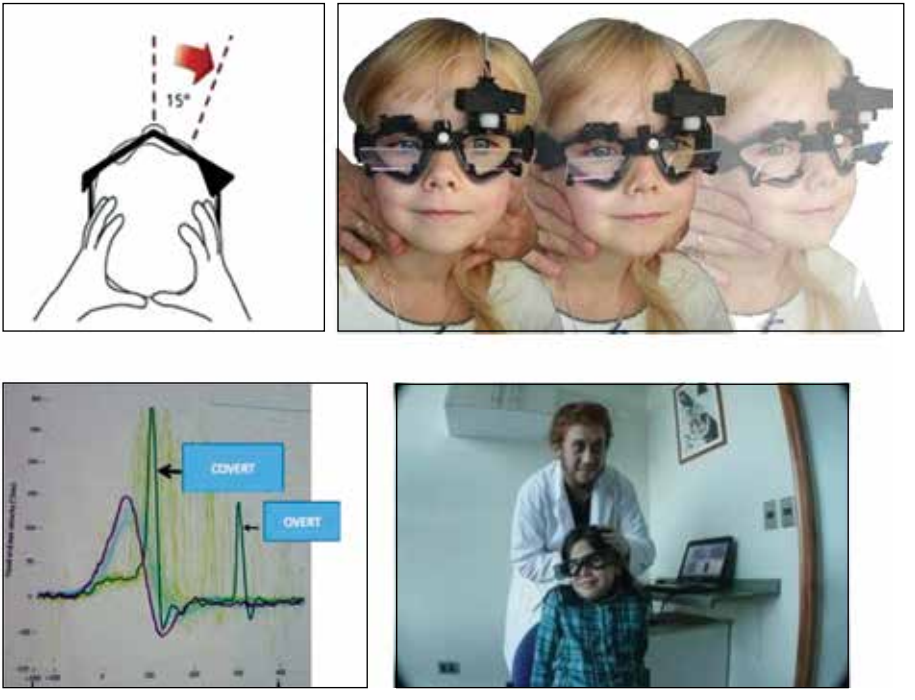

Figure 3. Video Head Impulse Test/VHIT.

– Nevertheless, the procedure has some practical limitations:
– Lack of cooperation in very young children (fix the gaze on the target).
– Goggles with camera were originally designed for adults (cannot be adjusted well on small faces).
– The degree of hypofunction is not determined ("on" – "off").
– Variability in the results (control of the pulse stimulus by the examiner that initiates the test).

Vestibular Evoked Myogenic Potentials (VEMP)

As mentioned above, the semicircular canals that are in charge of detecting **angular accelerations** are assessed using the caloric test and vHIT. Nevertheless, these tests do not evaluate the otolith organs (saccule and utricle) responsible for reacting to **linear accelerations**. Therefore, VEMP is used for this purpose.

There are two VEMP responses, depending on the structure and the nerve that is tested. For the inferior vestibular nerve, that originates from the saccule, cervical vestibular evoked myogenic potentials (cVEMP) are used and for the superior vestibular nerve, arising from the utricle, ocular vestibular evoked myogenic potentials (oVEMP) are used.

This acoustic stimulation is generated by mechanical stimulation, produced by the sound wave and not by the sound itself, i.e. it is not relevant whether or not the patient hears the sound, but that the sound wave reaches the otolith organs; there should be no obstruction, which is only possible if there is no disease in the outer ear or middle ear.

– The main advantage of the test is that it can diagnose a variety of conditions:
– Vestibular neuritis.
– Acoustic neuroma.
– Labyrinthitis.
– Brainstem stroke.
– Ménière's disease.
– Superior semicircular canal dehiscence (SSCD).

Cervical Vestibular Evoked Myogenic Potentials (cVEMP)

cVEMP are an objective, non-invasive, fast, easy-to-perform and comfortable test in children to assess function of the saccule and the lower vestibular nerve (Figure 4).

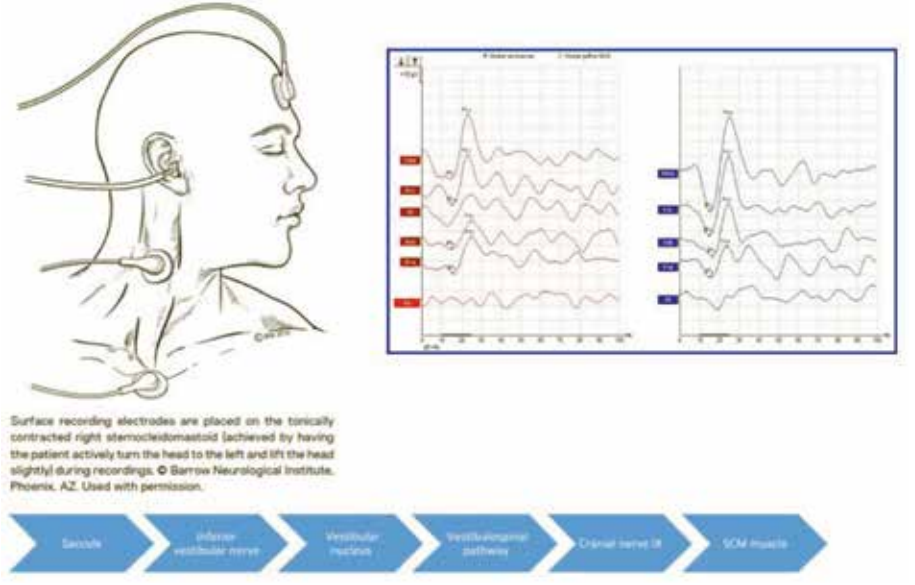

Figure 4. Cervical Vestibular Evoked Myogenic Potentials.

Surface electrodes are placed on the sternocleidomastoid muscle, on the sternal vertex and insertion; insert phones are also used for acoustic stimulation.

The test assesses the generation **of the vestibulo-collic** reflex, a disynaptic reflex that arises when the acoustic stimulus activates the saccular macula generating an electrical potential that travels along the lower vestibular nerve until reaching the lateral vestibular nucleus, and follows the course of the medial vestibulospinal tract. Stimulation of the saccule with a high-intensity sound has an inhibitory effect on the tonic contraction of the ipsilateral sternocleidomastoid muscle. As a result, a biphasic response is obtained, with a vestibular component generating p13 and n23 waves, and a cochlear component generating n34 and p44 waves. The latter are inconstant and without current clinical use (Córdoba M, 2015).

It is important to take into account that the inhibition of the ipsilateral sternocleidomastoid muscle contraction is measured; thus, to perform this measurement, a minimum level of contraction of this muscle is required.

The following parameters are assessed:
– Presence of p13 and n23 waves.
– Interaural amplitude difference (>36% is pathological).
– Increased latencies suggests injury to the vestibulospinal tract (Córdoba M, 2015).
– Response threshold at intensities lower than 70 dB suggest a third window syndrome.

Ocular Vestibular Evoked Myogenic Potentials (oVEMP)

oVEMP evaluates ocular muscle response evoked by sound stimulation. o**VEMP** is initiated by active acoustic stimulation of the utricular macula, triggering an electric potential that travels along the superior vestibular nerves ascending along the medial longitudinal fasciculus crossing the midline up to the nucleus of cranial nerve III. High-intensity sound stimulation of the utricle has an excitatory effect on the inferior oblique ocular muscle contralateral to the ear that is studied. The potential is composed of two sets of biphasic wave forms. The first biphasic potential has a negative peak (N) with a mean latency of 10 ms, followed by a positive peak (P) with a mean latency of 15 ms, termed N1 – P1 (Silva Tatiana Rocha, Resende Luciana Macedo de, Santos Marco Aurélio Rocha.2016). (Figures 5 and 6).

oVEMP is performed by placing surface electrodes on the skin just below the eye on the side contralateral to the auditory stimulus. (Silva Tatiana Rocha, Resende Luciana Macedo de, Santos Marco Aurélio Rocha.2016.)

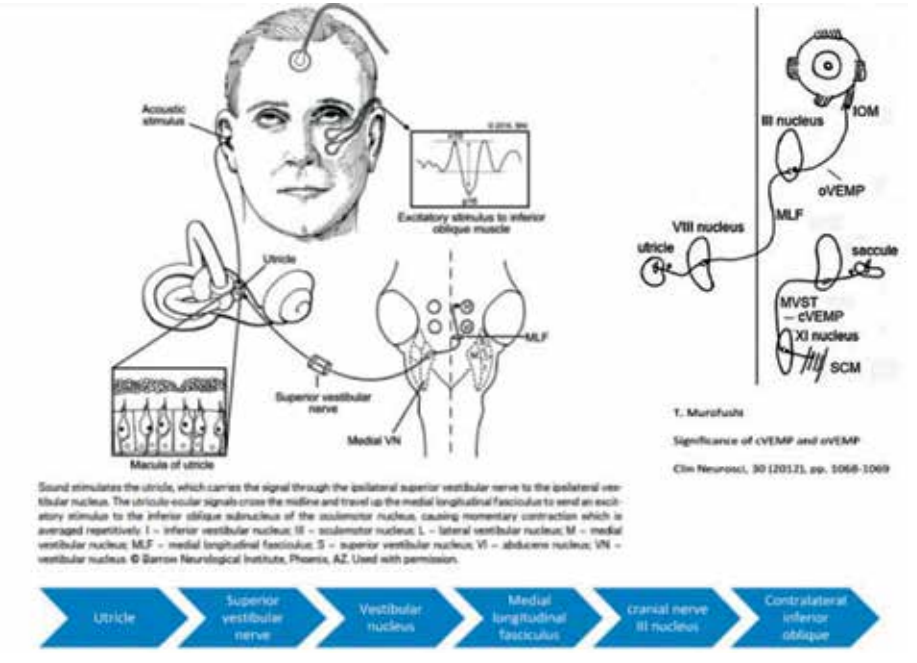

Figure 5. Ocular Vestibular Evoked Myogenic Potentials.

The following parameters are evaluated:
– Presence of n10 and p15 waves.
– Interaural amplitude difference (>30% is pathological).

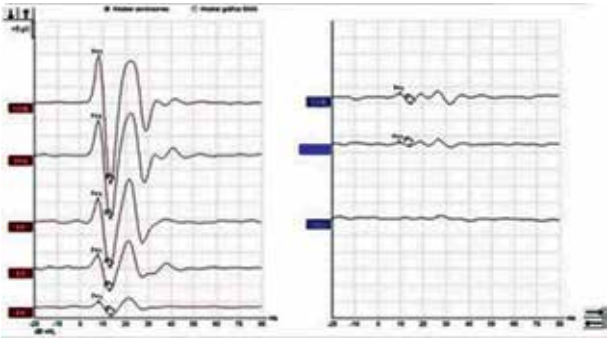

Figure 6.

Summary of functionality:
Figure 7.

Figure 7. Functionality cVEMP-oVEMP.

Posturography

Posturography is a useful method to quantify the functional state of balance of the patient, particularly when he or she presents with ongoing symptoms that, in spite of evaluation with different tests, could not be diagnosed: when assessing these alterations together and the side of the injury or which of the 3 systems (visual, vestibular, proprioceptive)is involved cannot be determined.

Posturography is used to assess the vestibulospinal reflex (VSR) and provides data on:
– Degree of dysfunction.
– Degree of compensation.
– Identification and monitoring of rehabilitation patterns

There are currently two types of posturography: static and dynamic (Furman et al., 1993). In our clinical practice, we only use static posturography, since dynamic posturography basically aims to quantify, through different tests, **voluntary control** of the limits of stability, and is therefore, in our opinion, not useful in patients with active vestibular disease.

Static posturography

Static posturography is performed on a fixed platform with a changing visual surrounding and a computer system that detects the center of body pressure, similar to

the center of gravity, in different situations of sensory conflict. The test provides the **angle of balance** (Visser J et al., 2008), useful to quantify the real magnitude of the symptoms described by the patient, especially those regarding gait imbalance.

Analysis of this set of clinical data may lead to different diagnostic options, such as (Table 2):

	Cranial nerve VIII/ VNG	cVEMP	oVEMP	vHIT
Ménière's disease	Caloric test: hypofunction of the involved ear	Abnormal, with wave amplitude asymmetry or absence	Abnormal only in the late phase with wave amplitude asymmetry or absence	Normal Abnormal Hypofunction with gains less than 0.8 and/or compensation saccades
Perilymphatic fistula	Caloric test: hypofunction of the involved ear if LSC is involved	Abnormal. Decreased threshold and increased amplitude in the affected ear	Abnormal. Decreased threshold and increased amplitude in the affected ear	Abnormal only in relation to SC involved, with hypofunction and gains less than 0.8 and/or compensation saccades
Vestibular migraine/ paroxysmal vertigo of childhood	Normal	Normal	Normal	Normal
BPPV	Positional nystagmus	Normal (amplitude symmetry	Normal (amplitude symmetry $\leq$ 0.36)	Normal: gains > 0.8 and $\leq$ 1.2 0.36) Absence of compensation saccades

Table 2.

Sensitivity and specificity of the different tests.

Test	Sensitivity	Specificity
-SOT (sensory organization test) [1]	40%	
-Romberg.[1]	63%	
-ROT (Rotatory test) [1]	37%	
-ROT+ENG (electronystagmografia) [1]	77%	
-Romberg/ tandem romberg [2]		
• ROT [2]	49% 53%	95% 95%
HIT (HEAD IMPULSE TEST) [3]	48%	95%
HIT [4]	34-45%	91-100%
HIT [5]	71% (unilateral vestibular deficit) 84 % (bilateral vestibular deficit)	84%
HIT + caloric test (VNG) [6]	47.6%	83.9%
HIT+ caloric test (VNG)+ minimal caloric test [6]	52.2%	89.7%

Table 3. Sensitivity and specificity of the different tests.

Final comments

In the pediatric population, prevalence of vestibular disorders is significant, and therefore this diagnostic option should be considered in a child that, with no apparent cause, suddenly stops physical activity, or in case of sudden-onset crying or the feeling of sudden terror.

Understanding the physiological limitations of the most common tests as well as the difficulties that may arise when performing them adequately is essential for the correct interpretation of the results.

Currently, there are several diagnostic procedures that allow us to comprehensively evaluate the child. Tests, such as vHIT to assess the function of the semicircular canals, or VEMPs to evaluate the otolith organs, and posturography, which enables us to determine the magnitude of the symptoms described, allow us to base our diagnosis on objective measurements and define the areas or pathways involved.

Regardless of the diagnostic power of the current testing tools, only adequate training and thorough theorical knowledge of this clinical field by the professionals allows for the adequate performance of these tests. Currently, human resources are more relevant than ever and they become more necessary with the increase in technological options and complexity of the equipment. These human resources will remain an irreplaceable factor in making the final diagnosis.

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LARYNX AND NECK

Aspiration from an otolaryngologist's perspective

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Introduction

Pediatric dysphagia is a complex condition that has become a model for multidisciplinary care team-based management. Collaborative relationships between subspecialty clinicians such as pediatric otolaryngologists, pulmonologists, gastroenterologists, and geneticists; therapists such as speech-language pathologists and occupational therapists, nutritionists; and parents, afford the most sensitive and robust patient care teams [(1)]. This multidisciplinary model, often referred to as the aerodigestive model, also appears to reduce the cost and time required for the diagnostic workup of children with dysphagia and related conditions [(1)]. The purpose of this chapter is to describe dysphagia and aspiration from the perspective of the pediatric otolaryngologist. It cannot be overemphasized that this role is best executed within a collaborative aerodigestive team.

Surgical correction of conditions contributing to dysphagia is predicated on understanding the complex, essential, and interdependent functions of the pediatric airway. The "airway" (i.e. larynx) serves multiple functions, and disorders may affect these differentially or together as depicted in Figure 1. Surgical management and decision-making must take into consideration this concept of the unified aerodigestive tract, carefully balancing treatment of one function (such as swallowing) with possible tradeoffs in another function (such as respiration or vocalization).

Figure 1. Depiction of interdependent functions of the pediatric airway.

Otolaryngology considerations in the workup of suspected aspiration

Initial evaluation of the child with suspected dysphagia or aspiration beings with a detailed history and physical examination. It is our practice to begin with vital signs, height, and weight/length. Vital signs include respiratory rate and pulse oximetry, with a note of any supplemental oxygen. Heart rate may be useful as well, because some congenital cardiac disorders may affect growth and therefore confound assessment of dysphagia. Standardized, age-appropriate growth charts demonstrating growth trends over time are considered part of vital signs, and growth charts are easily visualized on the electronic medical record interface or in paper charting systems. One commonly used option has been developed by the World Health Organization. (https://www.cdc.gov/growthcharts/who_charts.htm).

History includes detailed questions about the child's current feeding plan, specific consistencies or textures the child is taking by mouth, feeding techniques, alternative routes of nutrition such as nasogastric or gastrostomy tubes, previous feeding history, and current symptoms. Frequency and duration of respiratory illnesses and pneumonias are documented, as is history of noisy breathing, apneas, or episodes of color change or cyanosis during or after feeds. In infants, a previous BRUE (brief resolved unexplained event) episode is especially salient as aspiration is thought to be a leading cause of such events [2,3]. Any history of choking, needing Heimlich maneuver, or food impaction is elicited [4]. Caregivers are also asked about signs of aspiration such as throat clearing, coughing, wet vocal quality, congested throat or nasal sounds with feeding, attempts to disengage in feeding, and red/watery eyes. Caregiver perceptions of the effect of a nasogastric tube on their child's feeding and swallowing function are also elicited [5]. In our experience, nasal obstruction, whether due to nasal devices or anatomic obstruction, may disrupt suck-swallow-breathe coordination during infancy, and is a commonly overlooked or underestimated contributor to dysphagia in this age group. A history of prior breathing and airway problems, including previous intubations, tracheostomy, "beard-distribution" vascular lesions, and dysphonia or vocal fold problems may also clarify contributing factors to dysphagia.

Past medical and surgical history, especially as it relates to the complex action of swallowing, is noted with focused attention to cardiopulmonary, gastrointestinal, neurologic, and musculoskeletal systems. Medications are carefully reviewed, with special note of those having a known relationship to dysphagia such as anti-reflux medications and inhaled medications. Immunization status may provide useful data to explain respiratory infections. Perinatal oxygen requirement may suggest primary ciliary dyskinesia, while recurrent sinus or ear infections in conjunction with recurrent respiratory infections may suggest immunodeficiency or a ciliary disorder; all of these conditions may confound assessment of dysphagia in a child.

Physical examination includes a general assessment of head control, tone, and any evidence of respiratory distress such as nasal flaring, tracheal tugging, stridor, and retractions. A full head and neck exam is performed with special attention to the nasal cavity, oral cavity and oropharynx, sucking mechanism in infants, palate movement and palpation, evidence of sialorrhea, cranial nerve exam, and stigmata of genetic syndromes. If the patient has a tracheostomy in place, the size and ability to tolerate speaking valve or capping is examined. Pulmonary exam is performed before and after feeding.

Evaluation of swallowing in children

There are several tools available to investigate pediatric swallow function. The clinical evaluation of swallowing, or bedside swallow assessment, is a non-instrumental evaluation conducted by a speech-language pathologist or occupational therapist. This assessment is critical in generating a gross hypothesis regarding dysphagia, framing next steps, and choosing an appropriate instrumental swallowing evaluation. Clinical swallowing evaluation alone, however, has been shown to have poor sensitivity in predicting aspiration risk in children, and we therefore have a low threshold to obtain instrumental swallowing evaluations [6].

Instrumental swallowing evaluations in the pediatric population are varied and include flexible endoscopic evaluation of swallowing (FEES), videofluoroscopic evaluation of swallow (VFSS), high-resolution manometry, gastroesophageal milk scan, upper gastrointestinal tract series, and others. The two instrumental assessments most

commonly employed by otolaryngologists are flexible endoscopic evaluation of swallowing (FEES) and videofluroscopic evaluation of swallow (VFSS).

When deciding between FEES and VFSS, the clinical history and feasibility of obtaining the study are considered. At times, both studies are utilized; data obtained from each study are often complementary. FEES is most often performed by an otolaryngologist and a speech-language pathologist or occupational therapist with the goal of recreating the patient's typical feeding. A flexible nasolaryngoscopy is performed while swallowing across consistencies is observed (Figure 2). If there is strong suspicion of anatomic abnormality, FEES gives an endoscopic view of the patients anatomy and is then the preferred initial assessment under most circumstances (Figure 3). FEES can evaluate the structure of the upper aerodigestive tract from the nasal airway to the glottis and esophageal inlet, as well as the function of the cranial nerves involved in pharyngeal and laryngeal motor function and sensation [1]. Control of secretions and endoscopic evaluation of velopharyngeal sufficiency and the ability to conduct vocal tasks are evaluated. It may also be useful to evaluate sensory function via the laryngeal adductor response by mechanical stimulation of the supraglottic larynx.

At times, a bolus is given to the patient prior to passage of the nasolaryngoscope and the clearance of this bolus is determined via endoscopic visualization. This is called a static endoscopic evaluation of swallow (SEES) and may be particularly useful in children with neurologic causes of poor pharyngeal clearance and those behaviorally unable to tolerate FEES [8]. The ability to perform these evaluation in the breastfeeding patient is a distinct advantage of FEES and SEES. Details of the breastfeeding FEES technique are outlined in the literature [9].

VFSS, also known as modified barium swallow study (MBSS), or "cookie swallow", is performed by a speech-language pathologist and radiologist [10]. The speech-language pathologist presents food and liquids mixed with barium and, if necessary, employs different feeding strategies to help determine the safest feeding plan. The speech-language pathologist is responsible for interpreting the data obtained from the study as it relates to swallowing [11]. The radiologist is responsible for identification of any anatomic abnormalities, and management of the machinery and radiation exposure.

The major differences between FEES and VFSS are summarized in Table 1. With either study, the otolaryngologist must consider if the study is going to change clinical management prior to ordering the study, as both studies can expose children to procedures that would be otherwise unnecessary. Both studies may worsen oral aversion in some children.

Figure 2. Otolaryngologist and speech language pathologist performing FEES evaluation with bottle feeding.

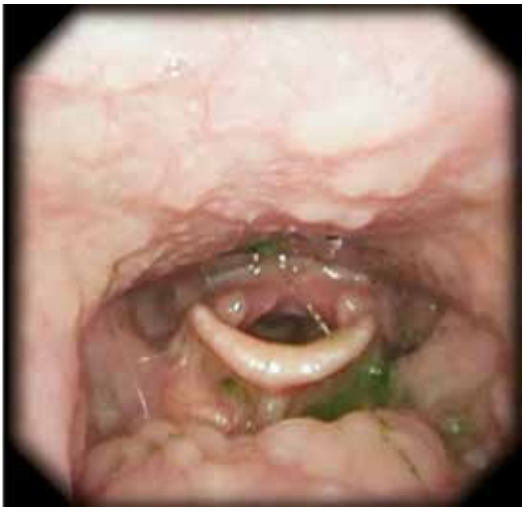


Figure 3. FEES image showing amounts of residue in left vallecula and postcricoid space after a swallow of applesauce. Image courtesy of Laura Orvidas, MD.

FEES	VFSS
Clear view of upper airway anatomy, nares to glottis	Inferred 3D anatomic details from sagittal view; multiplanar views available at some institutions
Clear view of vocal fold motion, ability to test laryngeal sensation, and determination of laryngeal lesions	Questionable
"Whiteout" at instant of swallow; cannot view oral phase or esophageal phase	Comprehensive view throughout the swallow
Clear view of location and amount of residue	Inferred details
Harder to separate penetration and aspiration	Definitely separates penetration and aspiration
Cannot tell clearance with cough, etc.	Definitely confirms/refutes clearance
Can do anywhere, on any patient tolerant of the nasolaryngoscope (most difficult between ages 2 years to 4 years)	More limited Access
Unlimited exposure time	Frequency and duration of study limited by radiation exposure

Table 1. Comparison of FEES and VFSS.

Airway evaluation in dysphagic children

For patients with a suspected anatomic predisposition to dysphagia, operative evaluation of the aerodigestive tract allows for further evaluation and potential intervention. Rigid airway endoscopy allows for a detailed view and examination of a patient's anatomy. It is our practice to conduct this exam in conjunction with flexible pulmonary bronchoscopy to evaluate for upper airway obstruction, laryngomalacia, tracheobronchomalacia, and to evaluate the segmental and subsegmental bronchi. Bronchoalveolar lavage may be useful during flexible bronchoscopy to evaluate for active lower airway infection or inflammation as well as for airway pepsin, which may signify aspiration of refluxed material. Often, the esophagus and upper gastrointestinal tract is also examined by our gastroenterology colleagues under the same anesthe-

tic. The order of these procedures is important, as a shallow depth of anesthesia is critical to an accurate display of dynamic function during the flexible bronchoscopy. Therefore, multidisciplinary aerodigestive evaluations are performed from the least anesthesia to the deepest anesthesia in a structured fashion, ideally with a dedicated team of anesthesia colleagues astute in these nuances.

Rigid airway endoscopy is best performed in a standardized and reproducible manner with complete evaluation of anatomic structures involved in the patient's differential diagnosis. This exam is ideally performed with the patient breathing spontaneously and without an endotracheal tube in the larynx. Necessary equipment includes tools to expose, examine, palpate, measure, and photo-/video-document the examination. Our basic setup comprises a variety of laryngoscopes, bronchoscopes, zero degree and angled telescopes, right angle probe, suctions, and uncuffed endotracheal tubes. If the larynx needs to be examined or operated upon with a two-hand technique, the patient can be placed into laryngeal suspension. It is our practice to examine the same basic battery of structures in every patient, with additional examination based on the patient's history and preoperative diagnostic workup.

First, the laryngoscope is placed, and topical lidocaine is applied to the larynx. The difficulty and grade of exposure is noted, and the laryngoscope used is documented in the electronic medical record for quick reference [12]. The supraglottis and glottis are examined and photodocumented. Microscopic exam of the subglottis, mid-trachea, carina, and segmental bronchi is completed. A right angle probe is used to evaluate for laryngeal cleft and to palpate for a submucous cleft of the posterior cricoid, and a photo is captured in all patients to document this portion of the exam. The cricoarytenoid joints are also palpated with the probe. The subglottis is sized using progressive intubation with uncuffed endotracheal tubes using techniques previously described [13]. The trachea and bronchi are evaluated for tracheoesophageal fistula, complete tracheal rings, inflammation, and malacia or compression.

In children with 22q11.2-deletion syndrome, special attention is paid to palpation of the palate and examination for glottic web (Figure 4), as well as tracheobronchomalacia and vascular compression of the lower airways (Figure 5) [14]. Children with history of VACTERL and CHARGE association should be carefully evaluated for tracheoesophageal fistula. Children with history of tracheoesophageal fistula and with wheezing should be carefully evaluated for other midline anomalies of the aerodigestive tract such as laryngeal cleft.

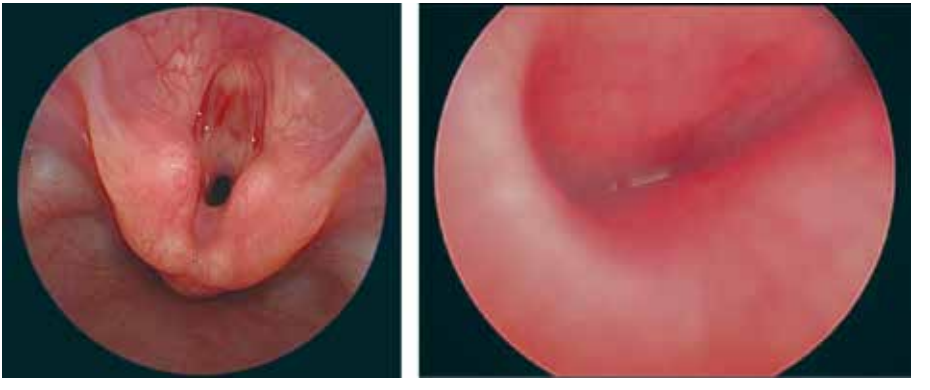


Figure 4. Rigid endoscopic view of Grade 3 congenital glottic web in a neonate.
Figure 5. Flexible endoscopoic view of severe left mainstem bronchial compression in a child with 22q11.2 microdeletion.

Ancillary studies

Other diagnostic studies may provide useful information in evaluating the child with dysphagia. Plain chest radiographs may demonstrate lung inflammation, areas of consolidation, or even cavitary lesions in cases of severe lung injury. Computed tomography (CT) may provide more detailed information about areas of consolidation, air trapping, bronchial wall thickening and bronchiectasis (Figure 6). These findings are not specific to aspiration and should of course be interpreted in the larger clinical context of the individual patient. CT or CT angiography may also provide information about anatomic anomalies of the heart and great vessels that may contribute to dysphagia. Echocardiograms may demonstrate congenital cardiac defects that may affect respiration (and therefore feeding) and growth.

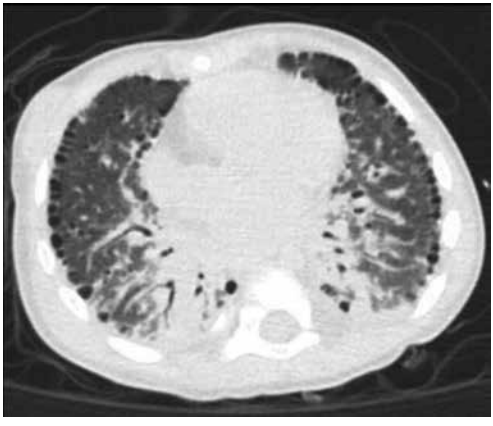


Figure 6. Axial CT image showing lung injury in a child with severe aspiration of refluxed gastric contents.

Common anatomic contributors to aspiration

Many conditions across multiple body systems may directly or indirectly contribute to aspiration in pediatric patients [15,16]. Examples of these are outlined in Table 2, along with an expanded differential for diagnoses within the purvey of the pediatric otolaryngologist [10].

Laryngomalacia

Laryngomalacia is the most common cause of stridor in infants, usually presenting around 2 weeks of age, and peaking between 2-4 months of age [17]. Stridor that is present at birth should always be assessed by awake flexible laryngosocopy, as lesions such as bilateral vocal fold immobility, congenital laryngeal web, and laryngeal dystonia may closely mimic laryngomalacia.

Most laryngomalacia symptoms resolve by 12-24 months; 90% of children do not need surgical intervention. The need for surgical intervention is driven by failure to thrive, severe obstructive sleep apnea, or chronic airway resistance sequelae such as pulmonary hypertension. There are several classification systems to describe laryngomalacia. Clinically, our practice has found the Thompson classification to be useful for patient evaluation and parent counseling, as outlined in Table 3 [18,19].

Table 2: Disorders associated with an increased risk of aspiration

General, genetic, neurologic conditions	Prematurity, spinal muscular atropy, cerebral palsy, Moebius syndrome, CHARGE syndrome, general hypotonia, TUBB3, 22q11.2 deletion syndrome, Chiari malformation	
Cardiopulmonary disorders	Bronchopulmonary dysplasia, congenital heart disease	
Gastrointestinal disorders	GERD, eosinophilic esophagitis, congenital diaphragmatic henia, omphalocele	
Medicalized/iatrogenic	Nasogastric tube, supplemental oxgen/ventilatory support, tracheostomy	
Otolaryngologic	Nose/nasopharynx	Nasolacrimal duct cyst Nasal or nasopharyngeal masses Choanal stenosis or atresia Piriform aperture stenosis Cleft palate Adenoid hypertrophy Nasal airway obstruction
	Oral/oropharyngeal	Velopharyngeal insufficiency Micrognathia/retrognathia Ankyloglossia Macroglossia Poor suck/oral incompetence Epilus and congenital oral masses Pharyngomalacia Tonsillar hypertrophy Lingual thyroid, lymphovascular malformations, Other tongue base masses
	Larynx/hypopharynx	Laryngomalacia Vocal fold immobility Laryngeal cleft Posterior glottic diastasis Subglottic pathology: hemangioma, stenosis, cysts Tracheomalacia Bronchomalacia
	Esophageal	Post-cricoid venous plexus Tracheoesophageal fistula GERD/Laryngopharyngeal reflux Esophageal dysmotility Cricopharyngeal achalasia Eosinophilic esophagitis

Table 3: Classification and management of laryngomalacia

Thompson Classification	Symptoms (Thompson)	Management (authors)
Mild	Inspiratory stridor, occasional episodes of feeding-associated symptoms; maintain coordinated suck, swallow, breathe;	Positioning during feeds, early monitored “tummy time”, consider medical management of reflux
Moderate	Frequent feeding-associated symptoms; difficulty with feedings; stridor in multiple settings	Close clinical monitoring (28% progress to surgical intervention), medical management of reflux
Severe	Persistent stridor, possible apneas, feeding intolerance, failure to thrive, severe OSA, BRUEs/cyanotic events	Surgical management guided by sleep endoscopy or flexible bronchoscopy (nasal airway to carina)

The common saying, "babies who do not breathe well, do not feed well" is embodied by the pathology at play in the setting of laryngomalacia. Indeed, feeding difficulties that occur in the setting of laryngomalacia most often reflect dyscoordination of the suck-swallow-breathe cycle as a consequence of supraglottic airway obstruction. However, in a subset of children, feeding difficulty and laryngomalacia occur simultaneously in the setting of a larger, overarching diagnosis that may not yet be established at the time of consultation. It is therefore important to completely assess the child for other neurologic abnormalities or physical exam characteristics which may influence the patients long-term feeding and swallowing prognosis.

Gastroesophageal and laryngopharyngeal reflux are thought to be closely associated with laryngomalacia, although the exact relationship remains a topic of controversy. From a physiologic standpoint, breathing against supraglottic resistance creates negative intrathoracic pressure, which has the ability to promote reflux. Reflux then instigates supraglottic and glottic edema and decreases laryngeal sensation, worsening breathing and swallowing. Anti-reflux medications, therefore, are often used to break this positive feedback loop.

The approach to the infant with laryngomalacia should include a history with attention to characteristics of stridor, history of apnea, history of tracheal tugging or retractions, and feeding difficulty. Plotting the growth curve and flexible fiberoptic laryngoscopy are considered essential components of the physical exam. Auscultation of the lungs and trachea, as well as inspection of the accessory muscles is given careful attention. Parents are asked to bring the infant in clothing that facilitates a full respiratory exam, and to withhold feeds in hopes of being able to examine symptoms during feeding. We do not routinely obtain polysomnogram or instrumental swallow study unless it is felt that either study would significantly change management. Clinical swallow evaluation is based on the patient's presentation and can help introduce strategies such as feeding in side-lying position or changing the flow rate of feeds.

Infants that demonstrate failure to thrive, concern for aspiration, significant difficulty with feeds, or obstructive symptoms despite medical management are offered surgical intervention. The operative approach most often includes either a sleep endoscopy or flexible bronchoscopy (from the nasal airway to the carina) to evaluate the anatomic locations of obstruction (such as epiglottic prolapse, arytenoid prolapse, and glossoptosis) and evaluate for concurrent or secondary airway conditions (the most common being tracheomalacia and subglottic stenosis) [20]. The steps of a supraglottoplasty are tailored to the patient's obstructive pattern, but most often include adequate exposure and suspension with spontaneous ventilation, release of the aryepiglottic folds, trimming of any excess arytenoid mucosa to the depth of the corniculate process, and consideration of epiglottopexy [21]. The specific techniques to achieve these goals are variable and include cold steel, laser, and powered instrumentation such as the microdebrider [22]. Decreasing operative time to less than 30 minutes has been shown to decrease the need for postoperative ICU admission and should be considered when choosing a specific technique [23]. Recent literature has favored bilateral procedures, with the caveat that care must be given to avoid denuding the opposing interarytenoid mucosa which may result in scarring and laryngeal stenosis [24].

Feeding after supraglottoplasty is reintroduced to mirror the preoperative feeding regimen, as early as the same day. If a patient has increased coughing or difficulty managing feeds shortly after surgery, feeding therapists are consulted for clinical swallowing evaluation and initiation of compensatory strategies. These may include slower-flow nipples on feeding bottles, breastfeeding after a brief period of pumping,

or alternative positioning strategies for the infant. It is our practice to consider FEES at the time of postoperative laryngoscopy, if necessary. Unless the child appears overtly unsafe, we generally do not obtain VFSS during the immediate postoperative period. Patients are maintained on anti-reflux medications for 6-12 weeks postoperatively, and the growth chart is carefully evaluated in coordination with the child's pediatrician.

Vocal fold immobility

Vocal fold immobility is a common cause of dysphagia in the pediatric population, across a range of ages and from various causes. It is the second most common cause of stridor in infants, behind laryngomalacia. Vocal fold immobility can be unilateral or bilateral, and congenital, acquired, or iatrogenic. "Immobility" and "hypomobility" are used to agnostically describe absent or reduced motion when the cause is unknown. If a neurologic cause is confirmed, either by laryngeal electromyography (LEMG) or confirmation of normal cricoarytenoid joint mobility by palpation, the terms "paralysis" and "paresis" are used. Finally, if a mechanical cause of immobility is suspected, such as cricoarytenoid joint dislocation or laryngeal scarring, the term "fixation" is used.

Common signs of unilateral vocal fold immobility are weak voice, stridor, dysphagia, feeding difficulties, and rarely respiratory distress. These symptoms may be positional, particularly in young infants. In contrast, bilateral vocal fold immobility, especially in the adducted position, is more likely to present with respiratory distress, stridor, and dysphagia.

Most often, vocal fold immobility is unilateral, neurogenic, and iatrogenic. Iatrogenic unilateral vocal fold paralysis and paresis are most commonly associated with injury to the recurrent laryngeal nerve or the vagus nerve during congenital cardiac surgery, birth trauma, head and neck tumor excision such as thyroidectomy, tracheoesophageal fistula (TEF) or esophageal atresia repair, neurologic disease, or other head, neck, and chest procedures. Birth trauma may explain up to 38% of "congenital" immobility. It is more likely to be unilateral and more likely to resolve spontaneously [25]. The aforementioned causes can also result in bilateral vocal fold immobility, albeit more rarely [26]. It is important to recognize that unilateral approaches, such as thoracoscopic approach to TEF repair, can result in bilateral vocal fold immobility secondary to traction injury, thermal injury, other iatrogenic causes, and anatomic predisposition.

Congenital bilateral vocal fold paralysis represents 12-30% of congenital vocal fold immobility [27,28]. The most common association is with Chiari malformation, but other causes such as Moebius syndrome, Charcot-Marie-Tooth disease, birth trauma, and idiopathic reasons are also implicated [29]. Acquired bilateral vocal fold immobility from vincristine therapy is observed in the pediatric oncology population.

Flexible laryngoscopy is critical to initial evaluation of vocal fold motion. This exam allows the clinician to document the movement of each vocal fold, any concurrent vocal lesions, the shape and degree of glottic gap during adduction, and the resting position of the immobile vocal fold. More subtle findings such as vocal fold height mismatch, atrophy of the vocal fold, bowing of the vocal fold, and asymmetric medial rotation of the affected arytenoid cartilages are also identifiable on flexible laryngoscopy without or without laryngeal stroboscopy. There are limitations, however, to this exam including difficulty in determining hypomobility and only moderate inter-rater agreement for degree of mobility; this is enhanced when sound and visual information obtained during vocal tasks are used together [30]. Laryngeal ultrasound is an emerging tool for assessing laryngeal motion and is especially helpful in patients with tenuous respiratory status such as those with congenital heart disease and children intolerant of awake flexible laryngoscopy [31].

Illustrating the multiple functions of the larynx, the impact of vocal fold immobility depends upon the resting position of the immobile vocal fold(s) and the compensation of other swallow mechanics. When adduction results in a moderate to wide glottic gap, voice and swallow may be poor while respiration is preserved; if the immobile vocal fold(s) rests in a median position, respiration may be impaired while voice and swallow are relatively preserved. Because of the complex neural anatomy of the larynx, it is not possible to reliably predict the resting position of the paralyzed vocal fold base on the site of nerve injury [32-34]. Importantly, patients should be followed at regular intervals to evaluate for recovery of function as well as changes in the resting position and compensatory laryngeal function [35].

In infants and children, laryngeal function is prioritized as breathing, then swallowing, and finally voice. The goal of any intervention or surgical procedure is to maintain the airway while improving the swallow and voice. In general, we prefer to wait until post-pubertal voice before performing procedures which could result in long-term laryngeal deficits because of continued growth of the larynx.

Unilateral vocal fold immobility

Management of unilateral vocal fold immobility is governed by clinical symptoms. Often observation, feeding and swallow therapy, and voice therapy (for children ages 3 years and older) are all that is required. If there is dysphagia, however, surgical management is more readily considered [36].

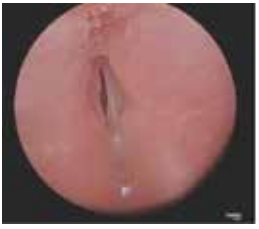
Injection laryngoplasty is a minimally invasive, quick, and safe procedure across a variety of pediatric populations [37]. For infants and children, this is typically performed in the operating room under general anesthesia with spontaneous ventilation. Multiple injection materials are available, and choice is guided by surgeon experience, desired duration of the material, and availability. It is our practice to admit all children under 30kg, children receiving hyaluronic acid injection (given the possibility of allergic reaction), children living more than 2 hours from the hospital, or any child with developmental delay for overnight observation with continuous pulse oximetry.

For children with vocal fold immobility persisting greater than 18-24 months after suspected injury, laryngeal reinnervation using the ansa cervicalis to recurrent laryngeal nerve is considered. Reinnervation has been successful in children less than 2 years of age, and as long as greater than 10 years following injury [38]. The data surrounding pediatric dysphagia following laryngeal reinnervation is more sparse, but Carroll found normal VFSS in select patients beginning 6 months after reinnervation [39].

Bilateral vocal fold immobility

When the bilateral vocal folds are immobile and resting in a median position, there is often severe airway obstruction (Figure 7). Again, the goal is to improve the airway while maintaining swallow and voice [40]. The most readily available option is to bypass the obstruction with a tracheostomy tube. The mainstay of alternative treatments for bilateral vocal fold immobility is to enlarge the glottic opening, which can be accomplished in various ways (Figure 8). Alternative treatments include cordotomy/arytenoidectomy (Figure 9), suture lateralization, and reinnervation with the phrenic or bilateral ansa cervicalis to recurrent laryngeal nerve. A relatively straightforward approach is the endoscopic anterior posterior cricoid split [41]. It is our practice to offer this in the infant population up to age 6-9 months with a swallow that is otherwise anticipated to be grossly normal. Patients with multiple cranial nerve abnormalities, such as those with CHARGE or Moebius syndrome, are not ideal candidates as they cannot

compensate for the increased aspiration risk postoperatively. In older patients, endoscopic posterior costal cartilage graft laryngoplasty is another alternative for bilateral vocal fold immobility and posterior glottic stenosis. It is our practice to perform a full multidisciplinary aerodigestive evaluation prior to offering this operation in order to better characterize the patient's baseline swallowing function and pulmonary health.



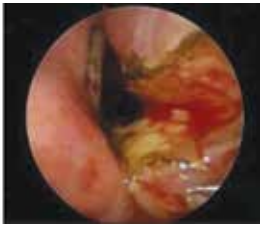


Figure 7. Narrow/obstructed glottic aperture in a child with bilateral vocal fold immobility.
Figure 8. Endoscopic posterior cartilage graft laryngoplasty to widen glottic aperture for the patient in Figure 7. Image shows the graft immediately after placement.
Figure 9. Endoscopic view of glottis immediately after laser cordotomy and partial arytenoidectomy for bilateral vocal fold immobility.

Laryngeal/laryngotracheoesophageal clefts

Laryngeal/laryngotracheoesophageal clefts are congenital (or rarely iatrogenic) anomalies of the larynx which are commonly considered in the differential diagnosis of pediatric dysphagia and aspiration. Clefts may present with dysphagia and/or respiratory symptoms. The most commonly used classification system for laryngeal clefts is the Benjamin-Inglis system, as outlined in Table 4, and is based on the most distal extent of the anomaly [42]. The degree of symptoms ranges from near-normal to life-threatening. One recent study found that in children with persist or recurrent wheezing, 17% had a laryngeal cleft [43]. Patients demonstrating a "posterior pattern" of aspiration on videofluroscopic swallow study are sometimes considered to be at risk for having a laryngeal cleft, though it is not necessary for diagnosis. Diagnosis and management of laryngeal cleft is controversial, partly owing to the variable clinical presentation of Type 1 & 2 laryngeal cleft. Furthermore, some clinicians feel that bolstering the interarytenoid tissue and height results in functional benefit for some patients, even in the absence of a true anatomic cleft [44].

Beyond the standard history and physical exam performed in patients with dysphagia, physical exam is focused to include stigmata of syndromes most commonly associated with laryngeal cleft: VATER/VACTERL, CHARGE, Opitz G (also known as Optiz G/BBB, Optiz-Frias; facial anomalies, midline gentitourinary defects), and Pallister-Hall (bifid epiglottis, polydactyly, hypothalamic hamartoma, hypopituitarism). It is our experience that increased severity of the cleft is associated with a higher likelihood of the patient's having a genetic syndrome. In addition, there is a high concordance of syndromic laryngeal cleft and other airway anomalies, particularly tracheoesophageal fistula [45]. At our institution, each patient with tracheoesophageal fistula or esophageal atresia undergoes a baseline airway examination for co-morbid airway anomalies including laryngeal cleft [45,47].

Rigid laryngeal endoscopy is the current gold standard for diagnosis of laryngeal cleft [48]. Flexible bronchoscopy has been shown to identify 69% of clefts, compared to rigid endoscopy [37]. This reduced detection with flexible endoscopy is because rigid

endoscopy allows a better approach angle to visualize the posterior larynx, allows for manipulation of redundant tissue which can obscure the cleft, and allows for palpation with a right angle probe or alligator forceps to feel the depth of the interarytenoid space and the integrity of the cricoid cartilage [49]. Rigid laryngeal endoscopy is also necessary to diagnose recurrent communication after prior cleft repair, or iatrogenic cleft after prior laryngeal reconstruction involving the posterior cricoid.

Treatment of laryngeal cleft is dependent on the patient's presentation and history including age and co-morbidities, and the depth of the cleft [48]. The goal of treatment is to promote a safe swallow and allow for sufficient nutrition to support growth and development. Type 1 cleft can often be managed by observation or manipulation of feedings such as thickener for thin liquids or limiting the rate of feeds. Injection of the type 1 cleft or deep interarytenoid notch with a temporary substrate to bulk the cleft (such as carboxymethylcellulose gel) is sometimes performed at the time of diagnostic endoscopy as a litmus test to inform decision making about suture closure [50]. Because many of our diagnostic endoscopies are performed as part of a coordinated procedure with pediatric pulmonary and pediatric gastroenterology, the depth of anesthesia can sometimes limit the feasibility of cleft injection during this exam. Timing of repeat clinical swallow evaluation and instrumental swallow studies following injection or suture closure is controversial and may depend on the patient's initial presentation [51,52]. Safe swallowing function is also known to improve with patient age, increased head and trunk control, and matured coordination regardless of the presence or absence of a laryngeal cleft, adding to the controversy surrounding deep interarytenoid notch and type 1 cleft [53]. Furthermore, swallowing is a complex function and surgical intervention on the posterior larynx may not improve swallow function or decrease aspiration [54].

Management of type 2 and 3 clefts is also driven by symptoms, but these lesions generaly need to be repaired. This repair is most often accomplished by an endoscopic approach, though some type 3 clefts are best served by an open approach [52]. Type 4 clefts result in a "common cavity" between the trachea and the esophagus, necessitating complex management and expedient reconstruction of the airway to prevent gross aspiration and respiratory failure. Open repair with interposition grafting is typically employed. Pre-operative and post-operative management are often the most difficult aspects of care of patients with complete laryngoesophageal cleft. After repair of type 4 and some type 3 clefts, patients are at high risk of significant tracheomalacia and poor management of secretions. Therefore, candidacy for tracheostomy should be evaluated once the cleft repair has sufficiently healed.

Table 4: Benjamin-Inglis classification of laryngeal cleft and common symptoms

Type	Anatomy	Symptoms
I	Supraglottic interarytenoid cleft, generally involving the interarytenoid muscle	Normal* to aspiration symptoms (which may only be present with thin liquids or drinking rapidly) ± stridor
II	Partial cricoid cleft	Aspiration symptoms ± stridor
III	Extends to cervical trachea	Severe aspiration; respiratory distress
IV	Extends to thoracic trachea or beyond	Rapidly fatal if not repaired early

*=controversy exists regarding making a diagnosis of "incidental" laryngeal cleft. That is, in the setting of no clinical history of aspiration or stridor.

Other surgical options for aspiration

There are other surgical options directly addressing laryngeal aspiration which, albeit rare, are important to consider in the surgical armamentarium.

Laryngotracheal separation is a safe, relatively fast operation. It is considered a surgical cure for aspiration in the sense that the aerodigestive tract becomes separated into the respiratory and the digestive tracts by closing off the pharynx and converting the patient to become a total neck breather akin to a laryngectomy [55]. In theory, this is potentially reversible, though not often performed clinically. The major consideration is that children are no longer able to vocalize. Even if a child is non-verbal, many families appreciate and greatly value vocalizations.

Some consider a narrow-field (or near-field) laryngectomy to be better for alaryngeal speech as it preserves the pharyngeal mucosa, along with the hyoid bone and strap muscles [56].

Laryngeal closure techniques are rare but relatively straightforward procedures, with some reporting performing glottic closure under local anesthesia [57]. Essentially, the mucosal of the true vocal folds, false vocal folds, and possibly a third layer are denuded and approximated to "seal" off the airway. These are done through a transcervical approach, and all require a permanent tracheostomy.

Finally, management of sialorrhea is an important consideration in the management of children with chronic aspiration. A step-wise approach should be considered in consultation with the family and other specialists, especially neurology and pulmonology. First line therapy is often medication, such as glycopyrrolate or atropine drops [58,59]. Occasionally, nebulized ipratropium can offer good benefit without systemic side effects, but the caveat that frequent administrations are required. Salivary chemodenervation, such as Botox injection, is also an option. When performed under ultrasound guidance, the complication rate is low but risks of worsening dysphagia, accidental facial nerve paresis, potential need for repeat procedures, and intravascular injection are discussed with parents [60]. Children that do not respond to more conservative measures, or in those children where medications are contraindicated, can be considered for surgical management. Ligation of the submandibular and parotid ducts is a quick, potentially reversible option. The outcomes have been reported to be similar to gland excision with less operative time [61,62]. Excision of the bilateral submandibular glands and ligation of one or both parotid ducts is the most often employed technique at our institution and affords nice reduction in salivary flow [63,64]. The safety for the patient to undergo general anesthesia from a pulmonary standpoint must be carefully considered.

Future directions

Recognition that management of dysphagia cannot be performed in isolation but instead requires a multidiscliplinary approach has shifted the paradigm towards integrated collaboration in the diagnosis, management, and follow-up of infants and children with aspiration symptoms [1]. This had led to the creation of Aerodigestive Centers at medical institutions across the globe. Future work will determine best practices and outcome metrics for such centers, and which patients benefit most from these resource-intensive programs. Coordinated care will play an increasing role in institutional efficiency both in the outpatient setting and in the operating room [1].

Telemedicine and patient wearables will inform clinicians on the day-to-day aspiration symptoms experienced by our patients. With this longitudinal data, we will move away from basing recommendations on only what can be elicited in the clinic visit and hopefully towards a more robust depiction of aerodigestive function for each patient.

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Anesthetic considerations for pediatric Drug Induced Sleep Endoscopy (DISE)

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Pediatric obstructive sleep apnea syndrome (OSAS) affects approximately 1-4% of children in the United States [(1)]. The most significant contributor of OSAS to this population is adenotonsillar hypertrophy, and the first-line treatment for pediatric OSAS is a tonsillectomy and adenoidectomy (T&A). Even after T&A is performed, 20-75% of children still have some degree of sleep-disordered breathing (SDB). Children that are less than age 3 years or greater than age 7 years, have severe OSA on their initial polysomnography (PSG), obesity, craniofacial anomalies, hypotonia, or Down syndrome are especially at risk for having residual SDB after T&A [(1)]. Polysomnography is considered the gold standard for the diagnosis of OSA, but there are many barriers to obtaining PSG in this patient population. Not every child can tolerate a PSG and the test itself can be stressful to the patient and/or the parents. PSGs can be costly and not every patient has access to a sleep center. In addition, PSG does not identify the specific site of obstruction, help direct further therapies, or predict which patients will benefit from additional surgical versus medical intervention. For these reasons, drug induced sleep endoscopy is being utilized as an additional tool to help identify and direct therapy for pediatric patients with OSAS.

Drug induced sleep endoscopy, or DISE, was first described in the United Kingdom by Croft and Pringle in 1991 [(2)]. It is essentially an "assessment of the upper airway using a flexible endoscope while patients are in a pharmacologically-induced sleep-like state" [(1)]. It uses sedative-hypnotics to simulate sleep in order to identify anatomic causes of airway obstruction, such as the tongue base, adenoids, inferior turbinates, velum, or lateral oropharyngeal walls (Figure 1). However, there may be more than a single site of obstruction. Multilevel obstruction can be as common as 97% as noted

by Atkins and his colleagues [3]. DISE has been reliably used in adults and children to diagnose the cause of OSA. It can help provide prognostic information regarding therapeutic interventions, but there is no clear DISE phenotype that predicts successful outcome after surgery [1].

There are several indications for DISE. It can be used before or after T&A to identify causes of OSA or to help diagnose sleep-dependent laryngomalacia. Before T&A, it can be helpful in evaluating children with significant sleep disordered breathing symptoms, those with OSA but without large tonsils or adenoids, and those that are at high risk for residual OSA after T&A, such as children with obesity, severe OSA, Down syndrome, craniofacial anomalies (Pierre Robin, Treacher Collins), hypotonia, or neurologic impairment [1]. Using DISE before T&A can help guide management of residual disease after T&A, but it is also possible that airway dynamics may change after T&A which may limit the usefulness of pre-T&A DISE.

From an anesthesiologist's point of view, DISE is a challenging procedure to manage. DISE is performed to look for anatomic causes of airway obstruction. These obstructions occur most frequently during REM sleep, but unfortunately there is no known anesthetic agent that replicates REM sleep [1]. In addition, while DISE requires spontaneous ventilation via a native airway it also requires a level of sedation that allows the patient to tolerate the invasive procedure. Too much sedation can cause apnea, desaturation, and need to intervene to rescue the airway. If severe, the procedure may be aborted [4]. Too little sedation can cause a false negative result or an obstruction that may not actually occur during natural sleep.

If the patient desaturates, there is no consensus on when the anesthesiologist should intervene. In many cases, it is a "judgement call" based on patient factors, the anesthesiologist's experience, and his or her comfort level in managing the patient at this lower level of oxygen saturation. It is difficult to know when or if one should intervene to improve the SpO2 knowing that any intervention could affect or invalidate the DISE results. Supplying supplemental oxygen during the study is also controversial, since even low flows of oxygen (as low as 2 L/min) can provide some continuous positive airway pressure (CPAP) and stimulate pharyngeal receptors [5]. This again can affect the DISE results. Generally speaking, most anesthesiologists would be comfortable with an oxygen saturation level of > 90% for mild OSA patients and > 85% for moderate or severe OSA patients before intervening, but again this is variable among anesthesiologists and institutions [5].

There are many different ways to evaluate a patient's depth of anesthesia. There are 4 classic stages of anesthesia first described by Guedel in 1927 [6]. Stage 1 achieves a level of analgesia in which the patient has decreased pain awareness with or without amnesia and may also have impaired consciousness. Stage 2 involves disinhibition, typically characterized by delirium, excitement, amnesia, enhanced reflexes, irregular respirations, and incontinence. Stage 3 is surgical anesthesia which involves loss of consciousness, loss of pain reflexes, regular respirations, and maintained blood pressure. Stage 4 is the deepest level of anesthesia which involves medullary depression with severe cardiovascular and respiratory depression requiring pharmacological and ventilatory support. With the advent of modern inhalational anesthetics, a new way to describe surgical anesthesia was introduced. MAC or minimum alveolar concentration refers to the alveolar concentration of anesthetic gas at which 50% of patients do not respond to a surgical stimulus [7]. It can be increased or decreased by various patient factors or pharmacological agents. Factors that increase MAC requirements include chronic alcohol abuse, infants (highest MAC requirements at age 6 months), and

hyperthermia. Factors that decrease MAC requirements include acute alcohol intoxication, very advanced age, hypothermia, anemia, hypoxemia, and severe hypotension [8]. In addition, agents such as opioids, benzodiazepines, ketamine, dexmedetomidine, and cholinesterase inhibitors can decrease MAC requirements [8].

There are several newer monitors and devices that can help guide anesthesiologists' evaluation of anesthetic depth. Though each has its own benefits and drawbacks, there are some that are more useful than others. Perhaps the most well-known and widely used monitor to help evaluate depth of anesthesia is the BIS or bispectrectal index monitor. This monitor integrates electroencephalography (EEG)-based data into a single number from 0 to 100. 0 is indicative of electrical silence, or no brain wave activity, whereas 100 is indicative of full wakefulness. It is generally accepted that a BIS of 40-60 is suitable for surgical anesthesia [9]. This monitor is applied to the forehead of an awake patient prior to induction, like the other standard ASA monitors, and monitored throughout the anesthetic. In children, it has been found that BIS is inversely proportional to end-tidal sevoflurane concentrations, but this association weakens with infants [10]. Because there are age-related differences in brain maturation and synapse formation in childhood, BIS monitors may not be as useful to monitor depth of anesthesia in children, especially infants, as it is in adults.

Because DISE involves endoscopy of the native airway during sedated REM-like sleep, it is impossible to perform the procedure with inhalational agents only. The typical anesthetic of choice involves a TIVA or total intravenous anesthetic. This can be administered with either boluses of medication, which is "fast and dirty," or with an infusion of IV medication, which is slow and controlled. With the bolus method of administration, it may be difficult to manually titrate to and maintain the desired level of sedation. It can be easy to give too much, causing apnea, desaturation, or an aborted procedure. It can also be easy to give too little, causing a prolonged procedure and possible patient discomfort. With an infusion, the variability of boluses can be avoided. In many countries, a target-controlled infusion or TCI can be used to give a precise continuous dose of IV medication to achieve a pre-calculated target plasma concentration. This requires a computer model that is developed based on pharmacokinetic parameters with the idea that drug effect is more related to plasma concentration than infusion rate. Unfortunately TCI is not available in the United States because it is not FDA approved. TCI was first submitted for premarket approval to the FDA in 1995 but the application was shifted between the drug and device centers before it was withdrawn in 2004 [11]. Because TCI is still not available in the United States, simple infusions with a set rate are typically used at the author's institution instead.

As noted previously, there is no known anesthetic agent that simulates REM sleep. However, there are some characteristics of an "ideal" anesthetic agent for DISE. An ideal agent would provide predictable anesthesia and simulate natural sleep without causing respiratory depression, cardiovascular effects, or airway collapse beyond what is seen during natural sleep [5]. In addition a predictable duration of action and smooth awakening are preferable [5]. With the pediatric population, an additional challenge is that most children undergoing a general anesthetic require an inhalational induction to tolerate IV placement. These inhalational agents decrease upper airway muscle activity and can confound DISE findings [1].

There are several anesthetic agents that are commonly used in pediatric DISE studies which we will review here. Propofol is the most well-known agent. It acts as a GABA-receptor agonist and NMDA-receptor antagonist but its mechanism of action is poorly understood [8]. It causes global central nervous system depression and respira-

tory depression. It has a rapid onset (within seconds), short duration (minutes), slow elimination half-life, and rapid extrahepatic clearance [8]. Typical induction doses can cause decreases in blood pressure, systemic vascular resistance, a slight decrease in cardiac output, and variable changes in heart rate [8]. With children, larger induction doses are needed but the dose is also rate-dependent [7]. Unfortunately, propofol can cause decreased upper airway cross-sectional area and increased obstruction at the level of the tongue base which can confound DISE results [12]. In infants, propofol causes anterior-posterior (AP) narrowing that is uniform throughout the pharyngeal airway, while in older children this decrease in cross-sectional area is seen at the epiglottis [12]. In adults, propofol administration to a BIS goal of 50-60 is associated with increased airway collapse and more complete collapse at affected sites [13].

Dexmedetomidine is a newer agent that is becoming more widely used because of its analgesic effects without causing respiratory depression. It is a selective alpha-2a adrenergic receptor agonist that acts as a sedative, anxiolytic, and analgesic without respiratory depression [8]. It replicates NREM sleep and has a moderately fast onset of approximately 4 minutes after an initial loading dose [1,8]. It has a long duration of 2-4 hours [8]. With bolus dosing, hypertension may be observed, but with an infusion, hypotension and bradycardia commonly occur [8].

Various methods of administering propofol have been attempted for DISE procedures. In 2016, Kellner and colleagues found that the level of sedation affects the degree of airway collapse [15]. Specifically, there is a dose-dependent increase in collapsibility under increasing levels of sedation. There were various areas of collapsibility noted, including the velum, uvula/palate contact to the posterior pharyngeal wall, and the tongue base. In their study, only 36 of the 50 patients could even complete the DISE evaluation with a goal BIS of 40. All the other patients desaturated to < 65% limiting the use of further sedation. In 2017, DeVito and colleagues examined target-controlled infusions (TCI) versus conventional bolus methods to see if either method was superior. In this study they found that they were better able to achieve physiologic patterns of sleep and apnea using TCI [16]. Physiologic sleep was achievable in 81% of patients versus only 30% of patients who received the conventional bolus method.

Because of the limitations of propofol-only sedation, various groups have tried other agents and regimens to find a better anesthetic for DISE exams. A study by Yoon and colleagues in 2016 examined propofol versus dexmedetomidine sedation regimens in adults undergoing DISE. They found that DISE findings were similar for both groups at all levels of sedation, but the degree of upper airway narrowing was slightly lower with dexmedetomidine [17]. In addition, they found that with propofol, more hemodynamic changes (blood pressure, heart rate) and lower saturations were observed. They concluded that there was more hemodynamic stability and less respiratory depression with dexmedetomidine. Another adult study by Cho and colleagues in 2015 examined propofol versus propofol/remifentanil versus dexmedetomidine/remifentanil regimens for DISE [18]. Remifentanil is a rapid-acting opioid that is metabolized by blood and tissue esterases; it is not dependent on liver or kidney metabolism and has a short and predictable elimination half-life [7]. Half-life is similar across all age groups and the pharmacokinetics of remifentanil are unaffected by cardiopulmonary bypass. The study by Cho and colleagues showed that there were higher rates of desaturation with propofol/remifenanil (77%) versus with dexmedetomidine/remifentanil (45%) [18]. The use of remifentanil helped reduced the patients' cough reflex. The dexmedetomidine/remifentanil combination caused less respiratory depression but was not able to provide adequate sedation for completion of the DISE procedure. Many patients in this arm

required additional propofol boluses even with the dexmedetomidine at maximum rates of 1.4 ug/kg/h.

Unfortunately there are very few studies examining anesthetic regimens for DISE in children. Many of the existing studies are in children undergoing cine MRI exams, which are another tool to identify sites of obstruction in patients with OSA. They provide a high-resolution examination of the airway during sleep and allow for identification of site(s) of airway obstruction [19]. Children with severe OSA are more likely to need an artificial airway during cine MRI if propofol is used versus dexmedetomidine [20]. In children without OSA, there are minimal dose-dependent changes to airway morphology with dexmedetomidine anesthesia [21]. In children with OSA, propofol and dexmedetomidine had similar effects on upper airway morphology but these changes were not statistically significant when upper airway dimensions were measured [22]. Finally, when Kandil and colleagues compared propofol to sevoflurane/propofol and dexmedetomidine/ketamine, they found that children in the dexmedetomidine/ketamine arm had fewer desaturations to < 85% and higher DISE completion rates than those in the other 2 arms [14].

When planning the ideal DISE anesthetic, the goals are adequate sedation, hemodynamic stability, fast onset/offset, an ability to maintain the native airway and spontaneous respirations without intervention, and an ability to simulate REM sleep [20]. In children for example, an optimal DISE anesthetic would likely involve an inhalational induction, IV placement, and transition to a TIVA anesthetic as soon as possible. As soon as the inhalational agent is turned off, a dexmedetomidine bolus can be started since it should be infused over 10 minutes. If using ketamine and glycopyrrolate, they can be given once the IV is in place. Once the dexmedetomidine bolus is complete, the continuous infusion can be started and the surgeon can proceed with the procedure.

If dexmedetomidine is not available, a low-dose propofol infusion with or without ketamine can be utilized. Propofol is fast on and fast off and is associated with reduced risk of laryngospasm. However, it is important to remember that propofol can affect the airway at multiple levels and may cause desaturation. The addition of ketamine may reduce the amount of propofol needed for the anesthetic. Ketamine is a NMDA-receptor antagonist that has sedative and analgesic properties. It has a short onset of 10-15 minutes and short duration of action of 15-30 minutes [8]. Importantly for DISE, it has a minimal effect on upper airway cross-sectional area, preserves airway reflexes, and has a minimal effect on central respiratory drive [1,12,14]. However, ketamine does cause increased secretions which can lead to laryngospasm. It also causes increases in heart rate, blood pressure, and cardiac output [8].

If an endotracheal tube is already present and DISE needs to be performed at the end of a case, there are some strategies for anesthetic management in this situation. Of course one should only extubate the patient when he/she is spontaneously breathing. Prior to extubation, ensure adequate hemodynamics, tidal volume, respiratory rate, and end-tidal CO_2. If an inhalational agent was used for the case, it should be turned off several minutes prior to extubation and the patient should be transitioned to IV agent(s). Avoiding opioids during the case is also preferable.

In summary, OSAS is very common in the pediatric population. Drug induced sleep endoscopy is a method to identify anatomic causes of obstruction, but finding the "perfect" anesthetic regimen for DISE is difficult. Based on the pediatric studies available, dexmedetomidine with or without ketamine is most likely the best option for DISE. It allows for adequate levels of anesthesia, less respiratory depression and desaturations,

and the least need for airway intervention. Going forward, it is important to develop a universally accepted anesthetic regimen so that we can interpret, report, and compare findings and optimize surgical outcomes.

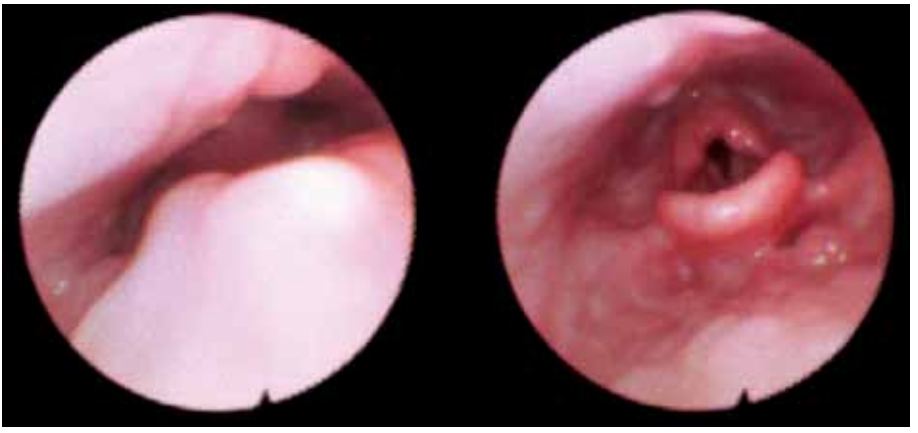

Figure 1. View during DISE without (left) and with (right) jaw thrust maneuver.

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Management of post intubation laryngitis

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Introduction

Post intubation laryngitis (PIL) is an inflammation of the larynx related to intubation, which is often accompanied by stridor, retractions, dysphonia and/or dry cough and presents itself from the time of planned extubation until hours/days after this. There is some confusion in the literature regarding nomenclature and this situation may be referred to as: post intubation laryngeal injuries, post extubation stridor, post extubation laryngitis, intubation lesions, acute laryngeal injuries. Despite the different names given to this situation, clinical evidence of obstructive upper airway symptoms following extubation are generally suspected to be caused by traumatic inflammation caused by a tracheal tube. Nevertheless, a definitive diagnosis is established through endoscopic confirmation of characteristic laryngeal lesions.

Reported occurrence rate of PIL varies from 3.5% to 30%. This wide variation reflects the heterogeneity of the study populations, individual healthcare characteristics and diagnostic criteria. PIL is associated with increased morbidity including prolonged hospital stay, risks of reintubation, prolonged use of sedation, airway trauma, nosocomial infection and development of laryngeal stenosis [(1)].

Endoscopic assessment of the airway and correct management may improve the healing process of laryngeal lesions and prevent definitive stenotic scarring of the airway.

Pathophysiology and predisposing factors

In 1969, Lindholm et al. [(2)] first reported intubation to be responsible for larynx and trachea injuries and suggested that the size and shape of the tube might contribute to these lesions.

Because of its oro-pharyngeal curvature, the endotracheal (ET) tube regularly lies in the posterior glottis and causes inflammation that can result in ischemic damage. Maximum pressure is exerted on the posterior laryngeal commissure, posterolateral circumferential subglottis and the medial aspect of the arytenoid cartilages. Edema, erosions, ulcerations with exposed perichondrium and cartilage are the main features of this evolving process [(3)]. This mechanism is reinforced by capillary hypoperfusion of the mucosa, frequently associated with severe systemic diseases that led to the patient's intubation in the first place. As reported by Hawkins, the process of an airway lesion begins slowly, with granulation tissue formation creeping from the ed-

ges of the denuded cartilage that is progressively replaced by collagen [8]. As granulation tissue grows significantly faster than the epithelium, it often leads to excess tissue that may cause airway obstruction and subsequent scarring and stenosis.

Laryngeal lesions can happen even after a short period of endotracheal intubation particularly in traumatic and difficult intubations. There is no consensus within the medical community as to the safe upper limit for the duration of intubation in children [4]. This is why knowledge of pathophysiology and recognition of these lesions through endoscopy is paramount in pediatric intensive care units.

Predisposing factors for PIL include: oversized ET tube, presence of systemic diseases, gastro-esophageal reflux, undiagnosed congenital airway narrowing, as well as faulty intubation techniques (traumatic and/or multiple intubations) particularly in the insufficiently anesthetized patient [5]. Other risk factors related to the intubation period have been suggested such as: excessive ET tube motion, poor patient sedation, traumatic nasogastric tube or ET suctions [6]. Some reports have also suggested that premature babies are more prone than older children to develop this condition [7].

Clinical assessment and diagnosis

As a rule, when planned extubation fails a second time due to presumed PIL or when dysphonia and/or stridor persists beyond 3 days after extubation endoscopic inspection of the larynx and subglottis is indicated. Endoscopic assessment may determine the degree of acute post-intubation injuries and help decide on the best treatment options and plans for elective extubation. Close interaction should be established between the pediatric intensive care unit (PICU) team and the airway surgeon for optimal outcomes in the treatment of these lesions.

One of the most frequent manifestations of PIL is failed extubation. In general, intensive care medical staff will use clinical criteria to suspect PIL when extubations fails based on the presence of: stridor, respiratory effort, cyanosis, sternal or intercostal retraction and nose wing flutter. A clinical scoring system described by Downes and Raphaely in 1975 to grade the severity of upper airway obstruction is still very practical and has been used by other authors to compare results of treatment for PIL [9]. Five component items make up the score, as can be seen in Figure 1.

	0	1	2
Inspiratory breath sounds	normal	harsh with rhonchi	Delayed
Stridor	none	inspiratory	inspiratory and expiratory
Cough	none	hoarse cry	Bark
Retractions/ nasal flaring	none	suprasternal retractions/ present	Suprasternal and intercostal/ present
Cyanosis	none	in air	In 40% oxygen

Figure 1. Downes and Raphaely Score. Total score ranging 0-10 points

If the child can be maintained extubated even if symptomatic a first endoscopic evaluation maybe performed on the bedside with flexible fiber-optic laryngoscopy (FFL). This exam can show mild lesions such as: edema, hyperemia, hemorrhage and non-obstructive laryngomalacia and also moderate to severe lesions: obstructive laryngomalacia, ulceration, laryngeal immobility and granulation of the posterior glottic or subglottic tissue. On this first examination one should take into account that the first few hours of extubation may fail to reveal subglottic edema simply because of the stenting effect of the tracheal tube. Therefore, reexamination is essential in the first 24h to 72h depending on clinical symptoms.

Recently Schweiger et al., published a very practical classification system for acute laryngeal injuries that apparently shows good correlation with clinical evolution. FFL was performed within 8 h after extubation and lesions were classified according to the CALI classification as mild, moderate or severe. Edema and hyperemia in supraglottis, glottis and/or subglottis are classified as mild lesions. Glottis uni or bilateral ulceration, arytenoid granulation tissue and/or partial ulceration in subglottis are classified as moderate lesions. Inter-arytenoid ulceration or granulation tissue, glottis immobility and/or subglottis complete ulceration and granulation tissue are considered as severe lesions. Based on the CALI, 90% of children who developed subglottic stenosis had moderate to severe injuries on the initial FFL [10].

When clinical symptoms progress or do not improve over the first 72h a microlaryngoscopy under general anesthesia should be performed. This is also the case when second extubation fails rapidly over the first minutes and the child is reintubated before a bedside FFL is performed or when the bedside FFL findings are not compatible with clinical symptoms. One must remember that bedside FFL is limited in evaluation of the subglottis.

An algorithm (Figure 2) has been suggested in the First Brazilian Clinical Consensus on Tracheostomized Children to help define the indication for endoscopic airway evaluation (EAE). Findings from a meticulous EAE may define the best therapeutic approach based also on the child's clinical condition and associated comorbidities.

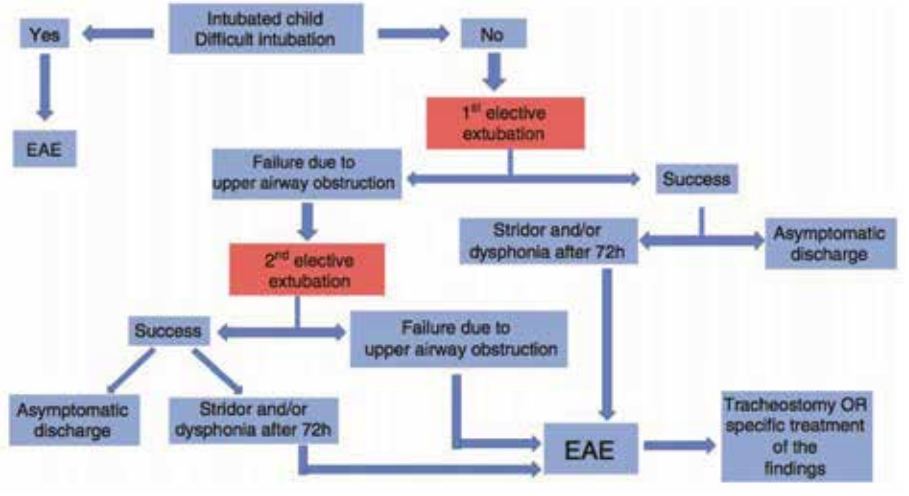

Figure 2. Flowchart indicating the need of endoscopic airway evaluation (EAE) in the intubated child.

Although infants are more tolerant to intubation than older children, an abnormally narrow larynx must always be suspected in the presence of congenital syndromic/non-syndromic anomalies or when resistance is felt while passing the ET tube through the vocal cords [5]. In this group of children an early airway endoscopic assessment may be considered.

The importance of clinical and endoscopic follow-up cannot be overstressed. The scarring process of acute laryngeal lesions may be quite unexpected since individual inflammatory reaction and scarring processes are variable and not completely unders-

tood. Clinical practice and observation have shown that most times mild lesions can be successfully treated with medical measures whereas moderate and severe lesions most probably will need endoscopic surgical treatment. Despite this, it is extremely important that parents and medical staff be aware that progressive obstruction of the airway due to scarring of acute lesions may occur up to approximately 6 weeks after extubation. Once the child is moved from intensive care unit to the ward one must not forget this possibility. Signs and symptoms of airway obstruction should be explained to the parents or caregivers and initially weekly reevaluations are suggested.

Treatment

Medical treatment modalities include use of systemic and nebulized medications, laryngeal rest and ventilatory support. Surgical modalities include removal of granulation tissue, dilation and endoscopic injection or topical application of medications. The rational for these treatments is to minimize exuberant and noticeably obstructive inflammatory reaction, maintain a patent airway and promote reepithelization of ulcerations.

Planned extubation with minimal, effortless breathing may be achieved with sedative drugs and/or noninvasive ventilation. The importance of close cooperation with the intensive care staff cannot be undermined to achieve this.

Although scientific evidence currently fails to support the use of inhaled epinephrine and corticosteroids to treat PIL, some studies and a 2009 Cochrane review have suggested a trend towards benefit [12-14]. Noninvasive ventilation has been the sole modality shown to have sufficient evidence to support its use [15].

Animal studies have shown that subglottic wound healing is significantly affected by pepsin and bile acid under acidic conditions justifying the use of acid-suppression therapy when there are glottis/subglottic lesions to prevent or reduce inflammation and subglottic stenosis [16].

This is why the suggested current protocol for suspected PIL is:
– 1-2mg/Kg/day IV dexamethasone (except if contra indicated due to clinical conditions)
– anti-acid suppression (ranitidine or proton-pump inhibitors)
– elective extubation in 48-72h with bedside FFL if tolerable.

If extubation fails, symptoms progress over the next hours or days or FFL reveals obstruction, a microlaryngoscopy should be performed under general anesthesia and maintenance of medical treatment is usually continued in the days following the procedure depending on findings and plans for extubation.

Endoscopic airway evaluation under general anesthesia

Operative direct laryngoscopy should be performed using a 0° telescope under anesthesia and spontaneous ventilation. This allows for differential or unsuspected diagnosis of other airway anomalies such as: laryngomalacia, tracheomalacia and vocal cord palsy although the later should be confirmed with an awake endoscopy. In the child who is still intubated adequate exposure of the larynx with suspension laryngoscope or the help of auxiliary surgeon should precede removal of the tracheal tube to maximize control of the airway.

The rigid telescope gives detailed imaging of the airway and working with four hands or using a suspension laryngoscope allows for examination and palpation, suction and removal of secretions and debris to grade and visualize the exact extension of

Figure 3. 3A- Endoscopic airway evaluation with a suspension laryngoscope and rigid telescope; 3B- Endoscopic airway evaluation with a rigid telescope working with four hands.

lesions (Figures 3 A and B). It is particularly important to define if there is circumferential mucosal lesion (Figure 4 A) or if there are islands of healthy mucosa between ulcerations (Figure 4 B) since these helps predict outcome [10]. The airway diameter can also be sized, particularly in the child that has been extubated but persists with symptoms. Age appropriate tubes can be used for this with the advantage of allowing intermittent ventilation while dilating or sizing if necessary.

Failed extubations may be due to clusters of granulation tissue obstructing the posterior glottis (Figure 4 C) and circumferential subglottic ulceration with granulation tissue and edema. Bilateral ulceration of the medial aspect of the arytenoids with interarytenoid fibrin bridge is the true precursor of fibrous interarytenoid adhesion [5] (Figure 4 D).

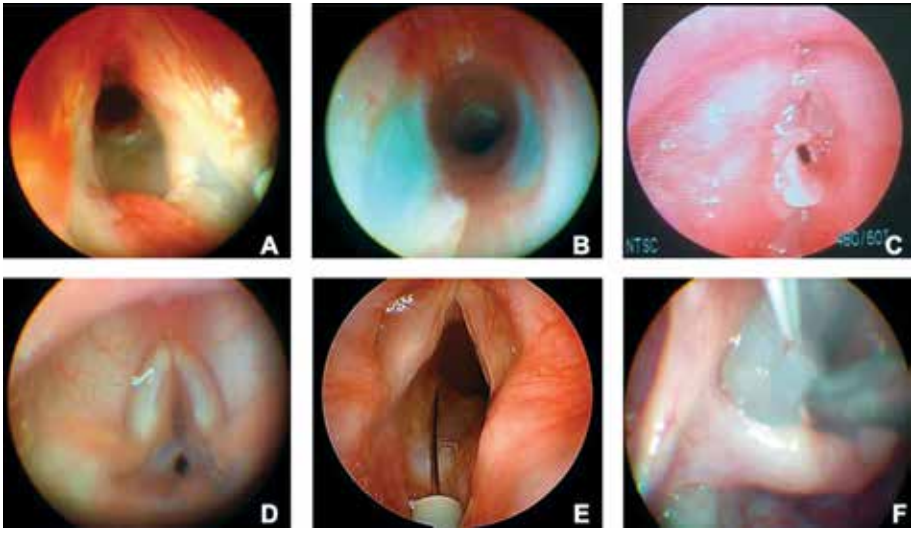

Figure 4. 4A- severe laryngeal lesions with circumferential subglottic ulceration and cartilage exposure; 4B- lateral cricoid exposure (non-circumferential subglottic ulceration); 4C- granulation tissue obstructing the posterior glottis; 4D- fibrous interarytenoid adhesion; 4E- inflammatory mucosa with corticosteroid infiltration; 4F- gentamycin-corticosteroid ointment placement around the ET tube.

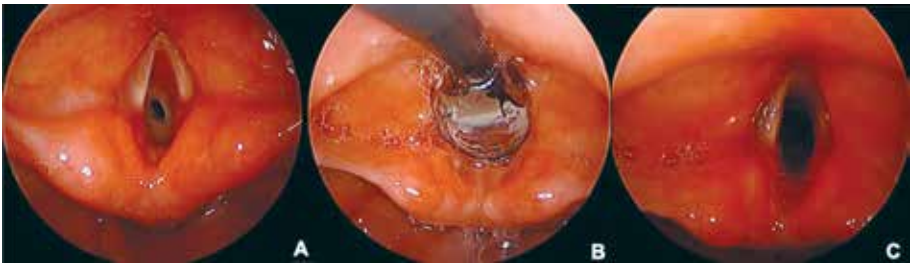

Figure 5. 5A- subglottic stenosis (20 days after extubation); 5B- airway balloon dilation; 5C- patent airway immediately after dilation.

Depending on the characteristics and intensity of the lesions, endoscopic measures are chosen following some basic principles:
– Removal of potentially obstructive granulation tissue.
– Removal of debris and fibrin from ulcerations.
– Infiltration of inflammatory mucosa with corticosteroid (triancinolone or metilprednisolone) shown in Figure 4 E.
– Securing a patent airway through dilation with age appropriate tubes or balloons (Figures 5A, 5B and 5C).
– Reintubation if needed with atraumatic nasotracheal intubation one or half a size smaller tube smeared with a gentamycin-corticosteroid ointment (Figure 4 F).

Mitomycin C (1–2 mg/ml for 2 min) can be administered topically onto granulation tissue as this delays the reepithelization process. However, it should never be applied on the denuded cartilage as it promotes necrosis by long-standing exposure of the cartilage in the subglottic lumen [5].

Endoscopic findings and prior use of systemic corticosteroids will determine the need for its further use and this should be discussed with the intensive care team. Extensive cartilage exposure may indicate the need for antibiotics since colonization by Pseudomonas aeruginosa may be an issue. Laryngotracheal cultures should be obtained to guide choice of antibiotics.

PICU staff is also asked to keep the child as comfortable as possible with sedation and minimal manipulation to promote laryngeal rest. Atraumatic pharyngeal or endotracheal tube suctions are also critical in minimizing the mucosal lesions and proper suspension of the ET tube connector to the ventilation tube, diminishes the risk of ET tube motion [5].

Systemic factors causing hypoperfusion of the mucosa (such as systemic shock, hypotension, anaemia and sepsis), gastro-oesophageal reflux or infections aggravating mucosal damage must be actively treated in order to prevent exacerbation of ET tube trauma [5].

Most patients can be extubated after a mean re-intubation period of 3–4 days after endoscopic treatment. Adrenalin aerosols (50 mg/kg in 4 ml of NaCl 0.9%), intravenous dexamethasone (2 mg/kg), continuous positive airway pressure (CPAP), and heliox when available can be delivered through a face mask. Noninvasive ventilation is particularly important overcoming this difficult post-extubation period [5] due to frequent abstinence syndrome after prolonged use of sedation drugs and weaning from ventilation.

If extubation fails again, the same treatment is repeated while the child remains intubated for a 3-day period (nasotracheal intubation) before a further extubation attempt is made. Depending on the childs' clinical conditions and symptoms presented on extubation another endoscopic assessment may be necessary to follow-up on the healing process of the acute lesions.

At this active laryngeal stage, performing a tracheostomy may worsen the laryngeal condition. Infected granulations evolve over time into contracting scars, leading to severe cicatricial sequelae. Most if not all post-intubation cicatricial sequelae of the larynx are preventable with adequate treatment administered at the acute stage. If a tracheotomy cannot be avoided despite adequate endoscopic treatment, proper tracheostomy tube placement [17] and follow-up are crucial.

When deciding for a tracheostomy one should consider: length of intubation due to failure in adapting non-invasive ventilation, comorbidities that might impact ventilation and swallowing on extubation and most importantly worsening of laryngeal injuries in sequential endoscopies. These factors should be discussed with the PICU team and with the patients' family in the decision process of a tracheostomy.

Figure 6 algorithm summarizes the proposed management of post intubation laryngitis.

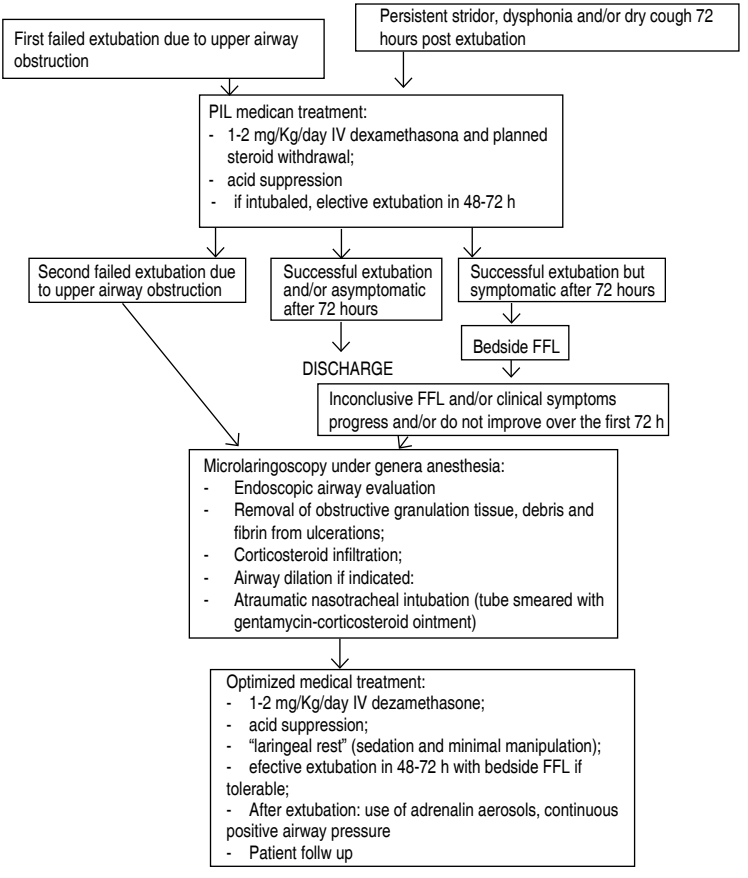

Figure 6. Flowchart summarizing how to proceed in children with post intubation laryngitis.

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Laryngomalacia: When is time for surgical treatment?

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Summary

Background: Laryngomalacia (LM) is the most common congenital anomaly of larynx that causes stridor in children. We evaluated the efficacy of epiglottic suture and laser epiglottopexy for treatment of infants with severe LM.

Methods: Surgical intervention was performed in 21 patients with severe LM, after the diagnosis was established using flexible laryngotracheobronchoscopy. Indication for surgical treatment was the presence of LM with at least one of the following: malnutrition, dysphagia or symptoms of gastroesophageal reflux and mean oxygen saturation (SaO2) <92% with oxygen desaturation index (ODI)>3.

Results: Epiglottic suture was performed in 12 patients, and laser epiglottopexy in 9, at mean age 4,7 months. Fourteen (66%) patients had recurrent cyanosis, especially during crying and feeding, and six (28%) had deformity of the chest wall (pectus excavatum). Five (24%) patients were intubated preoperatively. There was no need for

tracheotomy before the surgery. Oxygen saturation after surgery was between 95 and 99%. Oral nutrition was started immediately after removal of the endotracheal tube. Food intake was normalized in 19 (90%) children. One month after surgery, all patients gained in weight 500 grams to one kilogram. Two (9%) patients after laser epiglottopexy were still had stridor with associated dyspnea, and it was decided to redo the operation. In the second act, epiglottic suture was performed and in both cases dyspnea disappeared, with mild residual stridor

Conclusions: Epiglottic suture and laser epiglottopexy are efficient surgical techniques that lead to significant improvement of symptoms, oxygenation and nutritional status in patients with LM.

Key words: Epiglottopexy, laryngeal suture, laryngomalacia, stridor.

Introduction

Laryngomalacia (LM) is the most common congenital anomaly of larynx that causes stridor in children, and accounts for 60-75% of laryngeal anomalies [(1)]. LM typically manifests with inspiratory stridor that begins in first two years of life and resolves in most of the cases at until the age of two years [(2)].

Inspiratory stridor increases with acitivty, feeding, crying or agitation. Children with severe LM often have feeding difficulties. Feeding is prolonged and the child has to take breaks during the meal due to increased respiratory effort [(1)]. Desaturation can occur during feeding, but in more severe cases it can occur during sleep and at rest. In rare cases, due to these symptoms there is failure to thrive, episodes of upper airway obstruction and heart failure with pulmonary hypertension.

A definitive diagnosis is made with flexible nasopharyngolaryngoscopy. The hallmarks of LM are supraglottic tissue collapse and obstruction during inspiration [(3)].

McSwiney et al. have described three anatomical variations of LM: type 1- redundant bulky arytenoids that prolapse into the airway on inspiration; type 2- shortening of the aryepiglottic folds, resulting in tethering of the arytenoids to the epiglottis thereby narrowing the airway during inspiration; type 3 - elongation and lateral extension of the epiglottis (omega shape) that falls posteriorinferiorly on inspiration. Different combinations of these abnormalities may be seen as well. About 90% of cases do not require any surgical treatment, which is necessary in about 10% of cases [(2)].

We evaluated the efficacy of epiglottic suture and laser epiglottopexy for treatment of infants with severe LM.

Materials and methods

The study was conducted as a non-randomized prospective clinical study at Mother and Child Health Care Institute of Serbia. The study included 21 children, aged from two to nine months (mean 4.7 months), who were surgically treated due to severe LM from September 2014 to September 2018. All patients had pronounced stridor, failure to thrive and feeding difficulties. The diagnosis was made by pediatric and ENT examination, and confirmed with flexible laryngotracheobronchoscopy. According to the recorded findings, all patients had elongation of epiglottis (omega shape), that was falling posteriorinferiorly on inspiration. Indication for surgical treatment was the presence of LM with at least one of the following: malnutrition (body mass index [BMI] Z score < –2 SD), dysphagia or symptoms of gastroesophageal reflux and mean oxygen saturation on continuous night oxygen saturation (SaO2) trend <92% with oxygen desaturation index (ODI)>3.

Results

In our cochort 15 (72%) patients were male and 6 (28%) were female. Ten patients (47%) were born prematurely, and twelve (57%) had gastroesophageal reflux (GER). Among those diagnosed with GER, in six patients contrast gastroduodenal radiograph was done, and among the others the diagnosis was based on symptoms such as vomiting and episodes of upper airway obstruction during feeding. Fourteen (66%) patients had recurrent cyanosis, especially during crying and feeding, and six (28%) had deformity of the chest wall (pectus excavatum). The oxygen saturation at rest before surgery was between 65 and 88%. Five (24%) patients were intubated preoperatively. There was no need for tracheotomy before the surgery (Table 1).

	Epiglottic suture	Epiglottopexy
Number of patients	12	9
Oxygen saturation at rest	65% do 85%	70% do 88%
Preoperatively intubated patients	4	1
Tracheotomy	0	0
Associated anomalies	2	1

Table 1. The data before surgical interventions.

Epiglottic suture was performed in 12 (58%) patients, and laser epiglottopexy was performed in 9 (42%) patients. The first technique was epiglottic suture, aiming to correct the pathological shape of the epiglottis. It is a suture placed transversely on the lingual surface of the epiglottis that unfolds the folded epiglottis and shifts apart the adjacent aryepiglottic folds. Second technique was carbon dioxide laser epiglottopexy applied to the lingual surface of the epiglottis in a linear fashion (4-6 W continuous). (Figure 1).

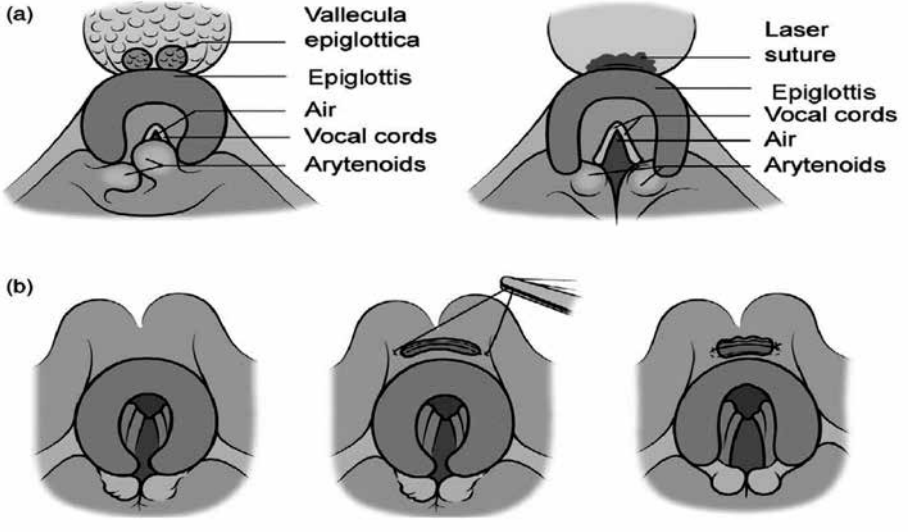

Figure 1. Schematic illustrations of (a) carbon dioxide laser epiglottopexy and (b) epiglottic suture for laryngomalacia.

Beside LM four patients had other congenital anomalies. Two children had unilateral choanal atresia, one had tracheal stenosis and Pierre-Robin syndrome, and one had congenital heart disease (tetralogy Fallot).

All surgical interventions were performed under general endotracheal anesthesia with nasal intubation, which allowed free access and surgical treatment on the epiglottis and surrounding structures, and all interventions were performed by the same surgeon. Postoperatively, the endotracheal tube was removed after four hours in nine (42%) patients, after 24 hours in 11 (52%) patients, and after seven days in one patient who developed bronchiolitis. Oxygen saturation after surgery was between 95 and 99%. Oral nutrition was started immediately after removal of the endotracheal tube. Food intake was normalized in 19 (90%) children. One month after surgery, all patients gained in weight 500 grams to one kilogram. One patient who underwent epiglottic suture after surgery developed bronchiolitis. Two (9%) patients after laser epiglottopexy were still had stridor with associated dyspnea, and it was decided to redo the operation. In the second act, epiglottic suture was performed and in both cases dyspnea disappeared, with mild residual stridor. In fourteen (66%) children, stridor disappeared after seven days, in five (24%) after one month, and in two (9%) patients mild stridor was present for another 6 months (Table 2).

	Number of patients
No stridor	14
Milder stridor	5
Aggravated stridor	2

Table 2. Stridor after seven days of surgical intervention.

After surgery, the children were in the intensive care unit for up to 24 hours after removal of the endotracheal tube. During this period, they received dexamethason and ceftriaxone parenterally. In the further course of hospitalization patients were receiving antibiotics.

The children were hospitalized for three to fourteen days after surgery (mean 5.7 days). Follow-up examinations were performed after seven days, one month, and then every three months until one year after surgery (Table 3).

	Epiglottic suture	Epiglottopexy
Extubation after		
4h	7	3
24 to 48h	4	6
7 days	1	0
Oxygen saturation at rest	95 to 97%	95 to 99%
Complications	1	2

Table 3. The data after surgical interventions.

Patients were followed up for two years after surgery, but in the second year controls were performed at six months. Control flexible endoscopic examination was performed one month after the intervention and then seven months after surgery. Within a month, the resorptive suture had disappeared and there was only a small scar on the lingual side of the epiglottis.

Discussion

Severe LM is more common in male children. In our study, 73% were boys, and in other studies the radio of boys and girls was 2:1 [4]. LM typically presents with inspiratory stridor, which can be present at birth or in the first weeks of life. A large number of our patients had dysphagia and choking episodes, and due to these symptoms, failure to thrive. According to other authors 40-58% of patients have feeding difficulty and choking episodes [2,5]. In severe LM, suprasternal and subcostal retractions can lead to pectus excavatum.

Children with LM often have GER that can be diagnosed either on the basis of clinical examination, contrast radiography or esophageal pH measurement [6,7,8]. Presumably, the negative inspiratory pressure generated in the upper respiratory tract may exacerbate GER. LM and GER may be associated because they are both the result of generally lower muscle tone in the upper airways [9]. In our study, 12 (63%) children had GER. According to the literature, GER is diagnosed in 36.4% - 75% of cases [8,10].

Diagnosis of LM is confirmed by flexible laryngotracheoscopy. Using the endoscope, we had a clear visualization of the supraglottic and glottic structures of the larynx. In order to determine the possible existence of associated anomalies, an endoscopy of the lower airways was performed as well, and one patient had tracheal stenosis that did not require additional surgical intervention. Hawkins and Clark also state that flexible laryngoscopy is very effective diagnostic procedure [11]. The advantage is that the dynamics of supraglottis can be evaluated. The disadvantage is that the mild forms of laryngomalacia can be missed due to crying. The stance on rigid endoscopy is controversial. Thus, Mancuso et al. in a study of 233 children with LM concluded that rigid endoscopy was not necessary [12]. We did not do rigid endoscopy in neither case.

Children with LM may also have other congenital anomalies that may complicate and prolong postoperative recovery. In our study, two children had unilateral choanal atresia, that was surgically resolved in the same operative act with LM. In one case, a heart defect was diagnosed that had been surgically treated a month earlier, and in one child, tracheal stenosis was present but there was no need for surgical intervention. In neurological patients with hypotonia recovery may be prolonged [5].

There are many surgical interventions for severe LM. The oldest surgical technique is tracheotomy, which is an outdated method because there are far less radical and invasive surgical techniques. Depending on the type of LM, epiglottopexy, ariepiglotoplasty, and variations of these surgical techniques are most commonly used. We performed a relatively new surgical technique, the epiglottic suture. We also used a CO_2 laser to perform epiglottopexy. Both surgical interventions have proven effective. With this research, we did not want to compare the two surgical techniques, but to present different surgical treatment modalities.

Of the total number of patients, 17 (89%) recovered after the first operation. In the study of Fajdiga et al. [13], all eight patients recovered successfully, and in the Whymark's study [14], who performed laser epiglottopexy in 76 children, 59 had a full recovery (78%). When bilateral division of ariepiglottic folds and / or excision of the mucosa is performed, the percentage of reoperation is from 4% to 17% [15, 16]. An alternative approach reduces the risk of complications, which is when one side of the larynx is operated, but then the percentage of reoperation is 15% to 50% [5, 15]. In addition, the described laser epiglottopexy and epiglottic suture reduce the risk of supraglottic stenosis in comparison to other techniques [14].

In two cases after laser epiglottopexy dyspnea and stridor persisted, so one month later we decided to redo the surgical intervention. With the laser we expanded the surface of the excised mucosa on the lingual side of the epiglottis and placed a suture on the epiglottis. The patients recovered completely. Since these were the second and third case in which we used laser surgery, it is possible that we did not remove sufficient amount of mucosal tissue on the lingual side of the epiglottis.

All patients recovered completely after the surgical procedures. Stridor disappeared completely in 89% of children within a month, which is comparable to published studies [5,17]. After removal of the endotracheal tube, oral nutrition was started and all the patients gained weight. Weight gain is one of the essential parameters for the successful surgery. Toynton et al. described prolonged postoperative recovery in children with associated neurological diseases [5].

Conclusion

Severe LM accompanied with failure to thrive, chest wall deformity, GER and episodes of clinically significant oxygen desaturations require surgical treatment. We successfully showed that epiglottic suture and laser epiglottopexy are valuable surgical procedures that provide the necessary strength and stability of the epiglottis. These procedures reduce the intensity of stridor while retaining the protective function of the epiglottis. No significant postoperative complications were noted and patients recovered completely.

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Current management of laryngomalacia

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Definition

Laryngomalacia is defined as the collapse of the supraglottic structures during inhalation, typically manifesting as inspiratory stridor, resembling the sound of a seal or a Canadian goose [1].

Laryngomalacia is the most common congenital anomaly of the larynx affecting 60 to 70% of children with congenital anomalies of the upper aerodigestive tract [2].

Its etiology remains unclear. However, hypotonia and the lack of neuromuscular control of the cartilaginous structures and laryngeal soft tissue due to immaturity or abnormal integration of the peripheral nerves, brainstem nuclei and pathways for swallowing and maintenance of airway patency for breathing are currently the most widely accepted hypotheses [3,4]. Inspiratory stridor is usually not seen at birth but becomes evident only after a few weeks with a progressively higher pitch until becoming more marked between 6 and 12 weeks, and slowly diminishes thereafter until disappearing at 18-24 months (Diagram 1).

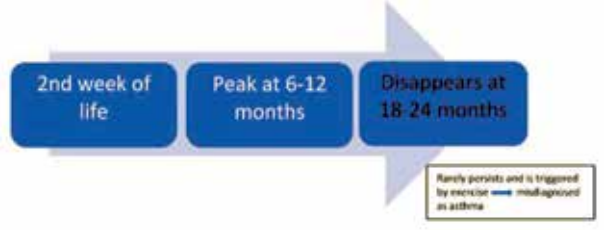


Diagram 1. Natural history.

Diagnosis

Evaluation of laryngomalacia is initiated with a good anamnesis, including questions regarding the stridor: whether it is inspiratory, expiratory, or biphasic; at what moment it appeared; and its behavior during sleep, crying, physical activity and feeding. Similarly, it should be investigated if stridor improves at any moment or in a certain position and if weight gain or breathing patterns when awake and during sleep are compromised. Prenatal and current history of the patient should be taken into account. In Table 1 Holinger's mnemonic for the evaluation of an infant with stridor is shown [3,5].

S	Severity	Caregiver's perception of severity and stridor pattern
P	Progression	Changes over time
E	Eating	Weight gain, feeding difficulties, failure to thrive
C	Cyanosis	Apparent life-threatening events
S	Sleep	Relationship between sleep and obstructive symptoms
R	Radiology	Findings on imaging studies, if performed.

Table 1. Holinger's mnemonic for the evaluation of an infant with stridor [5].

Inspiratory stridor that is characteristic of laryngomalacia typically worsens during crying, feeding, agitation, in the supine position, and during upper respiratory tract infections. It usually improves with neck extension and in the prone position. Most cases are mild or moderate, while between 5 and 10% are severe, associated with poor weight gain, bradycardia, tachypnea, cyanosis, dyspnea, difficulty breathing or hypoxemia, apnea, pulmonary hypertension, and cor pulmonale.

In the physical examination, weight and length, whether stridor is inspiratory or expiratory, and respiratory rate should be assessed and symptoms of breathing difficulties, such as nasal flaring and intercostal retractions, should be identified. In addition, anomalies such as pectus excavatum should be taken into account and auscultation of the neck and lung fields should always be performed.

The diagnosis of laryngomalacia is confirmed by flexible fiberoptic laryngoscopy in the awake patient in a supine position to dynamically visualize the supraglottis and identify structural characteristics as shown in Table 2.

1.	Airway edema.
2.	Erythema.
3.	Anatomical structure of the larynx.
4.	Laryngeal movements.
5.	Posterior rotation of the epiglottis and anterior rotation of the arytenoids.
6.	Areas of collapse of the supraglottis.
7.	Signs of gastroesophageal reflux.

Table 2. Features to evaluate on flexible laryngoscopy.

Exploration of the airway by rigid bronchoscopy is indicated when a clear diagnosis cannot be made or if the patient requires supraglottoplasty.

Classification

The traditional laryngomalacia classifications by Dr. Holinger [5] (Diagrama 2) or Dr. Monnier are useful and still valid. Nevertheless, on occasions they may be confusing due to the high incidence of combined types of collapse that may present in the same patient.

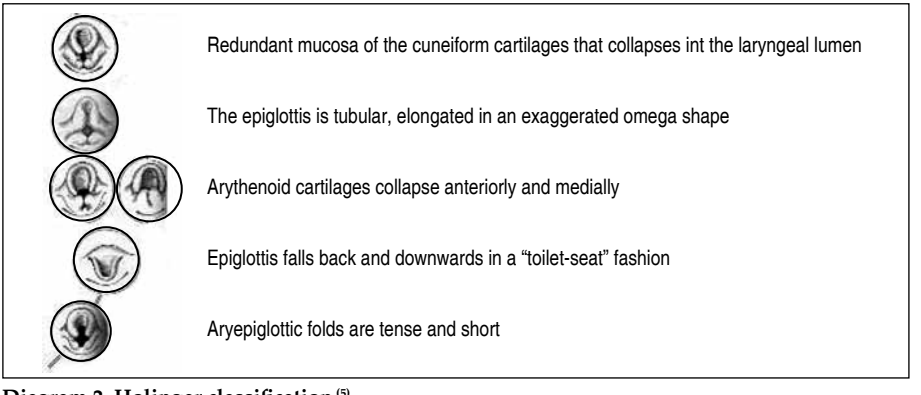


Diagram 2. Holinger classification [5].

Doubtlessly, the classifications are useful in the decision-making process for the treatment planning. Therefore, currently the Groningen classification is used6, providing a simplified list (Table 3) consisting of three types based on the dynamic changes of the larynx. For each type of collapse a different surgical approach is proposed.

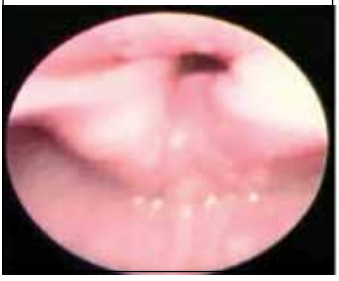
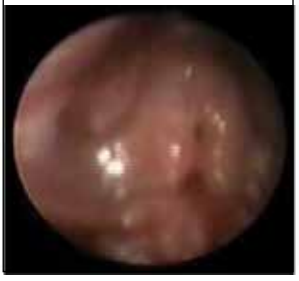
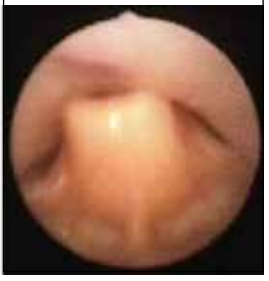
TYPE 1 Inward collapse of arytenoid cartilages	TYPE 2 Medial displacement of aryepiglottic folds	TYPE 3 Posterocaudal displacement of epiglottis against the posterior pharyngeal wall
		

Table 3. Groningen classification [6].

Differential diagnoses

Correct diagnosis is important for the adequate management of this condition, as inspiratory stridor is most often associated with laryngomalacia. Differential diagnoses, such as aryepiglottic or vallecular cyst, which may be life-threatening, or other, less aggressive, conditions, such as gastroesophageal reflux, should be taken into account.

Similarly, up to 40% of the patients with laryngomalacia may have synchronous lesions of the airway (SLA), Table 4, that should always be considered and may be diagnosed using flexible laryngoscopy or even rigid bronchoscopy. This latter tool should be preserved for those cases in which no clear diagnosis can be made.

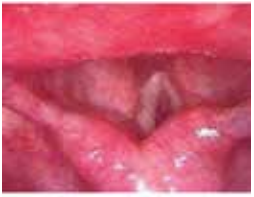
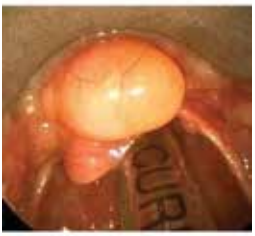
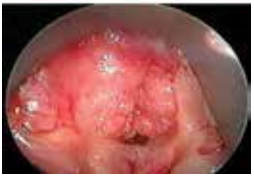
Lesion	Image	Lesion	Image
Tracheomalacia/ vascular rings		Vocal fold paralysis	
Vallecular cyst		Laryngeal papillomatosis	
Tracheal stenosis			

Table 4. Synchronous airway lesions.

Treatment

Treatment should mainly be focused on symptom severity (Diagram 3).

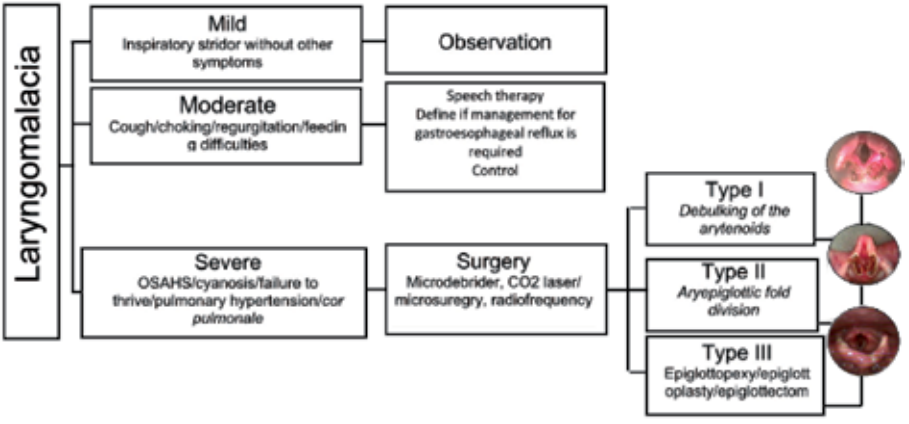


Diagram 3. Treatment algorithm for laryngomalacia.

In patients with laryngomalacia, the majority of symptoms resolve with conservative treatment and only require observation with adequate control of weight gain and development of severe symptoms [7,8].

Patients with laryngomalacia who also present with cough, choking, regurgitation, or feeding difficulties, management of comorbidities, such as gastroesophageal reflux, and evaluation by a speech therapist may be required [7].

Between 10 and 15% of the patients may have severe symptoms requiring surgical intervention. These are the patients with apnea, cyanosis, failure to thrive, pulmonary hypertension, or *cor pulmonale* in whom rigid laryngobronchoscopy should be considered and, according to the findings, supraglottoplasty may have to be performed [7].

Management of gastroesophageal reflux is controversial. Although the estimated prevalence is 65% in severe cases [9], currently no clear evidence exists on the association between gastroesophageal reflux and laryngomalacia. Reports on adverse effects of antireflux medication have been increasing [10]; therefore, treatment should be reserved for patients with confirmed disease.

Surgical management

For laryngomalacia the Holinger classification is commonly used and is currently still valid. Nevertheless, at the time of surgical treatment this classification causes some difficulties due to the possible combination of different types of collapse.

As mentioned above, the Groningen classification is a "new" system based mainly on the dynamic changes of the larynx that facilitates decision-making in surgical management. The Groningen classification divides laryngomalacia into three types [11]: 1. Inward collapse of arytenoid cartilages; 2. Medial displacement of aryepiglottic folds; and 3. Posterocaudal displacement of epiglottis against the posterior pharyngeal wall. The surgical approach according to this classification is as proposed in Table 5.

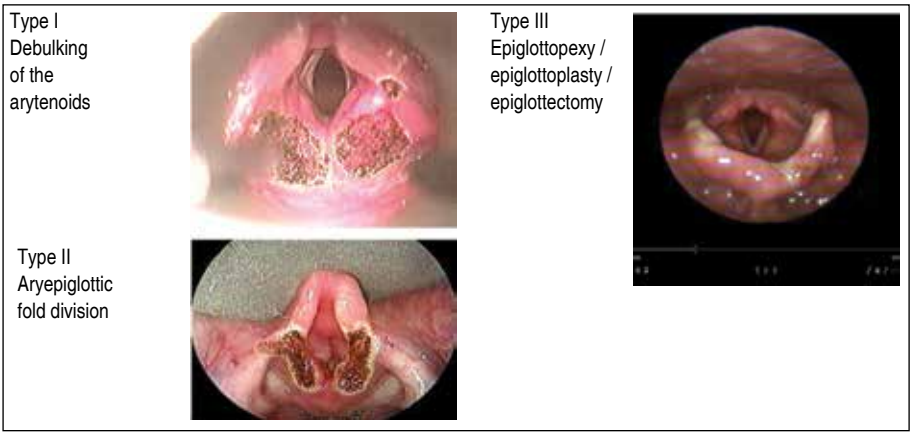


Table 5. Surgical approach.

Regarding the different surgical instruments, similar success rates have been reported for cold steel, CO_2 laser, and microdebriders. The experience of the surgeon and familiarity with the different instruments should guide decision-making in each particular case.

Surgeons that use CO2 laser advocate its hemostatic properties; however, the technique requires a longer time to prepare the patient, has a high cost, a risk of airway fire, and may cause thermal injury leading to increased postoperative edema, pain, and dysphagia [12].

When using cold steel, hemostasis is generally achieved with topical vasoconstrictors, such as epinephrine or oxymetazoline [12], and secondary effects in the immediate postoperative period are less.

Finally, microdebriders may be used as a surgical alternative, with the advantage that suction is provided, which clears blood and tissue from the surgical field, thereby improving visualization and reducing the risk of injury to the epiglottis and arytenoids [12] (Table 6).

Surgical instruments	Advantages	Disadvantages
CO_2 laser	Hemostasis	High cost Risk of airway fire Thermal injury Use of a special endotracheal tube
Cold steel	Low cost No thermal injury	Hemostasis
Microdebriders	Better visualization because of suction	High cost Hemostasis

Table 6. Advantages and disadvantages of surgical instruments.

Nevertheless, regardless of the technique or instruments used, there is solid evidence that supraglottoplasty is highly effective in the treatment of laringomalacia[13]. On

the other hand, tracheostomy, although rarely indicated, should always be considered as an extreme measure [3].

Complications of supraglottoplasty are uncommon. In the majority of series, the incidence rate is less than 10%. Possible long-term complications associated with supraglottoplasty include aspiration, supraglottic stenosis, injury to the laryngeal cartilage, airway fire, and granuloma formation [12].

Surgical failure is considered when no improvement of the symptoms is achieved or when symptoms recur [3]. Therefore, close postoperative follow-up is required to determine if the disease is definitively controlled or if it will persist in time.

Conclusions

Laryngomalacia is a common condition that resolves in the majority of cases without the need for additional treatment. The diagnosis should always be confirmed by flexible laryngoscopy in the awake patient. Synchronous lesions of the airway and comorbidities are associated with a worse outcome and should therefore be taken into account at the time of diagnosis and in the treatment. Anti-reflux medication should only be given when gastroesophageal reflux is definitively confirmed. Surgical management is indicated in patients with severe laryngomalacia associated with failure to thrive, severe apneic spells, or cyanosis. Supraglottoplasty has been shown to have excellent results with success rates higher than 90% [12]. Nevertheless, careful patient selection is warranted as results are generally not good in patients with CHARGE syndrome [14].

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Laryngomalacia: What is this and how to treat it?

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Introduction

Laryngomalacia (LM) is the most common congenital laryngeal anomaly, and the most common source of stridor in newborns. The definition of LM is the cyclic inward inspiratory collapse of supraglottic structures (Figure 1).

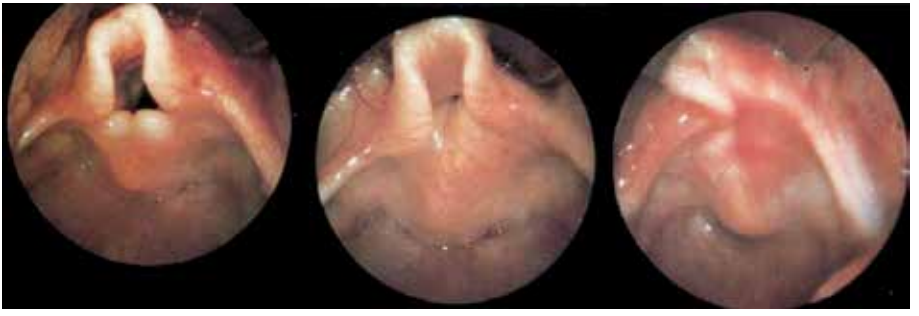

Figure 1. Laryngomalacia.

Laryngeal stridor

Stridor is a symptom, not a specific disease state; is the most prominent characteristic of obstructed airway in children. Stridor could be inspiratory, expiratory or biphasic, according on to its location and abnormality in the airway. Correct management of stridor can only be adequate after the precise diagnosis of its cause.

Epidemiology of stridor

The relative incidence of stridor causes does not vary widely regardless of where the data comes from. In infants, the main causes of stridor are congenital laryngeal abnormalities [1-4] and the most frequent is LM (Table 1).

Alteração	Lubianca (n=125)	Holinger (n= 219)
LM	58%	60%
Subglottis stenosis	19%	20%
Vocal fold paralysis	12%	13%
Other	11%	7%
Total	100%	100%

Table 1. Causes of stridor in children under 30 months of age in two otorhinolaryngological series [1,5].

Estridor evaluation

Most children may not present stridor in the first hours of life. If the stridor is present at birth, the cause usually is fixed obstruction (for example, laryngeal web and/or congenital subglottic stenosis). Commonly, LM associated stridor appears slowly in the second week of life or in exacerbation periods (feeding, crying, decubitus) causing dyspnea, cyanosis or apnea. However, there are cases of LM where the stridor is already present at birth.

Patient evaluation requires complete details of stridor, as appearance in the respiratory cycle, onset date, characteristic, intensity, aggravating and relief factors, progression and complications (for example, feeding difficulties, failure to thrive, cyanosis and sleep disturbances) [6]. Inspiratory stridor is typically associated with extra-thoracic obstruction and is originated by the collapse of laryngeal structures, resulting from the negative pressure created in the thorax by the inspiration movement. Expiratory stridor is typically of intra-thoracic obstruction and byphasic stridor denotes a fixed obstruction (for example, subglottic stenosis). The parents' subjective impression of the severity of the obstruction must be taken into account. Instantaneous or acutely progressive events are usually associated with infections or foreign bodies. Severe recurrent cases of "laryngitis" can hide subglottic stenosis and / or gastroesophageal reflux. The slowest progress, but with increasing severity, can be seen in cases of large papillomatosis and subglottic hemangiomas. Cases that present feeding difficulties, with or without aspiration, leading to failure to thrive, denote the need for intervention. Respiratory cyanosis is always a sign of severity and need for intervention. Another feature that means severity is breathing difficulty that persists and impairs sleep. Finally, cases in which previous imaging studies show pulmonary, cardiac or large vessel malformations, required immediate attention and evaluation under general anesthesia (Table 2).

Awake X Sleeping:
-Obstruction that worsens in sleep is pharyngeal (exception: laryngeal papillomatosis
-Especially tonsils
-Obstruction that worsens on vigil is laryngeal, tracheal or bronchial
-Exacerbated by exercise
Inspiratory X Expiratory:
-Inspiratory obstruction is extrathoracic:
-Occasionally nasal or pharyngeal
-Usually laryngeal
-Laryngomalacia
-Bilateral vocal fold paralysis
-Expiratory obstruction is intrathoracic:
-Mimic asthma
-Tracheal or bronchial
-tracheo/bronchialmalacia
-vascular ring, extrinsic compression

Table 2. Parameters to characterize respiratory obstruction (adapted from [7]).

Endoscopic examination is essential, since it determines the exact cause of the symptom, in addition to excluding other airway lesions. Around 30% of patients with stridor referred to the ENT by the non-specialist with a presumptive diagnosis have different disease from that for which they are being treated [8].

No other exam, such as fluoroscopy, barium esophagogram or lateral neck radiogram, is as definitive and enlightening as endoscopy [9].

Some authors advocate that in-office nasofibropharyngolaryngoscopy is sufficient and safe to diagnose the majority of patients with stridor with an extrathoracic characteristic without signs of severity, reserving the operating room exams for cases in which the initial findings are insufficient to explain the severity of the stridor or for those with history and presentation suggestive of intrathoracic injury [10]. On the other hand, there are those who prefer to initiate assessing the airway globally under general

anesthesia. These are supported by the chance of having a synchronous lesion in the airway in up to 37% of the cases, which can be undiagnosed by the nasofibropharyngolaryngoscopy in the office [1,11,12].

Laryngomalacia

Epidemiology

The prevalence of LM described on literature is widely variable (19.4 to 75%), regarding the criteria utilized in different studies and different Airway Centers [13,14]. LM accounts for approximately 60% of all congenital laryngeal anomalies. Boys are affected twice as often as girls. Although usually a self-limiting condition, in rare cases it can lead to obstructive apnea, dyspnea, cor pulmonale and failure to thrive [15].

Pathogenesis

LM is an enigmatic disease in which laryngeal tone is weak, resulting in dynamic prolapse of tissue into the larynx. The exact etiology is still unknown and remains a field of interest and research. There are three different theories proposed to explain LM pathogenesis: anatomic, cartilagineous and neurologic. Anatomic theory proposes the existence of redundant supraglottic soft tissue that prolapses causing stridor, associated with shortening of aryepiglottic folds when compared to other chlidren. The challenge in proving that this theory is the presence of anatomical findings similar to LM in asymtomatic children [16, 17]. In 1897, proposed a "cartilagineous theory" based on the study of 18 cases of laryngeal obstruction, relating LM with chondral immaturity [18]. Other authors failed to histologically prove this theory [19].

The weak laryngeal tone seen in LM could be more appropriately explained by the injuried neuromuscular support in the pharyngolaryngeal structures. Sensorimotor integrative function of the brainstem and peripheral reflexes are responsible for laryngeal tone and airway patency. In 2007, Dana Thompson showed in that this integrative function is altered in LM, and the degree of alteration correlates with disease severity. This indicates that factors that alter the peripheral and central responses of the Laryngeal Adductor Reflex have a role in the etiology of signs and symptoms of LM. According to this theory, laryngomalacia could be regarded as a laryngeal hypotonia [20].

Definition and diagnosis

The definition of LM was first published in 1942 [21] when it was described as the inward colapse of supraglottic structures on inspiration. Before that, congenital laryngeal diseases causing stridor were described as one group of "Congenital Laryngeal Stridor" [22]. Neverthless, other diagnosis cannot be ruled out without investigation.

It is mandatory to the pediatrician to distinguish LM from other conditions leading to noisy breathing. It is not rare cases of LM to be treated as asthma, bronchiolitis or tracheomalacia before the correct diagnosis is made.

A high pitched fluttering inspiratory stridor is the hallmark of LM. Usually, the course of the disease is self-limiting, with onset around the age of 2-4 weeks and progression to a culminating point at 6 – 8 weeks. The complete resolution usually occurs around 18 – 24 months. Diagnosis is usually made before the 4th month. Feeding difficulties, regurgitation, recurrent vomiting, occasional coughing or choking are seen in moderate to severe cases. Other severe symptoms are apnea, significant respiratory distress, and failure to thrive.

A complete physical examination of the infant must be done. A full birth history is necessary, including any surgical procedures or intubations the patient has undergone.

Parents should provide information about breathing difficulties noted in the home, focusing on noisy breathing or episodes of apnea. Noisy breathing that seems to worsen with feeding, crying or while supine is suspicious for LM.

Although it is controversial, some authors suggest a polysomnogram to quantify the presence and degree of obstructive sleep apnea occurring in a patient with LM, especially in older children; this is sometimes described as sleep-exclusive LM and has an incidence of approximately 4% [23]. In some cases, it could explain the persistent sleep apnea after adenotonsillectomy.

Proper evaluation of the patient with suspected LM requires an assessment of the supraglottic airway with flexible laryngoscopy. In mild cases (seen in 80-90% of this infants) the only diagnostic confirmation required is an awake transnasal fibreoptic laryngoscopy conducted in the outpatient clinic. If the examiner notes severe symptoms, the procedure must be a bronchoscopy in the operating room.

Flexible fiberoptic laryngoscopy is currently the gold standard for diagnosis LM due to the ability to assess the dynamic airway during awake respiration. For this to be possible, the patient should not be in deep sedation during anesthesia.

Infants with LM are often found to have shortened aryepiglottic folds that tether the epiglottis posteriorly, an omega-shaped epiglottis, and/or redundant arytenoid tissue that prolapses over the glottis (Figure 2). The Hollinger classification distinguishes five types of LM [7] and describes the various mechanical anomalies, but is not easy applicable in clinical practice.

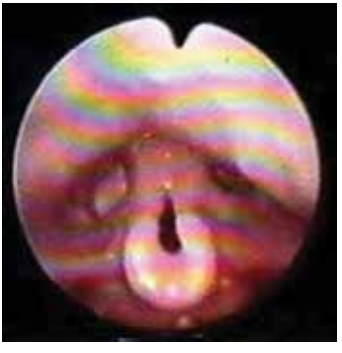

Figure 2. Nasofibrolaryngoscopy showing exacerbation of omega-shaped epiglottis and shortened aryepiglottic folds, preventing the vocal cord visualization.

Comorbidities

Gastroesophageal reflux disease:

The prevalence of Gastroesophageal Reflux Disease (GERD) in children with LM is described in literature as 65 to 100% [24,25]. Gastroesophageal reflux induces a posterior laryngitis and respiratory effort leads to a negative intrathoracic pressure that may also induce or worse the GERD. It is difficult to determine what comes first in this cycle of obstruction, GERD and edema, then the evidence for a causal association is limited.

In 2006, Suskind et al. described that GERD may result in decreased laryngopharyngeal sensitivity, which may contribute to pediatric swallowing dysfunction. Control of GERD, either by medical or surgical intervention, may improve swallowing function [26].

Hadfield PJ et al. compared gastroesophageal reflux rates in children in the pre- and postoperative period of supraglottoplasty and demonstrated a significantly improve in the reflux when it is relieved the obstruction in the airway [27].

On the other hand, if there is evidence that supraglottoplasty relieves GERD, there is also evidence demonstrating that the clinical treatment of GERD is effective in reducing the symptoms of LM [24]. Actually, is consensus that GERD should be treated in all patients with LM and feeding symptoms. There are no controlled studies demonstrating what would be the most effective treatment regimen for GERD in patients with LM. Usually hydrogen bomb blockers or H2 blockers and prokinetic agents are used. In children with moderate to severe disease, complementary studies (esophagogram, videofluoroscopy, and 24-hour pH-metry) may be useful for assessing prognosis and management. Depending on the results of these studies, complementary drug treatment or even fundoplication can be chosen.

Neurological disease:

Neurological disease is present from 20% to 45% of LM infants and include epilepsy, hypotonia, development delay, cerebral paralysis, Chiari malformation. Patients with associated neurological diseases need surgical procedure more frequently than patients with isolated LM [24]. Neuromuscular hypotonia also leads to musculature collapse with worsening of respiratory symptoms. These patients will commonly show more severe symptoms and for an extended time. Some of these may not solve their clinical condition despite supraglottoplasty. These patients will probably need tracheostomy.

Secondary or synchronic airway injures:

Synchronic airway injures incidence varies from 7.5% to 64% [24]. Tracheomalacia is the more common associated injury, followed by subglottic stenosis. These injuries have a cumulative effect on airway obstruction. Airway obstruction caused by LM combined with other injury can lead to a larger intrathoracic negative pressure. These negative pressure boosts gastroesophageal and laryngopharyngeal reflux, increasing symptoms severity [24]. Infants with mild to moderate disease associated with another airway injury present 4.8 times more chances to be submitted to surgical procedure [28]. The correct diagnosis of other injuries can lead to early intervention and affect disease progression. Similarly, LM surgery also reduce effects of other injuries in the airway.

Congenital heart diseases:

The congenital heart diseases occur in about 10% of infants with LM. These infants normally present moderate to serious diseases. Airway obstruction worsens cardiovascular function already compromised. Up to 34% of these kids will need surgical treatment to LM [20].

Congenital anomalies / syndromes:

Occur from 8 to 20% in LM cases [24]. This incidence can reach up to 40% of the infant with serious disease who need surgery. Infant with congenital anomalies commonly present other comorbidities which compromise oxygenation and breath, getting worse any degree of respiratory obstruction. These infants show a success fee lower when compared to infant with isolated LM [29]. Some of these patients, especially those with heart or neurological associated disease, will need tracheostomy.

Infants with LM and syndromes associated with micrognathia, for instance CHARGE (coloboma, heart disease, choanal atresia, delayed growth and development, hypoplasia of the genitals, anomalies of the ear / deafness) and Pierre Robin, present a poor

surgical prognosis. The retropositioned tongue base causes posterior epiglottis collapse, and the isolated supraglottoplasty is not efficient to correct. In some cases, these patients are submitted to tracheostomy until they solve their micrognathia by growth or other surgical intervention, for instance, mandibular distraction. Failure rates and tracheostomy requirement are higher in syndromic patients. In our department, we tend to correct the laryngomalacia and indicate the mandibular distraction precociously, as soon as possible (with days or few weeks of life).

Surgical treatment

Most patients are managed conservatively [3] and present resolution of symptoms by 2 years of age. About 10% to 20%, relative incidence depending on the casuistic described, may require surgical treatment for their symptoms. The surgery is indicated in children with apparent life-threating events, severe feeding difficulties, failure to thrive, cor pulmonale, pectus excavatum, respiratory distress (with significant neck and/or chest retractions), sleep apnea, cianosis and needed oral intubation. The surgical treatment is supraglottoplasty (with cold knife or laser) and should be individualized to the patient's laryngeal abnormality, then the technique could consist in excising shortened aryepiglottic folds, removing redundant arytenoid mucosa, performing an epiglottopexy, or a combination of these. Very uncommonly, children may require tracheostomy. Our results showed that supraglottoplasty is an efficient and safe procedure for severe LM in the great majority of the patients, with worst results associated with presence of comorbidities (cardiac, neurological, craniofacial) and pharyngomalacia [29].

Final considerations

Stridor is a symptom and not a diagnosis. It can be inspiratory, expiratory or biphasic, according to its location and anormality present in the airway. In infants, main stridor causes are laryngeal abnormalities. LM, vocal fold paralysis and subglottic stenosis are the most common.

Even in the cases with presumptive clinical diagnosis, it is mandatory the identification of the cause of the stridor as well as the associated comorbidities, through direct endoscopic visualization. This is the best way to diagnose and plan the treatment.

Clinical evaluation of patients with stridor requires complete symptom detailing. The inspiratory stridor is characteristic of extra thoracic injuries and the expiratory is characteristic of intrathoracic injuries. Subglottic abnormalities usually presents with biphasic stridor.

LM is the most common congenital laryngeal anomaly. Symptomatology is characterized by inspiratory stridor, which initiates around the age of 2-weeks and worse after agitation, crying and feeding. The clinical course is normally benign and symptom resolution occurs up to 18 months, usually opting for conservative treatment. However, severe cases should be treated surgically, through supraglotoplasty.

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Laryngomalacia: Supraglottoplasty and swallowing dysfunction

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Introduction

Laryngomalacia is the most common cause of childhood stridor and is estimated to have an incidence of 1 in 2100-2600 infants [1-4]. Stridor experienced with laryngomalacia is often described as a high-pitched, musical, or harsh sound. It occurs during inspiration and is caused by turbulent airflow due to dynamic airway collapse at the level of the supraglottis [1]. Laryngomalacia was thought to be more common in males, however more recent data suggest an more even gender distribution [1,2]. Symptoms

present commonly within the first month of life as intermittent stridor which may be exacerbated with feeding ("Feeding Variant Laryngomalacia" FVL), sleeping ("Sleep Variant Laryngomalacia" SVL), increased respiratory rate, forced inspiration, or supine positioning. Without intervention, symptoms will become more notable during the second four months of age (4-8 months) and improve in the following four months (8-12 months). Resolution is generally noted by 18-24 months [1,3,5].

Diagnosis

Laryngomalacia is diagnosed through history of illness and physical examination and confirmed by fiberoptic flexible laryngoscopy. Flexible laryngoscopy will often note a so-called "omega" shaped epiglottis (the epiglottis with lateral edges curled posteriorly toward the airway), and shortened aryepiglottic folds which exacerbate dynamic collapse of the supraglottis during inspiration. Excessive supraarytenoid soft tissue can also be noted and may prolapse into the airway with inspiration [1-3]. Of note, vocal fold movement should be evaluated to rule out vocal cord dysfunction as a possible cause of stridor or respiratory complaints. If parents note cyanosis with stridor, pulse oximetry should be used to rule out desaturation events. Polysomnography (PSG) may be considered when apneic events are noted or suspected during sleep or for patients who fail surgical intervention [5]. PSG can help to objectively measure the degree of obstruction cause by laryngomalacia. Genetic studies are not part of the standard workup but may be considered if there is concern that the laryngomalacia is part of a systemic or syndromic condition. Neck and chest radiographs may be used to rule out other tracheal or subglottic pathologies and to assess for underlying lung pathology [5].

Etiology

There are several theories used to describe the etiology of laryngomalacia. One postulates an abnormal laxity of the laryngeal cartilages leads to dynamic collapse. This theory does not account for cases in which the larynx has the endoscopic appearance of classic laryngomalacia, with a curled epiglottis and prolapsing tissues, but no clinical signs or symptoms of laryngomalacia. In fact, up to 50% of normal infants may have an "omega" shaped epiglottis [4]. The most accepted theory of etiology is the neurogenic theory of laryngomalacia [3,6]. The laryngeal adductor reflex (LAR) is a vagally mediated reflex activated by mechanoreceptors and chemoreceptors of the superior laryngeal nerve in the aryepiglottic fold [2,6]. Stimulation of these receptors sends afferent signals to brainstem nuclei responsible for regulation of respiration and swallowing. This in turn causes an involuntary efferent response via the vagus nerve causing vocal fold adduction and a swallow. The efferent response also impacts laryngeal tone. Laryngopharyngeal sensory testing (LPST), in which a specific amount and duration of pressure are applied to the aryepiglottic fold, demonstrates higher pressure thresholds for LAR stimulation in patients with laryngomalacia, supporting the theory of impaired laryngeal tone and sensorimotor coordination in affected patients [6]. The pressure thresholds for patients decreases over time, consistent with the natural history of disease including resolution by 24 months.

Severity of disease

Laryngomalacia can be categorized based on laryngoscopic appearance (the Olney classification) or based on the severity of the presenting symptoms. The Olney laryngoscopic classification categorizes laryngomalacia into three types [3]. Type 1 involves

solely foreshortened or tight aryepiglottic folds. Type 2 involves the addition of redundant tissue in the supraglottis which may or may not prolapse into the airway. Type 3 adds posterior inspiratory epiglottic collapse. The Olney classification does not directly correlate with degree of symptomatology or severity but does delineate the number of sites involved in the disease process. Another classification mechanism categorizes laryngomalacia based on symptom severity. In this classification, mild laryngomalacia is defined by inspiratory stridor without any other symptoms. Moderate laryngomalacia is characterized by stridor associated with feeding symptoms such as coughing, choking, regurgitation, or any other feeding difficulties. Severe laryngomalacia involves stridor with significant respiratory symptoms, such as apneas, cyanosis, pulmonary hypertension, cor pulmonale, pectus excavatum, or failure to thrive [2,3].

The severity of laryngomalacia has a direct impact on treatment options and optimal management. Mild laryngomalacia, which encompasses approximately 40% of all affected infants, is generally treated expectantly with monitoring, including growth assessments, and routine symptoms checks. Most cases of moderate laryngomalacia, making up another 40% of cases, do not require surgical intervention. Some children with moderate laryngomalacia may benefit from the use of gastric acid suppressing medications such as proton pump inhibitors (PPI), or histamine 2 (H2) blockers if there are any signs or symptoms of reflux. Despite a lack of clinical evidence confirming a causal relationship between gastroesophageal reflux disease and laryngomalacia, a link has long been suspected, and active management of reflux is standard practice for children with more severe laryngomalacia [2,5,7,8]. Some practitioners advise prophylactic medication even without reflux symptoms. While no standardized treatment protocol exists, many advocate for initiation of either a PPI or H2 blocker with escalation to dual acid suppression for persistent symptoms and de-escalation with a wean over several weeks for improved symptoms [5]. Severe laryngomalacia represents the remaining 20% of infants, and often requires surgical treatment.

Surgical treatment

Surgical intervention should initially involve operative laryngoscopy and bronchoscopy to rule out secondary airway lesions, and a supraglottoplasty performed at that time. The most commonly reported synchronous airway lesions are subglottic stenosis and tracheomalacia [2-4]. Epiglottopexy can also be considered if significant epiglottic prolapse is noted. If a secondary proximal airway lesion is suspected (ex. adenoid hypertrophy, pharyngomalacia), or severe SVL is noted, a drug induced sleep endoscopy (DISE) can be considered.

Supraglottoplasty involves a range of procedural steps to alleviate laryngomalacia. At its simplest, it involves division of tight aryepiglottic folds to release tethering and open up the supraglottic inlet. Further steps may be taken to trim redundant tissue from the region of the arytenoids. Supraglottoplasty including arytenoid reduction can be done with a variety of techniques including cold steel, microdebrider, CO2 laser, or coblator [9,10]. The cold steel technique is most commonly used as it is efficient, low cost, and lacks risk of thermal injury or airway fire inherent to other techniques. The patient is placed in a "sniffing position" with a ventilating laryngoscope. The procedure can be done with intermittent apnea, utilizing the laryngoscope for insufflation, intermittent intubation when needed, or even with an endotracheal tube in place, though this limits the exposure and mobility of instruments and tissues. An operating microscope is often utilized. Division of the aryepiglottic fold is done by grasping the arytenoid tissue and holding tension while dividing the fold down to the level

of the false vocal fold. This typically demonstrates an immediate visible release. To remove redundant arytenoid tissue, bulky mucosa is removed taking care to avoid injury to the arytenoid cartilage, false vocal fold, or medial surface of the arytenoid in order to prevent poor healing or scarring. If epiglottic prolapse is not improved after aryepiglottic fold division or persistent prolapse with glottic obstruction is present, an epiglottopexy can be performed during the same surgical procedure or in a staged fashion. To suspend the epiglottis anteriorly, tissue can be removed from the lingual epiglottic surface and tongue base to promote scarring and/or with a suture through the epiglottis and tongue base.

As with other endoscopic laryngoscopy procedures, the area must be topicalized with lidocaine prior to intervention to avoid laryngospasm, and judicious application of topical hemostatic agents such as oxymetazoline or adrenaline is often necessary to prevent and control airway bleeding. Risks include those inherent to airway endoscopy, including airway fire when laser or cautery is used, failure to improve patient symptoms, acute respiratory compromise including need for intubation, infection, and, rarely, worsening of symptoms from development of granulation or supraglottic scar tissue. Following surgical intervention, the child is monitored in the hospital to ensure continued airway safety, particularly in the immediate post-operative period when swelling may occur [2-4,11]. Steroids are routinely administered in the post-operative period [4,9,10]. While some endoscopists advocate overnight intubation following supraglottoplasty, this is typically not necessary for children without other risk factors for airway compromise [9,11]. Some evidence suggests there may be transient dysphagia after supraglottoplasty, but larger studies note patients with normal swallow function preoperatively do not have an increased risk of aspiration after the procedure [4,8,12].

Supraglottoplasty, although frequently successful, may not result in full resolution of symptoms, and patients may require a revision procedure, tracheostomy, or further airway intervention. Studies have shown patient age less than 2 months and medical comorbidities are significant risk factors for both revision supraglottoplasty and tracheostomy [4,12,13]. Patients with Down syndrome typically do well after supraglottoplasty if no coexisting cardiac or neurologic disease is present, while those with laryngomalacia in the setting of syndromes associated with retrognathia such as CHARGE syndrome or Pierre Robin sequence have worse outcomes due to persistent tongue base collapse [2,13]. Patients with other medical comorbidities are more likely to be diagnosed with laryngomalacia at a later age than otherwise healthy children, 6 months versus 2 months in one study [14]. Among patients with neurological comorbidities, 70% required revision surgery and 60% required tracheostomy, while patients with cardiac comorbidities have a tracheostomy rate of 30% [3,4,14].

Feeding variant laryngomalacia

Feeding variant laryngomalacia, present primarily with or exacerbated by feeding, requires a workup of both abnormal respiration and deglutition. Common symptoms of FVL include choking or coughing with feeds, emesis, "wet" cough, and inefficient feeds [4,15]. While the true prevalence of pediatric dysphagia is unknown, upper airway obstruction, including that of laryngomalacia, can affect the swallow-suck-breathe sequence. The overall incidence of feeding disorders in developmentally normal children is 25-45% but up to 80% in developmentally impaired children [16]. One series found silent aspiration in 98% of all patients with aspiration noted on modified barium swallow examination [15].

Feeding in the infant involves a complex coordination of oral, pharyngeal, and esophageal movements to transport nutrition to the gastrointestinal tract [1]. The movement involves coordination of a sucking motion, followed by a swallowing motion, and finally a full breath. In a normal swallow, epiglottic tilt and closure allows safe passage of the food bolus to the esophageal inlet, followed by opening of the laryngeal inlet and inspiration once the bolus has cleared the hypopharynx. Laryngomalacia is frequently identified in patients with swallow dysfunction, with feeding difficulty in up to 86% of patients [17]. Feeding difficulty is a common complaint in patients with laryngomalacia, second only to stridor [17].

Several factors predispose patients with laryngomalacia to dysphagia. The increased work of breathing and negative pressure of inspiration inherent with laryngomalacia cause increased negative intrathoracic pressure leading to gastroesophageal reflux and can lead to laryngeal penetration or aspiration. In addition, abnormal laryngeal adductor reflex (LAR) thresholds in patients with laryngomalacia predisposes to aspiration as these patients require increased pressures to initiate the LAR, resulting in increased episodes of aspiration from improper laryngeal closure [4,6,12,15].

A principal outcome of FVL workup is the identification of aspiration. Chronic aspiration can reduce lung function and predispose patients to recurrent pneumonia, bronchiectasis, and other long-term pathology [1,2,12-14,16]. The International Pediatric Otolaryngology Group (IPOG) Laryngomalacia consensus statement recommends chest radiograph followed by functional endoscopic examination of swallowing (FEES) or video fluoroscopic swallow study (VFSS) for any children with suspected aspiration [5]. The incidence of penetration and aspiration in children with severe laryngomalacia is extremely high, with studies reporting up to 88% and 72%, respectively, on preoperative FEES [12].

Assessment of dysphagia

When discussing dysphagia, there may be abnormalities in any phase of the swallowing process. Assessments of safe swallowing require any identification of aspiration, as this puts patients at risk for recurrent pulmonary infection and tracheobronchial inflammation. Laryngeal penetration, defined as the passage of bolus material into the laryngeal vestibule but above the vocal cords, is separated from aspiration, or the passage of material below the vocal cords into the trachea [6].

The workup for FVL differs from that of standard laryngomalacia in that an objective measure of swallowing is a critical component of the assessment. Clinical evaluation of swallowing, often referred to as a bedside swallow exam, is done by a speech language pathologist assessing a patient swallow various consistencies while watching for any signs or symptoms of aspiration. This assessment is fast, cost-effective, and does not involve radiation exposure. While a bedside swallow examination may identify overt signs or symptoms of aspiration (cough, desaturations with feeds, etc.), it cannot identify silent aspiration and cannot delineate aspiration and penetration. The sensitivity of bedside exam for assessing aspiration is less than 50%, and an instrumental assessment of swallowing is typically needed [6,8,17,18].

Instrumental assessment of swallowing

Two methods exist for instrumental evaluation of swallowing. A functional endoscopic evaluation of swallowing, or FEES, involves direct visualization of the larynx via flexible laryngoscopy performed with simultaneous feeding. FEES can be performed with breast milk, formula, or other liquids and foods of varying consistency. The food

items or patient secretions are dyed to allow improved visualization during endoscopy. Typically, an otolaryngologist performs the flexible endoscopy while a speech language pathologist performs the swallowing assessment and modifications.

If FEES is not possible due to anatomic anomalies, poor visualization, or patient compliance, a video fluoroscopic swallow study (VFSS, also termed modified barium swallow), may be performed. A VFSS may also provide information that is distinct or complementary to that of a FEES. A VFSS involves the patient swallowing various consistencies of barium-impregnated food items while fluoroscopy is performed of the upper GI tract. The exam requires a trained radiology technician to take the films, a radiologist to interpret the images, and a speech language pathologist to administer the food items.

Both objective measures of swallowing function have benefits and limitations [1,12,15,16]. A FEES exam allows direct visualization of anatomy with the laryngoscope allowing simultaneous evaluation of laryngomalacia or other anatomic pathology. A VFSS allows some visualization of anatomy, but not to the extent or viewpoint needed to assess for laryngomalacia. FEES also allows some assessment of a patient's own secretion management and sensation as the camera tip can be used to gently touch mucosa to observe response. In a FEES study, a "whiteout" occurs when the bolus passes over the camera, creating a time period on exam when no visualization is possible. A FEES also cannot assess the oral or esophageal phases of swallowing [9]. It also relies on the compliance of a patient to tolerate flexible laryngoscopy as patients struggling to calm or cooperate with the endoscopic exam may refuse to feed and may have increased work of breathing due to agitation. A VFSS eliminates the need to cooperate with endoscopic exam but requires a child to accept some amount of oral intake. VFSS allows for evaluation of the oral and esophageal phases of swallowing. Some centers will include a formal esophagram at the time of VFSS, allowing further anatomic assessment of possible esophageal pathology.

Exclusively breastfed infants pose a particular challenge when assessing objective measures of dysphagia. A VFSS is not possible in the breastfed infant as the bolus is not radiopaque and cannot be mixed with barium as can formula. While expressed milk can be used, it relies on acceptance of a bottle and cannot be used to modify feeding techniques during breastfeeding. Infants that refuse to accept a bottle nipple can still be assessed with FEES [16]. In this instance, food dye is added to the patient's mouth to help dye secretions and the expressed breastmilk. A breastfeeding FEES does not allow for adjustments in bolus consistency, but positioning and pacing techniques can be assessed.

For patients with significant dysphagia, additional assessments of the GI tract may be necessary. If esophageal motility concerns exist, such as achalasia or delayed gastric emptying, an esophagram or gastric emptying study can be performed. Signs or symptoms of refractory reflux may warrant a pH probe study to quantify reflux events. If central neurological anomalies are suspected, such as a Chiari malformation causing brainstem compression with vagal nerve impingement, an MRI may be used to fully evaluate the central nervous system [12-14,16].

Feeding modifications

Poor weight gain is a common problem with laryngomalacia and one of the factors delineating severity of disease. The poor weight gain is often from a combination of the increased caloric demand from work of breathing plus feeding difficulties. Prior to considering surgery, it is reasonable to consider other tactics for increased caloric

intake including high calorie formulas and consultation with a speech language pathologist for feeding techniques [3].

Feeding modifications can be done to improve or eliminate aspiration, including adjustments to patient position and bolus transit (via thickening or utensil modification) [4]. Positioning, pacing (either with adjustments to nipple flow or with monitored breaks in feeding by caregiver), and thickened feeds can all be done during a FEES or VFSS. The American Speech-Language-Hearing Association notes videofluoroscopy can be utilized to evaluate the effectiveness of postures, maneuvers, and bolus modifications in improving both swallow safety and efficiency [18]. For children with severe dysphagia in whom no oral diet is deemed safe, alternate nutrition and hydration via nasogastric or gastrostomy tube may be recommended.

Surgical intervention for feeding variant laryngomalacia

While conservative measures such as those described above may be sufficient to improve dysphagia symptoms, a proportion of children will have difficulty with feeding despite modification. A variety of symptoms may be noted in FVL including choking during feeding, dysphagia, aspiration, worsened respiratory status including stridor with feeding, and failure to thrive. Failure to thrive, along with severe or worsening respiratory symptoms including apparent life-threatening events, are the most commonly cited reasons to perform supraglottoplasty [9]. Resolution of both respiratory and feeding complaints after SGP has been shown in over 90% of patients [12,15]. Stridor improves sooner than feeding symptoms, which may last for months after supraglottoplasty [4]. As with respiratory symptoms, there are a subset of children with FVL who will have persistent dysphagia following supraglottoplasty. In particular, prematurity and neurologic disorders are risk factors for persistent dysphagia [8].

Summary

Laryngomalacia is the most common congenital anomaly of the larynx and the most common cause of stridor in newborns. Laryngomalacia is believed to be a neurologically mediated process, caused by an abnormal laryngeal adductor reflex. The diagnosis is made clinically and confirmed via flexible laryngoscopy. Mild and moderate laryngomalacia can often be managed expectantly, sometimes with inclusion of reflux therapy, as patients typically outgrow symptoms by 18-24 months of life. For those with severe symptoms, supraglottoplasty is a relatively straightforward procedure with high success rates. Patients with dysphagia related to laryngomalacia have significant benefit from supraglottoplasty. Caregivers of patients with multiple medical comorbidities including cardiac, genetic, and neurologic anomalies must be counseled on a higher rate of surgical failure.

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Laryngeal web: Diagnosis and treatment

Melissa Ameloti Gomes Avelino, MD, PhD and **Stela Oliveira Rodrigues**, MD.

Introduction

Laryngeal webs are rare congenital abnormalities that occur because of a failure in recanalization of the primitive larynx (that should occur between weeks eight and ten during embryogenesis). It can be considered the third of the three types of laryngeal atresia, described first by Smith and Bain [1]. The membrane is formed with mesodermal elements and the abnormal fibrous tissue is mostly common localized at the level of the glottis, extending across the anterior one third of the vocal folds, or extending varying degrees toward the posterior glottis and inferior to the subglottis [2,3].

Epidemiology

Laryngeal webs are rare and account for 5% of congenital laryngeal anomalies. Other congenital malformations may occur simultaneously such as congenital subglottic stenosis, trachea-esophageal fistulas and some syndromes (Fraser, fetal alcohol syndrome, cartilage hair hypoplasia, DiGeorge, CATCH22, duodenal atresia). Although a gene has not been identified as the cause of this malformation, the association with 22q11 microdeletion makes genetic investigation and counseling imperative, because approximately 65% of the patients presenting laryngeal web have Velocardiofacial syndrome (that is most frequently due to this variation) [3,4].

Classification

Traditionally laryngeal webs are classified in four subtypes proposed by Cohen (Figure 1).

– Type I membranes account for less than 35% of glottic involvement, are usually thin and do not extend to the subglottic region;
– Type II webs (Figures 2 and 3) although still thin or moderately thick have a 35% to 50% glottis involvement;

– Type III webs (Figure 4) have a 50% to 75% glottic involvement, are thick and potentially have a cartilaginous involvement of the adjacent subglottic region;
– Type IV webs (Figure 5) are uniformly thick and involve from 75-90% of the glottis area with cartilaginous subglottic extension [1,2].

It is important to point out that in all types of web, an additional subglottic stenotic lesion may possibly occur, regardless of the web itself (and probably due to a defect in cricoid development) [5].

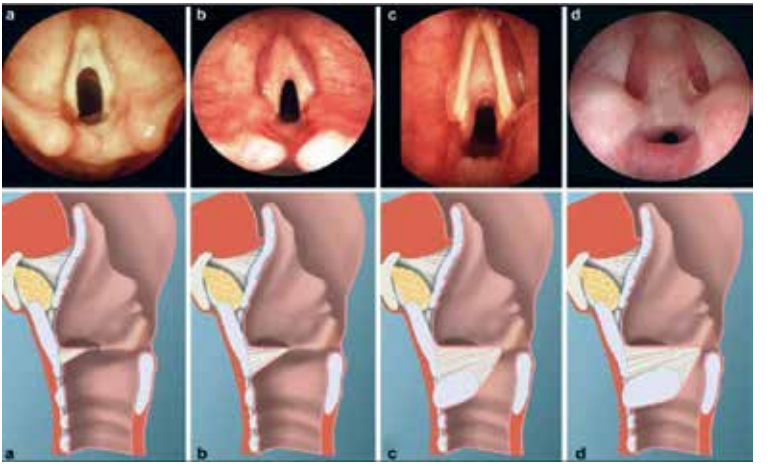

Figure 1. A. Laryngeal web type I, B. type II, C. type III, D. type IV [8].

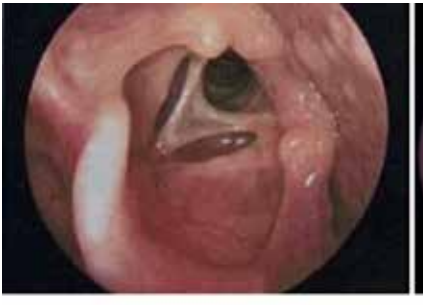

Figure 2. Laryngeal web type II.

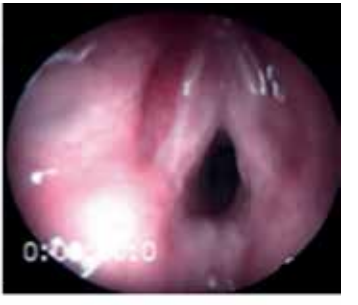

Figure 3. Laryngeal web type II.

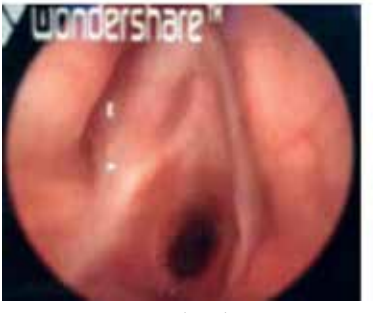

Figure 4. Laryngeal web type III.

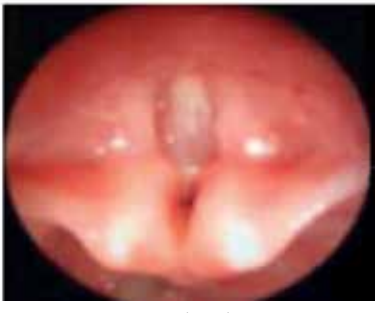

Figure 5. Laryngeal web type IV.

Clinical manifestation

Clinical manifestations vary according to the extent of glottis involvement and obstruction. More than 80% of the patients will show some symptom in the neonatal period. The most common symptoms observed are dysphonic crying and stridor (which may be biphasic or only inspiratory). Shorter webs account for dysphonia perceived as a weak cry and may also be the cause of respiratory distress depending on the degree of the obstruction or during upper airway infections. In types III and IV webs respiratory distress is usually noticeable since birth [6,7]. However, signs like recurrent croup (and at an atypical age) or episodic cyanosis may occur, with even individuals reaching asymptomatic adulthood [2].

The symptoms can be more frequently seen in the different types of web, as described below [8] (Table 1):

Type	Symptoms
I	Mild hoarseness, with no airway symptoms.
II	Weak husky cry, mild airway symptoms
III	Very weak voice, moderate airway symptoms
IV	Aphonia, severe airway symptoms with usually the need of a tracheotomy

Table 1. Symptoms of laryngeal webs.

Diagnosis

Dysphonia at birth may always raise suspicion towards laryngeal webs. Newborns with dysphonia and/or respiratory distress should be submitted to a nasalfibroscopy and this can make the diagnosis of a laryngeal web [1]. Nevertheless, microlaryngoscopy and bronchoscopy (MLB) under general anesthesia is imperative to evaluate the extension of the web to the subglottic area, size the airway with appropriate endotracheal tubes and search for other concomitant airway anomalies [2].

Imaging exams, such as computed tomography, may provide craniocaudal membrane extension, but by MLB it is possible to classify the types of congenital laryngeal webs [6].

The velocardiofacial syndrome, also known as DiGeorge syndrome or Shprintzen syndrome, is tested through fluorescent in situ hybridization (FISH) or direct sequencing [3].

Treatment

Not all patients with laryngeal web will need a surgical intervention. If the voice commitment is minimal and there is no respiratory discomfort, the patient can be followed only in observation [8]. But if needed, surgical treatment will depend on the extent of the web. In types III and IV webs a tracheostomy may be necessary as an emergency measure to assure the airway during the first days and/or months. Due to perioperative risks and technical difficulties of operating on a small airway, definite surgical treatment is not advised systematically before 6-12 months of age [9].

Endoscopic surgery with web incision with cold instruments or laser is very popular treatment choices particularly if there is no subglottic extension (as in types I and II). Nevertheless, there is potential for synechia formation at the anterior commissure [6,7].

The challenge for endoscopic cases is to avoid the anterior synechia. Some authors suggest the use of keels in endoscopic cases to avoid this problem, but the use of them

should be treated with caution in small children since respiratory insufficiency and scarring of the glottis area can occur [1].

The experience of our group and another Tertiary Hospital (UNICAMP) presented in the First World Congress of Pediatric ENT is to have better results when we used the LT-mold. Its triangular shape helps support the anterior commissure and expands the subglottic area at the same time during reepithelization. Although other materials and stents may be adapted, particularly in the small airway, the use of a smooth stent that perfectly fits the shape of an infant's larynx should help prevent secondary granulation tissue and scarring [1] (Figure 6).

Sztanó et al. described an endoscopic approach for a recurrent laryngeal web using CO2 laser to divide the web and Mytomycin C and a laryngeal stent to prevent synechia [10]. However, there is no consensus on how long the stent should be left in place [10].

If the web is thick or has a subglottic stenosis associated with it, an open procedure - anterior laryngectomy - is recommended. In some cases, cartilage graft (such as costal cartilage) is necessary anteriorly and/or posteriorly. The use of the costal graft is important in order to expand the airway when we have subglottic involvement [10] (Figure 7). The need of posterior graft occurs when the interarytenoid distance is markedly narrow due to the cricoid deformity [8]. Sometimes a tracheotomy is needed altogether. The tube or another kind of mold is necessary to prevent the formation of synechia [10]. As we have already discussed in regards to endoscopic surgeries, the use of a mold is important as to avoid anterior synechia, and again our best results are cases in which we have used the LT-mold. The difficulty is that the LT-mold is not available for commercialization nowadays.

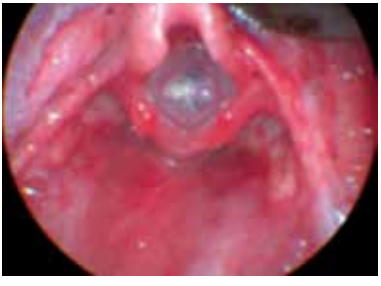

Figure 6. LT-Mold.

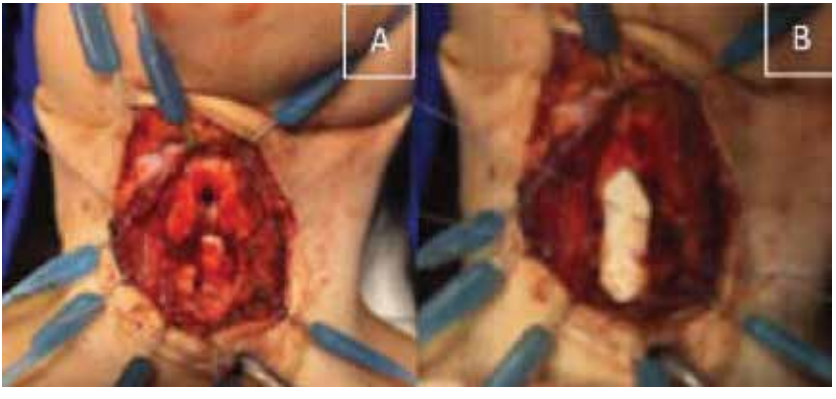

Figure 7. A. Posterior cartilage graft, B. Anterior cartilage graft.

Prognosis

Successful treatment should involve a patently functional airway and a satisfactory voice quality. Patients with type III and IV laryngeal webs are at greater risk for poor voice quality due to extensive glottic involvement and associated subglottic malformation [1].

In the study presented at the First World Congress of Pediatric ENT, we showed a series of six cases conducted in two tertiary centers in Brazil, with surgical treatments using LT-Molds kindly provided by Prof Dr. Philippe Monnier. In all cases, it was possible to decannulate and obtain good vocal quality, without anterior synechia.

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Airway hemangiomas

Cláudia Schweiger, MD, PhD, and **Denise Manica**, MD, PhD.

Introduction

The infantile hemangioma (IH) is a proliferative vascular tumor consisting of endothelial cells. Roughly 60% are found at the head and neck, holding the position as the most frequent pediatric tumor at this site.

Head and neck hemangiomas may be found in the airway and assume life-threatening presentations. The subglottic hemangioma (SGH) comprises approximately 1.5% of all laryngeal congenital anomalies and it is more common in female patients (2-3:1).

Clinical manifestations

Similarly to cutaneous forms, airway hemangiomas can be focal or segmental (also called diffuse). Airway segmental lesions are associated with segmental cutaneous lesions distributed along the mandible and chin (beard distribution – Figure 1). Therefore, concomitant lesions at the beard region should be kept in mind during evaluation because the total volume of the segmental laryngeal hemangioma is usually larger than the focal type, thus clinical manifestations and even response to therapy may present differently.

A recent study from Pittsburgh, from 2018 (McCormick et al.), performed at a Vascular Anomaly Center, included 761 patients evaluated at the center from 2013 to 2017 and showed that 13 patients presented a SGH (1.7% of their patients). Only 4 of them (30%) had an associated beard distribution hemangioma. On the other side, 31 patients presented facial hemangiomas in a beard distribution; of these, only 4 (13%) had a SGH as well. It means that a facial hemangioma should raise the suspicious of subglottic hemangioma in a child with symptoms of airway obstruction, not in all children. Mean time from the first signs of stridor to diagnosis was approximately 3 weeks.

The association between SGH and a beard distribution cutaneous hemangioma seems to be more frequent in patients with PHACE syndrome (posterior fossa defects, hemangiomas, cerebrovascular arterial anomalies, cardiovascular anomalies including coarctation of the aorta, and eye anomalies).

Generally, airway hemangiomas are not symptomatic at birth, developing symptoms as the tumor proliferates. At 6 months, around 80-90% will become symptomatically evident, mainly due to laryngeal lesions, that present with stridor and respiratory dysfunction usually because of subglottic compromise. Oral cavity and pharyngeal lesions do not frequently cause respiratory disturbance.

SGH symptoms (biphasic stridor and whooping cough) are frequently worsened by upper airway infection and may be misdiagnosed as acute laryngitis. As both diseases can show satisfactory responses to nebulized adrenaline and systemic steroids, it is not uncommon to present a significant diagnostic delay. Awareness is therefore essential and investigation should be warranted in patients with recurrent and persistent croup-like symptoms and in those with a progressively worsening of stridor. SGH should be the first hypothesis while evaluating a child with a clinical laryngeal disorder picture while presenting hemangiomas at the beard region.

Hemangiomas have a proliferative phase which is characterized by a fast growth in the first 3 to 5 months of life, that extends until 6 to 12 months. It is followed by an involutive phase that has a variable progression and a slow resolution of symptoms. Besides, growth of the child over time allows the airway to better accommodate the hemangioma, resulting in diminished frequency and severity of symptoms. The pathogenesis is not completely understood although the most accepted mechanism is that circulating endothelial progenitor cells migrate and find some favorable places to grow into placenta-like tissues.

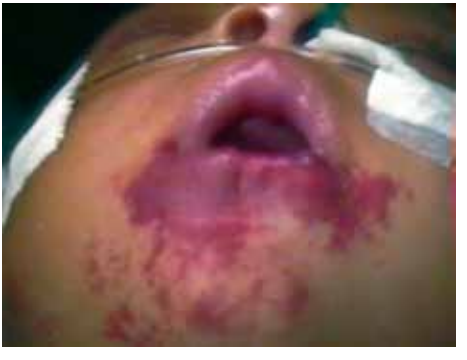

Figure 1. Beard distribution cutaneous hemangioma.

Diagnosis

Endoscopy under general anesthesia with spontaneous ventilations is gold-standard for the diagnosis of airway hemangioma. On examination, the presence of hemangioma can be confirmed, the degree of obstruction can be evaluated and other stridor-associated airway conditions can be excluded (Diagram 1).

The typical aspect of a hemangioma is a pink or blue lesion, often with surface teleangiectasias (Figure 2). It is more commonly found on the left side of subglottis. Palpation is an important tool for evaluation: hemangiomas tend to be very smooth, compressible, presenting differently from other lesions (e.g. fibrotic stenosis). It is, however, important to be very cautious when manipulating the airway as touching it can elicit an undesirable and dangerous edema. Lesion biopsy is usually unnecessary. However, when the diagnosis is not obvious, specimens from true hemangiomas stain positively for GLUT 1 (glucose transporter protein isoform 1) on immunohistochemistry examination.

Other diagnostic approaches may also be used. Magnetic resonance imaging (MRI) can help in some cases but it requires, unfortunately, a relatively long length of general anesthesia to be performed. On the other hand, computed tomography (CT) scan with angiography requires no patient anesthesia, although there is inherent radiation exposure. Anyway, in most situations a thorough and good quality endoscopic examination should obviate the need for any additional imaging exam.

A staging system for airway IHs has been proposed by Perkins et al. Its usage has not been widely accepted however due to the lack of correlation with treatment results or prognosis stratification.

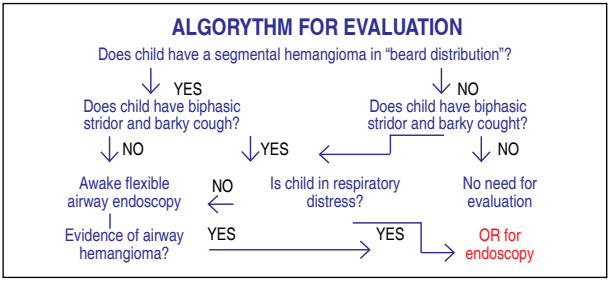

Diagram 1. David Darrow's algorithm for evaluation of a hemangioma.

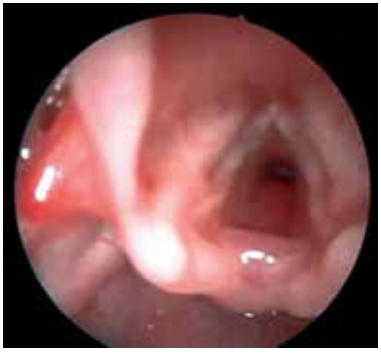

Figure 2. Subglottic hemangioma.

Treatment

Once diagnosis is established, it is important to ascertain an adequate timing and type of intervention. When considering which therapeutic approach, one should always recall that SGH is a self-limited condition and long-term airway sequelae should be systematically avoided.

Treatment options include observation, pharmacologic management, endoscopic and open surgical approach.

Observation is an acceptable approach when patients are minimally symptomatic. They should be closely followed up for obstructive symptoms especially in the first months of life.

Concerning the pharmacologic approach, propranolol holds the first line of treatment since 2008. Contraindications to use of the drug include cardiogenic shock, sinus bradycardia, hypotension, heart block greater than first degree, heart failure, bronchial asthma, and known hypersensitivity to the drug. Usually, drug is initiated at 1-2 mg/kg/day divided in 2 to 3 doses a day and then increased to 2-3 m/kg/day. Treatment is generally maintained through the first year of life.

McCormick et al. showed that from 4 patients presenting with subglottic hemangioma and in the beard region, two have failed therapy with propranolol (both with concomitant PHACE syndrome), while only 1 of 9 patients with subglottic hemangioma and no beard region lesions have failed the same approach. Beard region hemangioma (especially in the context of PHACE syndrome) has therefore been recognized as a risk factor for propranolol failure.

Corticosteroids act mainly on proliferative phase and have an important role in refractory patients and for obstructive lesions, where a combined approach with propranolol could be used for a faster response. For patients under propranolol therapy, steroids can also be prescribed to acutely decrease the edema of the airway in the event of respiratory infection. Steroids act mainly on proliferative phase. Doses of 2-3 mg/kg/day are generally necessary for 1 to 2 weeks before tapering. They should be used for the shortest period possible due to significant inherent adverse events. Alfa-interferon has also been described for refractory cases.

Due to advances in drug therapy, surgical treatment is currently only exceptionally required. It should be considered an option when obstruction is severe enough to prompt intubation for a long period until medications could exert a clinically significant effect, or when the patient remains symptomatic despite of optimal pharmacologic management.

Surgical treatment can be performed endoscopically or by an open surgical approach. Intralesional steroid injection is an endoscopic procedure that usually requires postoperative intubation. Laser treatment has been the most popular endoscopic surgical modality. It has been associated with a recurrence risk of subglottic stenosis ranging from 5% to 25%, more often seem with deeper resections and bilateral or circumferential disease. Debulking with microdebrider or shaver has also been attempted. Open surgery is of greatest advantage in patients with bilateral or circumferential lesions, precisely those with a major risk of recurrence upon endoscopic approach. It is more complex to implement however in those cases with extra-laryngeal compromise and can eventually lead to some degree of dysphonia.

An alternative to those with a severe respiratory compromise, precluding the lesion manipulation, is tracheostomy. Adequate care and associated risks should be taken

into account when considering this approach. Nevertheless, it can be a timely alternative in centers that do not have a pediatric airway management team.

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Current management of infantile hemangiomas

Christopher Liu, MD.

Infantile hemangiomas are one of the most common benign tumors of infancy—affecting approximately 4-5% of infants [(1)]. Up to 60% of infantile hemangiomas occur in the head and neck region. Presentation in this area of the body can have significant long-term impacts on cosmesis and function. Thus, a comprehensive understanding of the pathogenesis, clinical presentation, and treatment of infantile hemangiomas is essential to appropriate management.

Infantile hemangiomas are unique in that they demonstrate at least two distinct phases of evolution. Oftentimes, these lesions are not very apparent at birth and they may initially present as a small area of blanching or localized telangiectatic erythema. The growth phase usually begins within the first month of life due to endothelial cell proliferation. Growth is often rapid and most infantile hemangiomas will reach 80% of their maximum size by 3 months of age [(2)]. It is important to remember that growth is volumetric and expansile, not invasive. During the growth phase, ulceration may occur leading to bleeding or infection and ultimately scarring. Additionally, if the lesion is close to a vital structure, function may be compromised. Following the initial growth phase, there is a quiescent phase where proliferation and apoptosis are likely in equilibrium and no change in the size of the lesion is noted. This usually occurs during mid-to-late infancy. The involution phase typically begins at one year old when proliferative endothelial tissue begins to undergo apoptosis and the lesion is converted into fibro-fatty tissue. This process can last for several years and the rate and degree of involution can be highly variable. Involution does not necessarily mean resolution and many patients will have a residual lesion, such as scar, dyspigmentation or redundant skin, even after involution is complete [(3)].

Several risk factors for infantile hemangioma have been identified. They include: male gender, ethnicity (Caucasian), prematurity, twin birth, advanced maternal age, placenta previa, pre-eclampsia, and placental abnormalities such as retroplacental hematoma or infarction. Low birth weight is a very strong risk factor and every 500-gram reduction in birth weight confers a 40% increased risk of infantile hemangioma [(4)]. Based on these risk factors, many have theorized that a history of placental hypoxia during the prenatal period increases the risk of infantile hemangioma by triggering an intrauterine vascular response.

Clinical history is usually sufficient in making the diagnosis of infantile hemangioma. The clinical presentation and phases of growth are pathognomonic for this condition. Imaging is generally discouraged unless the diagnosis is uncertain or if there are more than 5 cutaneous infantile hemangiomas. The presence of 5 or more infantile he-

mangiomas increases the risk of hepatic lesions and screening abdominal ultrasound should be performed [5]. If the lesion is not behaving like an infantile hemangioma or has an atypical appearance, it is reasonable to obtain noninvasive imaging first such as ultrasonography. Ultrasound is preferred due to low morbidity, lack of radiation exposure, and low expense. Additionally, sedation is not required in order to complete the study. An infantile hemangioma will appear as a lobulated hyperechoic mass with diffuse vascularity and absent arteriovenous shunting when Doppler imaging is applied (Figure 1). Parotitis can also have a similar appearance and clinical correlation is necessary to make the appropriate diagnosis. Computed tomography (CT) and magnetic resonance imaging (MRI) are often not necessary to make the diagnosis of infantile hemangioma. However, MRI should be considered when there is concern for segmental facial hemangiomas and PHACE syndrome which will be discussed later in this paper. MRI characteristics depend on the phase of growth. Lesions in the growth phase will be isointense on T1 and moderately hyperintense (but not as intense as an arteriovenous malformation) on T2. During involution, the lesion will convert to fibrofatty tissue and will appear hyperintense on T1 (Figure 2).

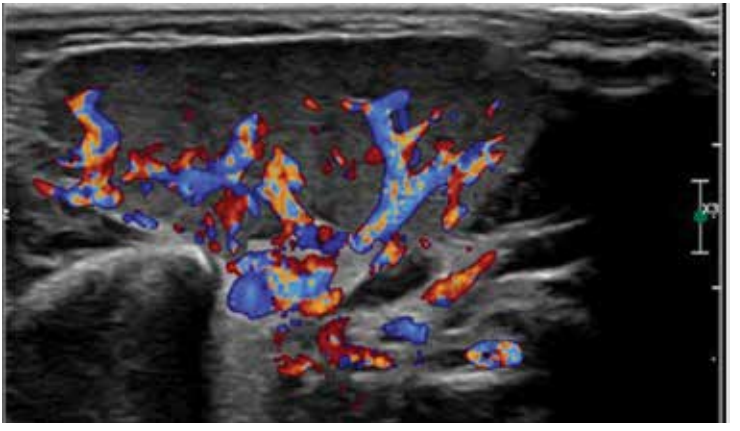

Figure 1. Doppler ultrasound image of a parotid infantile hemangioma.

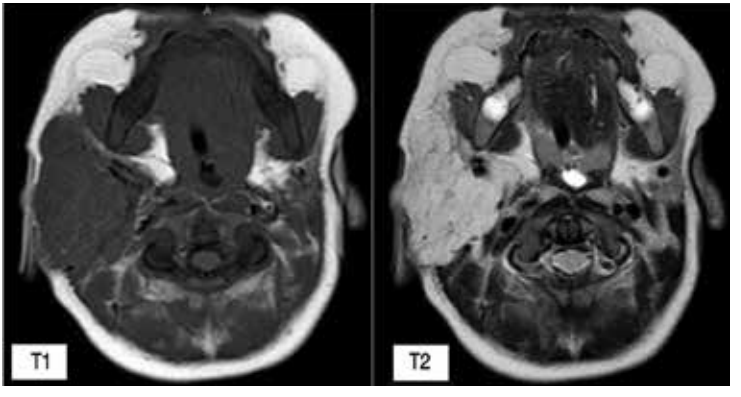

Figure 2. Magnetic resonance imaging of an infantile hemangioma in the proliferative phase. The lesion is isointense on T1 and moderately hyperintense on T2.

Treatment

Many treatment options are available when a child presents with an infantile hemangioma. The decision to initiate any therapy for an infantile hemangioma depends on the potential for pain, bleeding, ulceration, life-threatening complications, existing or imminent functional impairment, or disfigurement. Examples of locations where functional impairment requiring intervention may occur include: periocular (deprivation amblyopia), perioral (feeding impairment), nasal (nasal obstruction in an obligate nasal breather), and airway (airway obstruction). Additionally, one must always remember that the natural history of infantile hemangioma is involution with time. Therefore, watchful waiting with close observation is a very reasonable option in cases where the lesion is otherwise asymptomatic.

The treatment of infantile hemangioma has evolved significantly since the efficacy of propranolol was first reported by Leaute-Labreze et al. in 2008 [6]. As a result, oral propranolol has now replaced corticosteroids as first-line treatment for infantile hemangiomas requiring systemic therapy [7]. The exact mechanism of propranolol, a sympatholytic non-selective beta blocker, on infantile hemangiomas is unclear but may be related to vasoconstriction, inhibition of angiogenesis, and induction of apoptosis. A randomized control trial published by Leaute-Labreze et al. in 2015 demonstrated that a regimen of 3 mg/kg/day for 6 months was superior to placebo and shorter, lower dosage regimens (ie: 1 mg/kg/d for 3 months, 1 m/kg/d for 6 months, and 3 mg/kg/d for 3 months) [8]. Results were impressive as they reported up to 98% of infantile hemangiomas will respond to treatment and up to 60% will demonstrate complete regression.

Since propranolol is a cardiovascular medication, a thorough pretreatment evaluation is strongly recommended. This should include a history and physical that evaluates for a personal and family history of cardiovascular disease or arrhythmias. Vital signs (including heart rate and blood pressure) and a cardiopulmonary examination should be performed at the first initial office visit. The need for a screening electrocardiogram (ECG) is unclear. At this author's institution, ECG is not obtained unless there is a family history of a heart condition or an abnormal cardiac examination finding (bradycardia or arrhythmias). Routine echocardiography is not recommended unless there are concerns for structural heart abnormalities. If initial cardiopulmonary evaluation yields an abnormal finding, consultation with cardiology is recommended prior to therapy initiation. Contraindications for beta blocker therapy include conditions such as heart failure, hypotension, arrhythmia (heart block, sinus bradycardia), and bronchial asthma.

Prior to initiating treatment, caregivers should be counseled regarding medication administration and potential side effects. Families should be instructed to feed the child regularly and withhold the medication during periods of illness when there is poor oral intake in order to reduce the risk of hypoglycemia. Additionally, caregivers should be informed that they need to wait at least 6 hours between doses. Other potential side effects that parents should be informed about include bradycardia and hypotension, hypoglycemia (weakness, drowsiness, irritability), bronchospasm (wheezing, coughing worse with upper respiratory illnesses), sleep disturbances, cool extremities, and gastrointestinal upset.

Once the patient has been screened appropriately and the caregivers have been educated, propranolol can then be initiated. Therapy initiation should begin with a lower dosage (1 mg/kg/day divided into 3 doses) followed by weekly escalation until goal

dosage is achieved (3 mg/kg/day divided into 3 doses). Medication initiation and escalation should occur while the patient is in the clinic and not at home. At this author's institution, parents are instructed to give propranolol with a meal while in the clinic. Vital signs are re-checked one to two hours after medication administration. If heart rate and blood pressure remain stable, then the child is discharged home on the dose that was given in the clinic. Routine monitoring of blood sugar is not recommended. If the dosage is not tolerated, then the patient is brought back the following week and initiated with a half-dose (ie: 0.5 mg/kg/day divided into 3 doses) and observed. Patients that are less than 8 weeks corrected gestational age, have inadequate social support, or have medical co-morbidities such as cardiovascular, pulmonary, or endocrine abnormalities should be initiated in the inpatient setting for close monitoring of their vital signs. Once inpatient initiation is complete, subsequent escalations can be performed in the outpatient setting. Final dosage can be tailored to patient response and caregiver preference. Discontinuation of therapy involves halving the dosage for one week before discontinuing. Caregivers should be counseled that up to 15% of cases may begin to grow after discontinuation of therapy. If this occurs, propranolol should be re-initiated and the patient should be treated for a longer period of time (Figure 3).

More recently, topical beta-blockers, primarily topical timolol maleate in the form of gels or drops, have been investigated as a potential treatment option for infantile hemangiomas that has fewer systemic side effects. Its use for treating infantile hemangiomas was first reported in 2010 [9, 10]. Systemic absorption does occur but is usually low with minimal side effects. However, one should exercise caution when administering near mucosal surfaces [11]. Topical timolol has been demonstrated to be more effective in treating superficial infantile hemangiomas when compared to observation or ultrapotent corticosteroids [12, 13]. The medication is most effective for small, thin, superficial lesions that are <1 mm in diameter [14]. Administration of topical timolol in conjunction with systemic therapy should be undertaken with caution as absorption and blood levels of the beta-blocker may be difficult to predict and control.

Oral glucocorticosteroid therapy was previously the mainstay of infantile hemangioma treatment before the discovery of propranolol. Steroid treatment can be considered in cases where there is a contraindication to the use of propranolol or an inadequate response to propranolol therapy. The optimal dosage of steroid therapy has not been clearly established. Dose ranges reported in the literature range from 2 to 5 mg/kg per day of prednisolone or prednisone [15]. Steroid administration is associated with a significant side effect profile that includes: Cushingoid appearance, infection, immunosuppression, growth retardation, hypertension, and mood changes. In order to minimize systemic side effects, intralesional injection of steroids may be considered for bulky, focal lesions or lesions in critical anatomic locations. Much like systemic glucocorticoids, dosages for intralesional steroid injections are not well established. Most report using betamethasone and/or triamcinolone injection every 4-6 weeks [16-18]. In especially large lesions that require large quantities of local steroid injection, systemic side effects should remain a concern.

Laser therapy is another potential option for managing a cosmetically unappealing infantile hemangioma and can be used in conjunction with phamacotherapy. The most studied and reported laser is the 585 nm Pulsed Dye Laser (PDL). Laser therapy does not control growth but it may help improve the appearance of macular erythema and superficial telangiectasias in involuting infantile hemangiomas. However, multiple treatments are often required. Early laser treatment during the proliferative phase may increase the likelihood of complications [19]. Potential complications include skin atrophy, bleeding, pigmentary changes, scarring, and purpura.

Surgical intervention is always an option but has become less and less common due to the efficacy of propranolol therapy. However, it is an excellent treatment option for hemangiomas that have residual skin changes after involution. Waiting past four years of age is usually not necessary as most will not change significantly after that age [20, 21]. Surgical excision or debulking is often not performed during infancy. In addition to the risks of anesthesia in a young infant, early surgical intervention can lead to inferior outcomes due to the highly vascular nature of the tumor during the proliferative phase. Waiting until the tumor has involuted can reduce the risk of blood loss and also the number of operations needed to achieve a satisfactory cosmetic or functional result. Caregivers often express concerns regarding psychosocial implications if the lesion is not addressed early in life. Clinicians must keep in mind that long-term memory and self-esteem do not establish until the child is two to three years old—when the hemangioma is already in the involuting phase [15]. Therefore, early surgical intervention is usually not indicated unless there are extenuating circumstances.

Early intervention can be considered when the hemangioma is close to a vital structure and there is threat of imminent impairment during the proliferative phase. For example, early surgical excision of a periocular hemangioma may be indicated due to the risk of deprivation amblyopia from the obstruction of visual fields. When resecting or debulking an infantile hemangioma, it is important to remember that it is a benign lesion and thus, subtotal excision is appropriate if there is concern for injury to a vital structure such as a cranial nerve. Excisions can also be staged especially if the hemangioma is large and bulky. Basic cosmetic and reconstructive paradigms (such as using relaxed skin tension lines and respecting facial subunits) should be followed when excising a hemangioma.

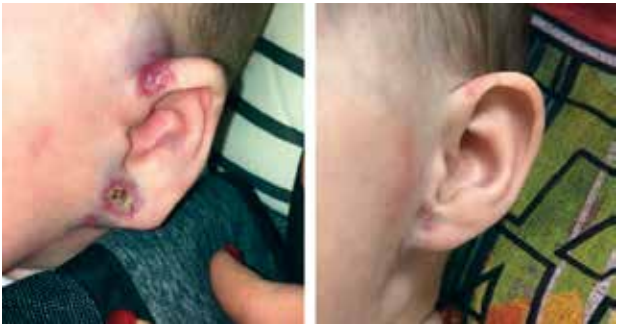

Figure 3. Ulcerated hemangioma of the auricle before and after completion of propranolol therapy.

Special considerations: PHACE Syndrome and airway hemangiomas

PHACES syndrome (posterior fossa anomalies, hemangioma, arterial cerebrovascular anomalies, cardiac defects, eye anomalies, sternal defects) is characterized by striking, large segmental infantile hemangiomas of the face, neck, or scalp. Posterior fossa abnormalities affect up to 40% of patients. The most common abnormality is unilateral cerebellar hypoplasia. Cerebrovascular anomalies are variable and can range from stenosis of an artery in the Circle of Willis to complete absence of an internal carotid artery. Furthermore, up to two-thirds of PHACES patients will have congenital cardiac anomalies such as coarctation of the aorta or double aortic arch. Due to these potentially life-threatening associated anomalies, an infant presenting with a large

(>5 cm) cervicofacial infantile hemangioma should undergo evaluation for PHACES syndrome. Initial screening studies should include MRI of the head and neck, MRA (from head to aortic arch), and echocardiography [22]. These studies are especially important prior to initiating propranolol, a cardiovascular medication that could potentially place these patients at risk for a neurovascular incident.

Infantile hemangiomas located in the airway (especially, in the subglottic area) require special attention due to their potential for causing airway compromise during the rapid growth phase. Early intervention is often needed to prevent life-threatening complications. Children with airway hemangiomas are typically asymptomatic at birth but develop breathing and feeding difficulties around one month of age when the proliferative phase begins. They will oftentimes present with a history of recurrent croup that eventually develops into persistent, worsening, biphasic stridor. The overall frequency of airway hemangiomas is rare, however, the presence of a segmental beard distribution hemangioma in addition to airway symptoms should raise a clinician's suspicion (Figure 4). The association of beard distribution and subglottic hemangiomas has been reported to be as high as 63% [23]. A recent paper by McCormick et al. reported a 10% association between beard distribution and infantile hemangiomas [24]. Thus, all patients who present with beard distribution hemangiomas should be screened for airway lesions. If the child does not have associated airway symptoms, initial evaluation can include awake airway flexible endoscopy or neck x-ray. If initial studies are negative, monitoring for development of airway symptoms is appropriate.

If the child has airway symptoms, then microlaryngoscopy and bronchoscopy in the operating room should be the next step. For those patients with large airway hemangiomas, intraoperative intra-lesional steroid injection or laser resection may be considered to temporize symptoms and propranolol therapy should be initiated postoperatively. One can consider leaving the child intubated while waiting for the child to respond to propranolol therapy. Eighty to ninety percent of airway hemangiomas will respond to propranolol therapy and stridor oftentimes will resolve within the first 24 hours of therapy initiation. Open resection can be considered if the size of the hemangioma would require prolonged intubation while medical therapy is being initiated or if the patient has failed medical therapy. Surgery for airway hemangiomas has fallen out of favor in the last decade due to the efficacy of propranolol therapy. The surgical approach would first involve intubation to secure the airway. The lesion would then be exposed via anterior laryngofissure approach and the endotracheal tube would be relocated to the inferior portion of the laryngofissure. The lesion would then be removed in the submucosal plane under microscopy. An anterior cartilage graft can be placed to enlarge the subglottic airway if necessary. The child would need to remain intubated for 3-7 days postoperatively [25].

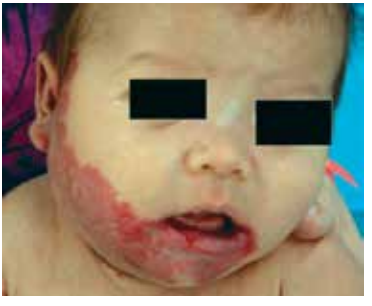

Figure 4. Beard distribution infantile hemangioma.

Conclusion

Infantile hemangiomas demonstrate a classic clinical course of proliferation and rapid growth in early infancy followed by involution that begins around one year of age. The diagnosis of infantile hemangioma is oftentimes a clinical diagnosis based on history and physical examination. Imaging for confirmation is not usually necessary unless there is uncertainty.

The decision to intervene depends on several factors including functional impairment, risk of disfigurement, infection, and ulceration. Management paradigms for treating infantile hemangiomas have evolved quickly over the last decade since the accidental discovery of propranolol as an effective treatment option. Propranolol, now considered first-line therapy, has essentially obviated the need for early surgical intervention and steroid therapy, which is associated with significant side effects. Pretreatment cardiopulmonary evaluation and caregiver counseling must be performed prior to initiating propranolol therapy and patients should be monitored when given their first dose and subsequent escalation doses. Topical timolol is a good alternative to systemic propranolol if the lesion is small and superficial. Surgical excision and laser therapy are always options if involution is incomplete. Ultimately, when managing infantile hemangiomas, the risks of any treatment option must be balanced against the knowledge that these tumors will ultimately undergo involution with time.

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Surgical options for the management of bilateral vocal fold paralysis in children

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Vocal fold paralysis is the second-most common congenital anomaly of the larynx in children, after laryngomalacia, accounting for 10% of all congenital lesions of the larynx [1,2]. In between 30% and 62% of the cases, the paralysis is bilateral, generally due to involvement of the recurrent laryngeal nerves (RLN), and manifests with symptoms of breathing difficulties due to obstruction of the airway by the abducted vocal folds [3-5].

Clinically, these children present with laryngeal stridor during crying associated with different degrees of respiratory difficulties (dyspnea, cyanosis, subcostal retractions, etc.), and may develop swallowing difficulties with a high risk of aspiration [6].

It has been estimated that 50% of the cases are congenital and Arnold-Chiari malformation is the most commonly associated congenital anomaly. Therefore, in children with laryngeal stridor from birth, bilateral vocal fold paralysis (BVFP) should be ruled out. In children, the etiology of BVFP is variable, including neurological diseases, iatrogenic causes, trauma, and is idiopathic in a large part of the cases [7].

Diagnosis of BVFP is made by fibronasolaryngoscopy, ideally in the awake patient, to evaluate the laryngeal anatomy and physiology during functional activity of the larynx to confirm the bilateral immobility of the vocal cords. Cricoarytenoid fixation should be ruled out as a cause of immobility (although in general, the term paralysis is reserved for immobility due to denervation). Complete evaluation of the airway using fibrobronchoscopy or rigid bronchoscopy is recommended to rule out concomitant conditions.

In children, a high rate of spontaneous resolution of the paralysis has been described, ranging from 48 to 71% between 6 and 12 months of life and up to 10% after 5 years of age [4]. Nevertheless, because of the potential risk of airway obstruction, respiratory difficulties, growth retardation, and failure to thrive, the majority of children with BVFP require some type of intervention to ensure airway patency. In most cases, it is preferable to wait for at least two years before performing definitive surgical treatment that modifies the anatomy of the larynx [7-9].

Surgical treatment options

There are multiple surgical options for the management of BVFP. However, the surgeon should keep in mind that there is no ideal surgical procedure and each case should be evaluated individually. Dynamic procedures seek to restore normal mobility of vocal folds (through laryngeal reinnervation), while static procedures are aimed to increase the diameter of the posterior glottis. In this chapter we will focus on the static procedures that are the most commonly performed in the management of BVFP in children.

Any surgery that increases the diameter of the airway can potentially compromise the quality and volume of the voice and may alter swallowing. Therefore, it is important to achieve an adequate balance between airway patency, maintaining a functional voice, and minimizing the risk of aspiration

In the initial treatment, more conservative procedures that do not alter the laryngeal structure are considered to avoid irreversible sequelae that compromise the late recovery of vocal cord mobility. This is especially relevant in children. However, if necessary, more complex complementary procedures may be performed. It is always important to explain the parents or caregivers that more than one intervention or a combination of surgical techniques may be required to achieve adequate results.

To understand the different surgical options, we should picture the airway as a tubing system and the paralysis as a site of obstruction at the level of the glottis. According to the Poiseuille law of fluid flow, the airway flow is proportional to the radius to the fourth power; In this way, when the diameter of the airway is smaller, the airflow obstruction will be much larger.

There are three options for the management of the obstruction that BVFP causes in the airway: 1) Create an alternative route that "redirects" the air flow (tracheostomy), 2) diminish the severity of the obstruction by resection or lateralization of the obstructive component, and 3) increase the diameter of the airway to allow increased air flow.

1. Create an alternative route: tracheostomy

Tracheostomy is a surgical intervention commonly performed in children with BVFP, either as temporary or as a definitive treatment. It is estimated that around 53% (50–65%) of the children with BVFP require tracheostomy at some moment8. Tracheostomy works as an "escape route" by which air flow is redirected bypassing the area of obstruction at the level of the glottis (Figure 1).

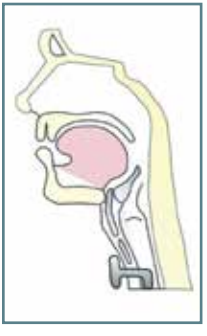


Figure 1. Diagram of the tracheostomy as an alternative route.
Figure 2. Patient in the early postoperative following tracheostomy.

Generally, this procedure is performed in children with severe airway involvement with marked respiratory difficulties and poor weight gain in whom a watch-and-wait strategy is not possible [10,11] (Figure 2).

In the vast majority of cases, tracheostomy is considered as a temporary measure that provides a safe airway, preserving the laryngeal structures and their function, while waiting for the immobility of the vocal folds to resolve (given the high rate of spontaneous resolution); or while other definitive surgical procedures are performed that improve airway patency and allow decannulation [7].

Tracheostomy is considered as the definitive treatment of BVFP in some patients. In children with, for example, little pulmonary reserve, difficulties to manage of secretions, neurological diseases, and other comorbid conditions, tracheostomy may be the best alternative.

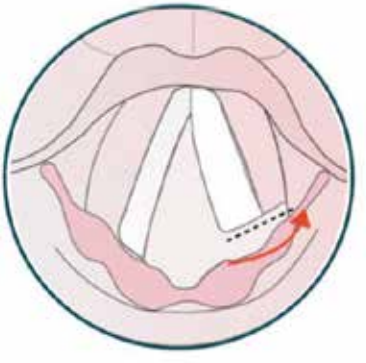
2. Diminish the severity of the obstruction.

In cases of BVFP in which the obstruction of the airway is caused by adducted vocal folds, there are several surgical options to diminish this obstruction. Some procedures are more "destructive" and irreversible, such as posterior cordotomy and arytenoplasty, in which part of the healthy vocal fold and/or part of the arytenoids are resected, while others are considered "non-destructive", such as suture lateralization of the arytenoid to secure the airway.

Posterior cordotomy and arytenoplasty

Posterior cordotomy CO2 laser is an endoscopic procedure aimed at enlarging the lumen of the posterior glottis (respiratory glottis) through partial resection of the posterior third of the vocal fold (Figure 3).

Using a surgical microscope, a wedge incision is made in the posterior third of the vocal fold immediately anterior to the vocal process of the arytenoid cartilage extending laterally up to the thyroarytenoid muscle to increase the airway lumen. Exposition of the cartilage should be avoided to prevent granuloma formation and to decrease the risk of re-stenosis [3,12] (Figure 4).



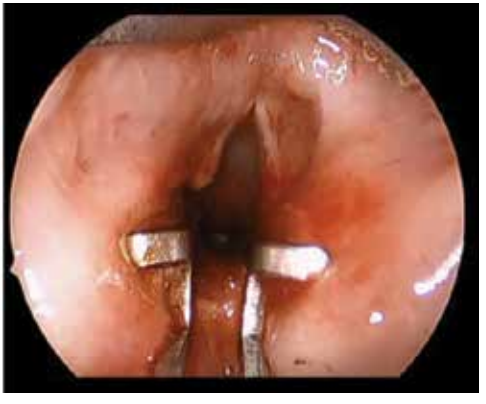


Figure 3. Diagram showing posterior cordotomy in the right vocal fold.
Figure 4. Intraoperative view of posterior cordotomy in the left vocal fold.

Cordotomy may be performed uni- or bilaterally, according to the preference of the surgeon, and may be accompanied by partial resection of arytenoids (arytenoplasty) to further increase the diameter of the glottis at this level, especially in cases in which this cartilage is medialized and obstructing the airway.

These procedures are non-reversible and may alter the quality of the voice of the patient by allowing air to escape leading to a breathy voice and hoarseness. In general, it is preferred to be the least aggressive possible, so as to achieve a good airway lumen sparing voice quality as much as possible.

Posterior cordotomy is one of the most common procedures performed in the management of BVFP in children and good results have been preported [12]. Nevertheless, an opening that is too large may result in decreased voice quality and aspiration. The need for re-innervation has also been described, as some patients present with excessive scarring.

Lateralization of the arytenoids

This procedure consists of the natural abduction of the cricoarytenoid joint, by placing a suture at this level, which is externally tied around the wing of the thyroid cartilage in the neck, lateralizing the vocal process of the arytenoids, thereby improving airway patency [3,13] (Figure 5).

One of the advantages of this technique is that it does not alter the laryngeal anatomy and may be reversed as the suture can be removed if necessary. However, especially in very young children, this suture may be very difficult to place endoscopically due to the small size of the larynx and the narrow airway.

3. Increasing the airway diameter.

Considering that, based on Poiseuille´s law, the main determinant of air flow is the radius, these procedures are aimed at exponentially improving airway patency by widening the diameter of the larynx at this level. When increasing the diameter, especially at the posterior glottis, the potential risk of aspiration and voice changes should be taken into account (Figure 6).

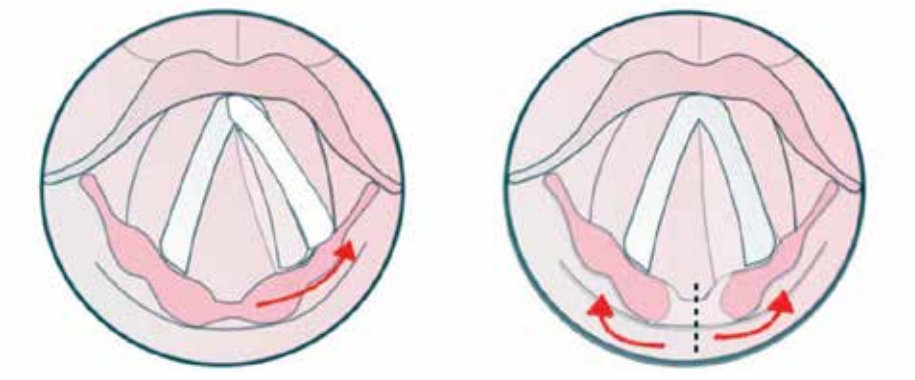


Figure 5. Diagram showing right arytenoid lateralization.
Figure 6. Diagram showing posterior cricoid split.

Endoscopic posterior cricoid split with graft insertion

This procedure consists of endoscopic incision of the posterior part of the cricoids and placement of a rib cartilage graft in this space to increase the transverse diameter of the posterior glottis [3,14] (Figure 7).

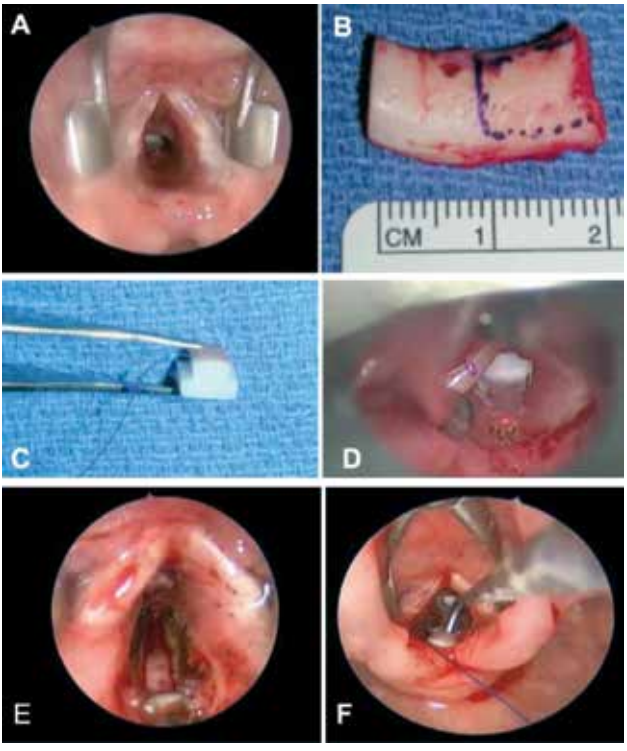


Figure 7. Intraoperative images of posterior cricoid split and rib graft insertion: (A) Preoperative endoscopic view of the glottis and subglottis. (B) Image of the rib cartilage graft (~2 cm). (C) Preparation of the graft (D and E) Posterior cricoid split with CO2 laser. (F) Placement of the graft in the pocket of the cricoid split.

Posterior cricoid split is a very good option for the management of BVFP in children as it does not affect spontaneous recovery of the fold mobility, expands the posterior glottic opening, and may even avoid the need for tracheostomy [7,14].

The harvest of a rib cartilage graft is associated with potential morbidities, such as pneumothorax, bleeding, pain at the donor site, and external scarring. Nevertheless, children have the advantage of possessing a significant cartilaginous component of the costal arch, which facilitates harvesting of the graft.

Endoscopic insertion of the graft may be challenging due to the narrow surgical field. In addition, cases of graft extrusion or reabsorption have been described.

Endoscopic anterior and posterior cricoid split

Recently, Rutter et al. [15] have described this technique in which both an anterior and a posterior incision are made endoscopically in the cricoid. Subsequently, a high-pressure balloon is used to dilate the area without the need for graft placement. The diameter of the balloon should be half a size larger than the diameter of the orotracheal tube calculated for the age of the patient.

This technique enlarges the airway while avoiding the morbidity associated with the harvest of a rib cartilage graft. Good results have been described in children with BVFP.

Conclusions

Vocal fold paralysis is the second-most frequent congenital anomaly of the larynx in children. Between 30% and 62% of the patients will have bilateral involvement, which is an important cause of laryngeal stridor in children.

Given the high rate of spontaneous resolution of vocal fold paralysis in the pediatric population, a watchful-waiting approach is recommended before embarking on any surgical procedure, except in children with marked respiratory difficulties. In these cases, tracheostomy is still the most commonly performed procedure, at least in the initial management of the disease.

Currently, multiple surgical options are available for the treatment of BVFP; however, there is still no ideal procedure or gold standard. Therefore, each case should be evaluated individually considering etiology, time of evolution, age, and symptoms and comorbidities of the patient, among others.

Generally, in children less "destructive" interventions are preferred, but multiple interventions and surgical techniques may be required to achieve an adequate balance between airway patency and voice quality.

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Management of bilateral vocal fold immobility: Endoscopic posterior cricoid split with rib graft

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Bilateral vocal fold immobility (BVFI) either with or without laryngeal stenosis is a challenging problem in the pediatric population. BVFI can be divided into two categories: bilateral vocal fold paralysis (BVFP) and cricoarytenoid joint fixation (CAJF). Etiologies of BVFP include neurological, cardiopulmonary malformations, anoxic injury, trauma, iatrogenic, and idiopathic [(1)]. These movement issues can be accompanied

by stenosis, either posterior glottic (PGS) and/or subglottic (SGS). CAJF, PGS, and SGS are usually related to intubation and subsequent scar formation. Many of these children will require a tracheostomy early in life due to upper airway obstruction.

In children with BVFP precipitating airway obstruction necessitating tracheostomy, there are multiple treatment methods to allow for decannulation. Surgery is performed to provide an adequate airway for breathing after decannulation but with minimal impact on speech and swallowing. Vocal fold cordotomy, vocal fold cordotomy and arytenoidectomy [2], vocal fold suture lateralization, open laryngotracheal reconstruction [3], endoscopic posterior cricoid split with rib grafting [4], and botulinum toxin injection [5] have all been described. Because more than 50% of BVFP will resolve spontaneously [3,6] many advocate surgical intervention to achieve decannulation only after the child turns one year of age [3].

In children with CAJF with and without PGS and/or SGS there are many treatment options, both endoscopic and open, to achieve decannulation. Endoscopic procedures include vocal fold cordotomy, arytenoidectomy, endoscopic mucosal advancement flap, and endoscopic posterior cricoid split with rib grafting. Adjunctive measures may also be employed including the use of Mitomycin-C, steroid injection, and botulinum toxin injection. Endoscopic techniques use either cold steel or carbon dioxide laser to remove scar tissue or open the airway. Open procedures include scar excision, mucosal grafts/flaps with and without stenting, and laryngotracheal reconstruction.

The decision to perform an endoscopic procedure vs. an open surgery depends on the ability to obtain good endoscopic exposure. Contraindications are listed in Table 1. Endoscopic approaches are preferred when possible due to decreased morbidity and faster recovery [7,8]. Compared to an open laryngotracheal reconstruction, EPCG does not disrupt the anterior cricoid ring, eliminating the need for stenting due to the intact spring of the cartilage. In addition to the contraindications for endoscopic procedures listed in table 1, open procedures should also be considered after multiple failed endoscopic approaches, as well as more severe stenoses.

Table 1. Contraindications for endoscopic approaches to glottic stenosis.

Poor endoscopic exposure of the larynx
Retrognathia
Micrognathia
Glossoptosis
Macroglossia
Retroflexion of the epiglottis
Severe transglottic stenosis
Grade 4 subglottic stenosis
Tracheal stenosis

Preparation

In cases of BVFI, direct laryngoscopy and bronchoscopy should be performed at the start of any endoscopic intervention. A full airway assessment including palpation of the cricoarytenoid joint is essential to confirm the diagnosis and appropriateness of the planned procedure. If necessary, laryngeal EMG may be performed to differentiate between BVFP and CAJF. If a diagnosis of BVFP is made, MRI of the brain and neck should be performed to assess for any neurological abnormalities or lesions along the course of the recurrent laryngeal nerves.

For all endoscopic approaches utilizing a laser, there are several key considerations for preparation and anesthesia. First, given the airway fire risk inherent to the procedure, it is recommended that the FiO2 be maintained at room air. In patients with tracheostomy tubes, the tracheostomy tube should be exchanged for an equivalently sized Jackson metal tracheostomy tube. Laser precautions are meticulously observed throughout the procedure. The patient's eyes should be covered with moist laser-safe eye pads. The face and any exposed skin should be covered with wet blue towels. All staff in the room must utilize appropriate laser-safe goggles, and the laser should be turned to standby whenever not actively in use.

Several key pieces of equipment are recommended for successful use of the described endoscopic techniques in this chapter. A microscope with laser adaptor and micromanipulator enables the surgeon to obtain excellent visualization and allows for efficient laser use. A carbon dioxide laser is ideal for these techniques especially for the thick plate of the posterior cricoid cartilage. A Lindholm laryngoscope and Lindholm laryngeal spreader (Figure 1) are ideal for achieving maximum exposure of the posterior aspect of the airway.

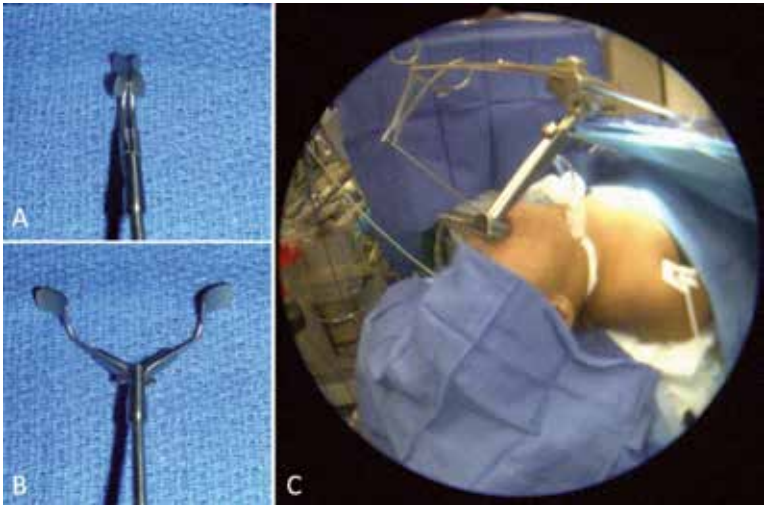

Figure 1. Lindholm laryngeal spreader in closed (A) and open (B) positions. Also pictured suspended in inverted fashion from suspension apparatus using rubber bands (C).

Procedure

Videos of the procedure can be found at www.csurgeries.com [9]. A Lindholm laryngeal spreader is then inserted in an inverted fashion to retract the false vocal folds and secured to the suspension apparatus with rubber bands (Figure 1). This keeps the grasp out of the way of instruments being used on the posterior aspect of the airway.

A low setting and small spot size in pulsed mode are used to avoid thermal injury and resorption or ablation of the cricoid cartilage. With the laser in position, the straight suction is used to protect and push the interarytenoid muscles posteriorly to expose the posterior cricoid plate. This also allows the surgeon to put pressure on the superior and posterior aspect of the cricoid cartilage which rotates the cricoid inferiorly and anteriorly allowing for better exposure of the posterior cricoid plate. The

CO2 laser is then used to divide the posterior cricoid plate (Figure 2) being sure to maintain the posterior perichondrium which protects the esophageal musculature. The perichondrium should not be undermined once the cricoid is divided to maintain a snug fit and prevent migration of the graft.

Once the posterior plate of the cricoid is fully divided, the length of the defect is measured with a straight suction. A 1.5-2.0 cm segment of rib cartilage is then harvested and carved in a T-shaped fashion with the perichondrium maintained on the luminal surface. The graft should be approximately 1 cm in length depending on the length of the patient's cricoid as measured intraoperatively, with a 5 mm width of perichondrium on the luminal surface and 1 mm flanges (Figure 3). A 5-0 prolene suture on a taper needle is used to place a rescue stitch through the superior aspect of the graft to assist with graft extraction should insertion be unsuccessful. Using a 0-degree 4 mm Hopkin's rod for visualization a stout laryngeal forceps are used to insert the rib graft into the lumen of the airway. A right-angled probe is then used to snap the graft into place with the flanges posterior to the cut aspect of the cricoid and the perichondral surface facing the airway lumen (Figure 4). The probe should then be used to ensure that the graft is a snug fit and will not migrate. If the graft does not snap in easily after multiple attempts, then it should be trimmed, and further attempts made. Once the graft position is confirmed with the Hopkin's rod telescope, the rescue stitch is cut and gently removed. The laryngeal spreader is also removed, and the airway reassessed with the Hopkin's rod telescope (Figure 5).

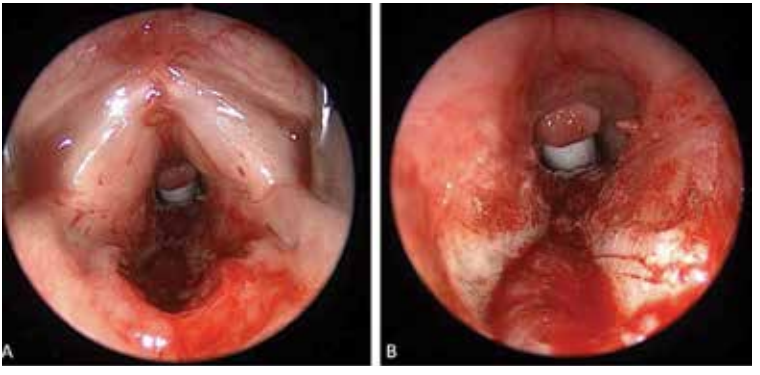

Figure 2. Views of posterior cricoid cartilage divided along its full length from above (A) and below (B) the level of the vocal folds. Note that the interarytenoid muscles and the posterior perichondrium of the cricoid are left intact.

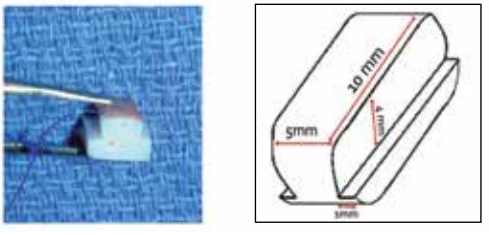

Figure 3. Rib graft following carving into T-shape with prolene rescue suture in place. Note the perichondrium is preserved on the luminal surface (A). Average dimensions of the rib graft (B).

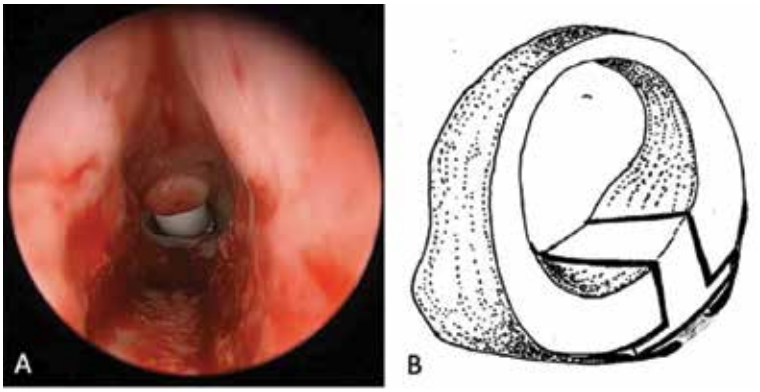

Figure 4. View after rib graft insertion distracting the posterior cricoid plate (A). Illustration of rib graft after insertion. Note the posterior cricoid perichondrium is left intact (B).

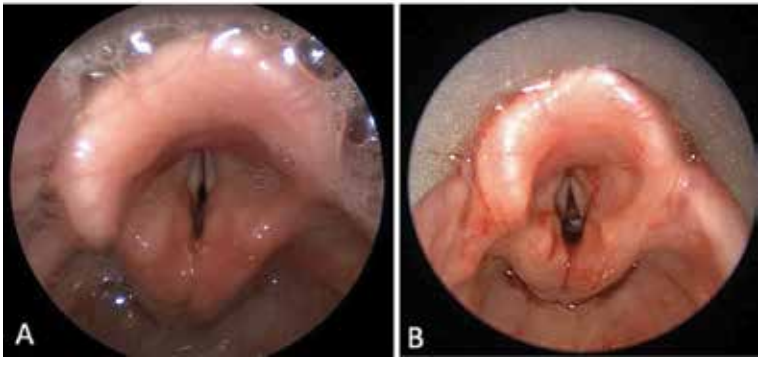

Figure 5. Preoperative view (A) and postoperative view (B) immediately after insertion of graft. Note the distraction of the vocal folds and elimination of posterior glottic stenosis.

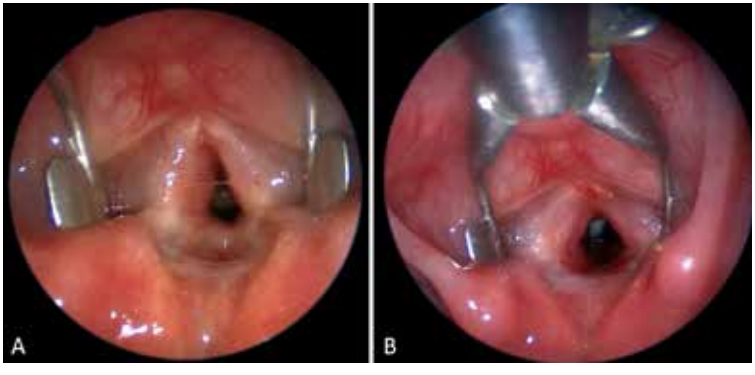

Figure 6. Preoperative (A) and three-month postoperative (B) laryngoscopy with laryngeal spreader.

Postoperative care

The patient should be admitted to the PICU postoperatively with pulse oximetry. Plugging of the tracheostomy tube with mucous and blood is common and tends to occur on day 2 post-operatively. In addition, the tracheostomy tube should not be removed unless in the operating room as its placement safeguards against the possibility of rib graft displacement and aspiration of the graft into the lower airway. They should receive humidified air via tracheostomy collar and resume their preoperative diet. The patient is usually discharged on postoperative day 3 if tolerating diet and pain is controlled with oral medications. Follow up laryngoscopy and bronchoscopy are performed on postoperative day 7 after which time the tracheostomy tube may be changed and downsized. Patient is decannulated when tolerating capping trials throughout the day, undergoes post-operative airway assessment, and passes a capped sleep study (Figure 6).

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Airway endoscopic care on intubated patients in pediatric intensive care units

Fabiano Bleggi Gavazzoni, MD.

As medicine evolves and saves more and more lives, intensive care units (ICUs) become a prominent place for this condition to be achieved. Therapeutic options in pediatric patients, clinical or surgical, related to different situations, such as extreme prematurity, severe congenital diseases, organ transplants, polytrauma treatment, among others, place pediatric ICUs as a fundamental part of this process, keeping alive children who would not survive some years ago. However, this advance brings with it, invasive procedures, although necessary and performed by competent and cautious professionals, that can determine definitive sequelae.

One of the often-affected systems, and the target of the present discussion, is the respiratory. Different situations need assisted ventilation and long-term intubation which may determine irreversible airway damage, from the nose to the lungs. Special attention should be taken to the post-intubatory lesions of the larynx [(1)], because their

frequency, seriousness and the fact that, when properly addressed, their sequelae can be avoided or at least minimized.

The pathophysiology of post-intubatory lesions is well known and results from the compression of the orotracheal tube over critical areas of the larynx, especially the posterior glottis and the cricoid ring [2]. Cannula pressure becomes greater than capillaries pressure, responsible for blood irrigation causing mucosal ischemia and tissue damage, evolving to edema, granulation, ulceration and, finally, fibrosis. The result of this event is laryngotracheal stenosis, which leads to changes in breathing, swallowing and phonation, with significant impact on the child's quality of life.

Monitoring of the larynx during the intubated period can be determinant to avoid such sequelae. The different variables associated with the occurrence of lesions, such as total intubation time, cannula fixation forms, degree of sedation of the patient, and others, may not always be adequately controlled. Then, airway endoscopy [3], using flexible and/or rigid laryngoscopy, can be able to manage the evolution of the disease, enabling to take the right decision to protect the larynx, such as keeping intubation, where no signs of tissue suffering are seen, or indicating tracheostomy, in cases where lesions are evident and the permanence of invasive ventilation is mandatory.

Reviewing the literature for airway monitoring of intubated patients in pediatric ICUs, we noticed just a few papers and protocols worried about the larynx. Although airway care is always present in ICU protocols, since most patients depend on orotracheal intubation (OTI) and assisted ventilation [4-6], the laryngeal damage itself is not emphasized. Intubation difficulties and complications of mechanical ventilation are the main focus [7]. The laryngeal evaluation ends up being requested only after some disease has been established, such as difficult extubation or even stenosis. The indication and performance of bronchoscopy was much more frequent [8,9] aiming the lower airway than upper lesions.

Midula et al. [10] and Bar-Zohar et al. [11] reviewed flexible bronchoscopy in pediatric ICUs, citing, among the most frequent indications, bronchopulmonary toilet, alveolar broncho lavage, endobronchial and transbronchial biopsy, laser therapies, broncography, intubation aid, application of pulmonary topical medication and placement of bronchial stents, concluding that it is a safe and necessary procedure, however, care for intubation damage and evaluation of post-extubation lesions were not considered.

It is consensual among ICUs guidelines the concern of bronchoscopy evaluating lung diseases [12,13], however, agreeing with Bush [14] and Walker et al. [15], we see the need to expand indications of bronchoscopy in pediatric ICUs, including laryngeal care of intubated children, even before respiratory distress appears. Post intubatory lesions related to tube changes and reintubations by accidental extubation [16] (unfortunately, a not so rare situation in the ICUs) are widely documented and may happen as early as 24 hours of intubation [17].

We believe preventive laryngeal examination and early endoscopic control of post-intubatory lesions, can avoid extubation difficulties and may reduce laryngeal damage, specially laryngotracheal stenosis. Late evaluation of patients with stridor are associated with difficult to treat laryngeal stenosis [18].

Our preventive airway endoscopy protocol suggests performing laryngeal evaluation to the following groups:

– Intubated children for more than 5 consecutive days.
– Extubated and reintubated children, for any reason (including accidental extubation).

– Extubated children with stridor, respiratory effort, need of oxygen and need of noninvasive ventilation (exception should be applied to neonatal patients, that frequently have respiratory distress following extubation. In this situation, the indication of preventive airway endoscopy will depend on the the clinical and pulmonary picture of each patient).
– Emergency tracheostomized patients.
– Tracheostomized patients coming from other hospitals who did not have previous airway endoscopy report.

The exam may be carried on in the ICU bed, in mild cases, or the children can be referred to the operating room, to allow a more comprehensive evaluation and intervention, if necessary. It is pre-defined that patients who undergo bedside examination and do not have an assertive diagnosis, will necessarily be reexamined under general anesthesia in the operating room.

Routinely, bedside examinations will be performed without anesthesia or sedation. If sedation is necessary, it should not compromise the respiratory pattern, in order to have spontaneous ventilation during all time. In the operating room situation, inhaled and venous general anesthesia will be used, with the child extubated all time and on spontaneous ventilation, using a nasal catheter with a mixture of oxygen and anesthetic gases, aiming to obtain the appropriate anesthetic plan for each moment of the examination.

The airway endoscopy can be performed with a flexible nasolaryngoscope or suspension rigid laryngoscope aided by a 0 degree, 4mm diameter and 20 cm length optic and/or microscope. The exam includes:
– Nasal Cavity - septal deviation, tumors, choanal atresia, malformations.
– Rhino pharynx - adenoids hiperplasia.
– Pharynx - palatine tonsils hyperplasia, pharyngomalacia.
– Hard and soft palate - cleft palates.
– Hypopharynx - lingual retro positioning (retrognathia), lingual tonsils hyperplasia, cysts, malformations.
– Larynx – laryngomalacia, short ariepiglottic folds, search for granulomas and/or ulcerations, evaluation of vocal folds mobility, paradoxical movements, arytenoids subluxation, posterior glottic stenosis (using a laryngeal spreader), subglottic stenosis.
– Trachea - injuries, stenosis, supra stomal collapses/granulomas (in case of tracheostomy), extrinsic compressions (vascular ring, mediastinal tumors).

Once the diagnosis is achieved, the decision of how and when therapy begins depends on a team decision. If the intensivist agrees the children has clinical conditions and the ENT surgeon define a surgical pathway, the surgery can happen just after the exam, during the same anesthesia. Each disease demands its own approach. Granulation tissue removal, a cyst marsupialization, a suppraglotoplasty are example of possible procedures. Treating underlying conditions is also addressed as soon as possible. A treatment suggestions list is as follow:

- Impossibility of nose breathing - use of Mc Govern pacifier.
- Faryngomalacia and retrognathia – nasolaryngeal probe, non-invasive ventilation.
- Laryngeal lesions - granulomas and ulcerations fibrin removal, application of corticosteroid/antibiotic ointment (diprogenta), inhalation with corticosteroid/antibiotic association (otociriax) .
- Mild/Moderate laryngomalacia – height/weight and dyspnea/cyanosis crises control.

- Severe laryngomalacia – supraglotplasty, epiglotopexy.
- Bilateral vocal fold immobility - little respiratory distress – observation, moderate to severe respiratory distress - lateralization of one of the vocal folds with Lichtemberger needle, tracheostomy.
- Aritenoid dislocation - reduction of dislocation.
- Fixation (posterior glottic stenosis) - posterior enlargement with costal cartilage graft, tracheostomy.
- Subglottic stenosis - balloon dilation (less than 3 months), tracheostomy.
- Supra stomal tracheal ring granuloma - surgical resection.
- Supra stomal tracheal ring collapse/fracture - resection of the fractured ring and end to end anastomosis.
- Extrinsic tracheal compression - treatment of the causal factor.

In conclusion, we expect that the use of preventive endoscopic care of intubated children in pediatric intensive care units, allow to avoid, or at least reduce, lesions and sequelae of the airway, especially the laryngeal ones.

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Subglottic stenosis: Post-intubation acute lesions, treatment

Cláudia Schweiger, MD, PhD, **Cátia Saleh Netto**, MD, MSc and **Denise Manica**, MD, PhD.

Introduction

Subglottic stenosis (SGS) is a well-recognized clinical entity since 1965, when the use of prolonged endotracheal intubation began to be used in children who needed longer

ventilatory support [1]. 1 In a recently published study, the overall incidence of SGS was estimated to be 11% [2].

Chronic laryngeal lesions after endotracheal intubation result from acute lesions, usually seen within hours or a few days after extubation. Thus, the presence of certain acute lesions could predict the development of chronic lesions, requiring intervention.

The endotracheal tube (ETT) exerts pressure on the posterior surface of the larynx leading to mucosal ischemia, which seems to be the triggering factor for the development of acute laryngeal lesions after intubation. Lesions occur at the areas of greatest contact with the tube: medial surface of the arytenoid cartilage, medial portion of the cricoarytenoid joint and vocal process, posterior glottis in the interarytenoid region, and subglottis surrounding the inner surface of the cricoid cartilage, usually the posterior part [3,4].

Although new techniques have been developed for the treatment of acute laryngeal lesions, early detection is essential for the successful use of these treatments and to prevent progression to chronic lesions [5].

Subglottic stenosis (SGS) prevention

Primary prevention of SGS consists of identifying risk factors and secondary prevention consists of identifying and treating laryngeal post-intubation acute lesions, in order to prevent the progression to SGS.

Risk factors

Knowledge of the risk factors for the development of SGS is necessary for adequate prevention. The various factors responsible for the development of acute laryngeal lesions are related to the ETT itself (size, material, cuff), intubation technique, and nursing care at the pediatric intensive care unit (PICU) [6].

The duration of intubation plays an important role in the pathogenesis of SGS, increasing the risk of outcome for those on prolonged use of ETT [7]. Sedation level seems to be a play a role in SGS as well. Children maintained at an inadequate sedation level during the endotracheal intubation period appear to develop higher rates of chronic injury, possibly due to ETT mobilization trauma, especially during episodes of agitation [2].

Furthermore, the need for ETT exchange was identified as a risk factor for the development of moderate-to-severe lesions, as well as the number of ETT mobilizations [8,9].

It was observed that many of the children who developed SGS had traumatic or repeated intubations [10]. Another particularly important factor is laryngotracheal reflux, which can trigger the progression and persistence of the SGS [11].

Cuffed ETT, respiratory infection, local infection and intrinsic factors have also been cited as risk factors for SGS.

Classification of post-intubation acute laryngeal lesions

The first classification of laryngeal lesions by intubation was proposed in 1969 by Lindholm, after extensive work in adults and considering the depth of ulcerations, and is described in Table 1 [12].

Colice et al. considered the degree of obstruction and classified the FNL findings as normal, mild lesion (erythema or mucosal ulceration without reduction in lumen size during inspiration), moderate lesion (erythema, ulceration and mucosal edema redu-

Grade I	Hyperemia and/or edema, without ulceration
Grade II	Superficial ulceration of less than one-third of the airway circumference
Grade III	Deep ulceration of less than one-third of the airway, or superficial ulceration of more than one-third of the airway circumference
Grade IV	Deep ulceration of more than one-third of the airway or ulceration with cartilage exposition/exhibition in any region

Table 1. Classification of intubation laryngeal lesions proposed by Lindholm. Adapted from Lindholm, 1969.

Degree of change	Endoscopic appearance
Early nonspecific	- Hyperemia - Edema - Patchy surface ulceration
Edema	- Protrusion of ventricular mucosa - Edema of vocal fold - Subglottic edema
Granulation Tissue	- Tongues" from vocal process - Subglottic GTa
Ulceration	- Ulcerated troughs - Annular in posterior glottis - Subglottic, within cricoid
Miscellaneous	- Bleeding - Arytenoid dislocation - Perforation - Cricoid ulceration

Table 2. Benjamin classification, 1993. GT = granulation tissue; SGS = subglottic stenosis.

cing laryngeal lumen during inspiration) and severe lesion (erythema, mucosal ulceration and edema reducing laryngeal lumen by more than 50% during inspiration) [13].

Benjamin classification, in contrast, does not score lesion severity, but refers to all categories of lesions that may eventually develop into glottic or subglottic obstruction (Table 2) [14].

A Classification of Post-Intubation Acute Laryngeal Lesions in Infants and Children (Table 3) has been published recently and showed high sensitivity (90%) and specificity (73%) to predict the development of SGS in children, and is a potentially valuable tool in identifying children at risk for the disease [5].

	Group 1 Mild	Group 2 Moderate	Group 2 Severe
Supraglottis	- Edema - Hyperemia		
Glottis	- Edema - Hyperemia	- Uni or bilateral ulceration - Arytenoid GT	- Inter-arytenoid ulceration - Inter-arytenoid GT Immobility
Subglottis	- Edema - Hyperemia	- Partial ulceration (<360o.)	- Complete ulceration - GT

Table 3. Classification of acute laryngeal injuries (CALI) as mild, moderate, or severe, according to anatomical location and type of injury.

GT= granulation tissue.

According to the CALI, 2% of the patients with mild acute injuries, 8.5% with moderate injuries and 50% with severe injuries progressed to SGS.

Treatment

Treatment of SGS in children remains a challenge and numerous open and endoscopic surgical techniques have been reported. Endoscopic techniques have the advantage of being less invasive and leave no external scars [6].

Combined glottic and subglottic stenoses are the most challenging to treat; they are found in very severe cases or when prolonged intubation has been preceded by a trauma [6].

Currently, significant improvements in airway endoscopy have allowed for the development of new endoscopic techniques in the treatment of subglottic and tracheal stenosis [15].

Fundamental endoscopic options:
– Re-intubation with steroids/antibiotic ointment around the endotracheal tube.
– Removal of granulation tissue.
– Balloon dilation.
– Rigid dilation (with tubes).
– Systemic corticosteroids.
– Steroids/ antibiotic inhalations.
– Tracheostomy ± laryngeal mold.
– Reflux therapy.

Elective re-intubation

Airway obstruction can occur within minutes or even hours after extubation, causing extubation failure. Laryngoscopy reveals acute laryngeal lesions, such as gltotic and subglottic edema, ulcers and granulation tissue, with airway involvement.

Hoeve et al. retrospectively studied the efficacy of therapeutic reintubation in a group of premature infants in whom extubation failed, as a result of a post-intubation injury confirmed by endoscopy of the larynx or trachea. They described 23 patients with a mean age of 37 days who re-intubated with a "loose fit" tube (inferior in diameter to what would be recommended considering patient age, permitting leakage of air at the end of an insufflation) for a period of 17 days. Only one of these patients progressed to tracheostomy. When the airway finding was edema or superficial lesions, mean time for intubation was only 8 days and more than half of these patients were extubated within 3 days. When ulceration and edema was found, the mean intubation time was 13 days. However, when granulation was present, intubation longed for weeks afterwards [16].

In a small group of 10 infants with subglottic stenosis caused by endotracheal intubation in the neonatal period, Graham reported a controlled reintubation study that allowed successful extubation in six cases. Six patients were successfully extubated; two were tracheostomized and decannulated afterwards, with no need for further surgical procedures; one underwent tracheal reconstruction; and the other tracheostomized patient died due to other causes [17].

According to Monnier, the treatment for acute laryngeal lesions consists of reintubation with a smaller ET tube with topical application of gentamicin-corticosteroid ointment buffer (Figure 1), systemic antibiotics following tracheal aspirate culture and systemic corticosteroids. Most patients can be extubated after an average reintubation

period of 2 to 4 days. Adrenaline aerosols (50 mg/kg diluted in 4 ml of 0.9% NaCl), intravenous dexamethasone (2 mg/kg), continuous positive airway pressure (CPAP) and heliox administered through a face mask are important tools to overcome this difficult post extubation period [6].

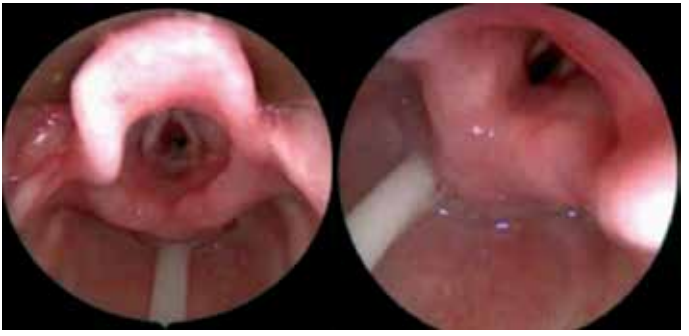

Figure 1. Intubation and steroid/antibiotic ointment applied. Left: Severe acute glottic and subglottic lesion. Right: Seven days after treatment.

Balloon laryngoplasty (BLP)

Balloon laryngoplasty (BLP) is an endoscopic procedure, first described in 1984 as a method to manage tracheal and bronchial stenosis [18].

Before the angioplasty balloon dilation was introduced or in cases when it was not available, dilation was performed with rigid bronchoscopes or with the endotracheal tube itself, but the results were unsatisfactory with poor control over the dilated area [15]. Balloon laryngoplasty seems to provide better results because theoretically it minimizes the risk of airway rupture or mucosal trauma by applying a radial force to the circumference of the stenosis and reducing the shearing force, reducing restenosis alterations [19]. In addition, due to the small diameter of the deflated balloon, it can be passed through extremely narrow areas without causing additional trauma [20].

In 2011, we published our experience in a tertiary hospital with a series of eight children with acute stenosis after intubation, submitted to dilatation with an angioplasty balloon (Figure 2). Complete resolution rate for the stenosis in evolution was of 75% (six in eight patients), but all the children were asymptomatic during follow up, even those with Grade 1 residual stenosis, avoidance of tracheostomy in all of them [20]. This study was included in 2 systematic reviews in 2014, which showed that BLP as a primary treatment for pediatric SGS is successful in most patients and reported complications are rare [21,22].

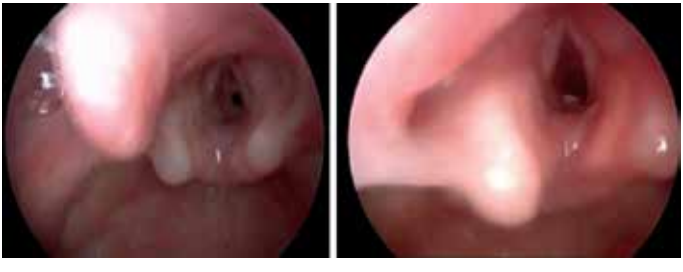

Figure 2. Balloon laryngoplasty (BLP). Left: Severe acute subglottic lesion. Right: Lumen improvement after BLP.

Accordingly, recent studies have shown that BLP in patients with acute SGS may have a good prognosis due to lower tracheostomy rates and higher decannulation rates, and reduces the need for open laryngeal surgery by 70% to 80% [19,23]. At last, BLP has the same success rate as tracheostomy and other airway surgeries for the treatment of acute subglottic stenosis, with the advantage of causing less morbidity and mortality [24].

The factors that did significantly contribute to treatment failure were gastroesophageal reflux disease, patient weight below 5 kg, concomitant airway disorders such as laryngomalacia, and the use of multiple dilations [22].

Although recent systematic reviews have concluded that balloon airway dilation is effective in treating SGS, there is no consensus on the optimal balloon diameter size. However, it is known that excessively large balloons may damage or rupture the airways, and very small balloons may reduce the effectiveness of the procedure leading to the need for repeated procedures for clinical improvement [25].

Complications of BLP are rare but can be potentially serious, including death by tracheal laceration. Increased severity of SGS seems to be associated with increased chances of treatment failure [21].

Schweiger et al. developed a successful reproducible SGS survival animal model using cautious endoscopic injury induced in the subglottis followed by intubation. This model paves the way for further translational research evaluating various surgical interventions for symptomatic SGS and for developing management protocols [26].

In an animal study using New Zealand White rabbits on balloon dilation, it was shown that from four balloon sizes (6, 7, 8 and 9 mm), the 8 mm balloon was the most effective in obtaining improved post-dilation cricoid lumen diameter without causing cricoid fractures. The results suggest that SGS may offer some degree of "protection" against cricoid fractures when using an 8 mm balloon.

Further research is necessary to define the ideal duration of balloon inflation during dilation, the optimal interval between dilations, and the role of adjunctive therapies in the management of acquired SGS.

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Endoscopic vs. open airway surgery

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The surgical decision to undergo an open versus endoscopic approach for a variety of airway procedures has become more complicated as technology and endoscopic techniques have advanced over the last 3 decades. Factors specific to the patient and pathology can help guide surgical decision making. As with any procedure, a discussion of the risks and benefits of the planned approach with the patient/family is important and helpful in the management of expectations.

The endoscopic approach in surgery has become popular and widely publicized among other surgical specialties as "minimally invasive" and offers an attractive way to decrease scarring and the overall morbidity. Endoscopic surgery also frequently involves shorter hospital stays. Endoscopic techniques can be more technically challenging for the surgeon due to limited surgical access. Advances in technology, specifically camera optics, have allowed for more effective visualization of difficult surgical targets. However, the surgeon must balance factors such as surgical time, safety, adequate resection, and likelihood of need for revision surgery during the decision-making process. The following pathologies represent some scenarios where the decision to do an open vs endoscopic procedure may be difficult.

Laryngeal cysts

Laryngeal cysts can be classified as saccular cysts or laryngoceles. Saccular cysts contain mucoid fluid and occur as a result of obstruction of the submucosal glands located around the ventricle. They can typically be found in an anterior location between the true and false vocal cords or in a lateral location in the false vocal cord and

aryepiglottic fold [1] (Figure 1). Laryngoceles are typically air-filled cysts which can be contained within the cartilaginous framework or in the neck via passage through the thyrohyoid membrane. Laryngoceles are thus classified as internal or external/combined. Diagnostic CT imaging is helpful to categorize these lesions as internal or external. Preoperative workup should also include evaluation for another laryngeal lesion, as supraglottic tumors may cause obstruction of the ventricle with subsequent laryngeal cyst development. This is not typically the case in the pediatric population and clinicians should have a higher suspicion for ventricular obstruction in adult patients at risk for laryngeal cancer.

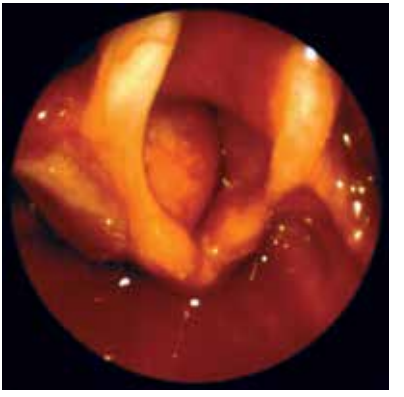

Figure 1. Saccular cyst obstructing the laryngeal inlet.

Endoscopic treatment of laryngeal cysts can be treated with marsupialization or excision depending on the extent and location of the cyst. Traditionally this approach was reserved for patients with an isolated internal laryngeal cyst, however, there are several cases in the literature where adult combined/external laryngoceles have been treated successfully with an endoscopic approach alone [2]. Vallecular cysts respond well to marseupialization. However saccular cysts tend to recur after marseupialization, with reports of them recurring 4-7 times despite multiple surgeries (excluding aspiration alone) [3]. Endoscopic technique commonly uses suspension microlaryngoscopy and CO2 laser to excise the false cord to expose the ventricle effectively marsupializing the cyst. Length of hospitalization for endoscopic resection is, however, typically shorter.

Open excision of a saccular cyst has traditionally been reserved for adult patients with an external component, however, in the pediatric population an external approach can be performed relatively quickly and is typically curative. The transcervical approach involves incision at the level of the thyrohyoid membrane. Dissection is carried down to the cyst and the medial aspect is traced to its laryngeal origin. Several techniques exist to gain access to the internal portion of the cyst. Historically, a lateral thyrotomy was performed, but an alternative approach which does not disrupt the thyroid cartilage involves incising the perichondrium along the superior aspect of the thyroid cartilage and dissecting the cyst out from the false cord and ventricle [4].

There are several important considerations in the decision-making process on whether to proceed with an open or endoscopic approach. One important characteristic is extent beyond the laryngeal cartilage as discussed above. History of prior neck surgery which would make dissection of the neck difficult would further enhance the

risk of possible injury to the superior and inferior laryngeal nerve during an open approach. During an endoscopic approach injury to the vocal cords is possible. Another important factor to consider is the risk of airway compromise. Saccular cysts may cause significant airway obstruction requiring tracheostomy until after definitive management. Typically, the airway compromise is from an internal component of the cyst and the option to proceed endoscopically is still a consideration in this case. Voice outcome data is limited due to the rarity of this condition, however, in one study in adults voice quality was improved in all patients who underwent resection despite endoscopic vs transcervical approach. There was no difference between preoperative and postoperative acoustic analysis [5].

Laryngeal webs

Laryngeal webs can be categorized as congenital or acquired, with the latter being much more common as a result of iatrogenic injury. Congenital laryngeal webs are rare and may present as a neonate with aphonia, stridor, or hoarseness. The Cohen classification has been used to describe the severity of the web based on the percentage of glottic obstruction. Congenital webs can be associated with the genetic deletion 22q11.2 which may manifest as DiGeorge syndrome or Velocardiofacial syndrome [1]. The web may also be variable in thickness, some cases of thin congenital laryngeal webs may go undiagnosed as a result of lysis from intubation.

Acquired anterior glottic webs are more common than congenital web s and may form as a result of prolonged intubation or iatrogenic injury during endoscopic or open airway surgery. These can be seen in cases of recurrent respiratory papillomatosis.

A recent study including 37 total patients (26 congenital and 11 acquired) demonstrated an average of 1.9 procedures/patient for congenital webs, while acquired webs required 3.1 procedures/patient [6]. In this study the majority of patients underwent endoscopic treatment. The laryngeal webs were surgically resolved in 39% of congenital cases with an additional 22% demonstrating improvement and 14% of acquired cases with an additional 29% improved. The overall recurrence rate was elevated in congenital webs, which was 44% and 39% in acquired cases [6].

Despite the recurrent nature of anterior glottic webs, endoscopic intervention is an attractive means of glottic web division since patients can avoid a tracheostomy. A variety of endoscopic techniques have been described including cold steel dissection, division with CO2 laser. Keel placement can now be performed endoscopically as well. Adjunctive agents such as mitomycin C and botox have also been used, however, the efficacy of these injectables has not been well elucidated in the literature [7]. An endoscopic approach is ideal for minor congenital or acquired webs and in patients who have voice complaints, rather than airway obstruction.

Open repair of laryngeal webs has typically been reserved for thick webs and webs with synchronous airway stenosis. In this regard, open repair is a more successful approach in the setting of a congenital webs, which tend to be thicker and have a subglottic component. Surgical technique typically requires a laryngofissure with careful division of the web and allows for the cut edge of the mucosa to be stretched up to the incised edge of the thyroid cartilage to recreate the mucosalized vocal cords (Figure 2). If mucosal coverage cannot be achieved, then placement of a laryngeal keel should be considered. If the cricoid cannot be closed over an age appropriate endotracheal tube, then an anterior cartilage graft may be placed. In very severe webs a posterior cartilage graft may also be a consideration.

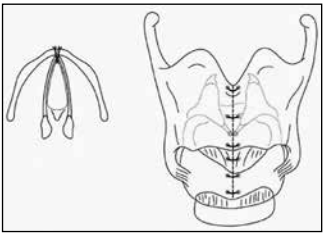

Figure 2. Repair of laryngofissure following glottic web division with resuspension of the vocal cords.

Laryngeal clefts

Laryngeal clefts (LC) and laryngotracheal-esophageal clefts (LTEC) are rare congenital anomalies which form as a result of incomplete partitioning of the larynx and esophagus. Multiple classification schemes exist for LCs and LTECs. The most common classification system used is the Benjamin-Inglis system (Table 1). We have also found that it is also helpful to breakdown the type 4 clefts into "short" which end above carina and "long" which extend to carina and occasionally down a bronchus.

Cleft Extension	Benjamin-Inglis
Interarytenoid	Type I
Extends into cricoid	Type II
Involves the complete posterior cricoid	Type II
Extends into cervical trachea	Type III
Extends to intrathoracic trachea	Type IV

Table 1. Benjamin-Inglis classification system.

Several genetic syndromes have been associated with clefts including Opitz-Frias syndrome and Pallister-Hall syndrome [1]. Patients with aspiration, recurrent pneumonias, or bronchiectasis on chest CT should be evaluated with microlaryngoscopy and bronchoscopy to exclude an H-type TEF, and with rigid instrument probing of the inter-arytenoid area to evaluate for a laryngeal cleft. While success rates are variable among published studies, the largest series of all cleft patients reports an overall success rate of 92% and 97% for those with and without additional airway anomalies [8]. Interestingly, a small percentage of type II and III cleft repairs failed greater than 1 year out from surgery [8]. This suggests that these patients require long-term follow up to reassess cleft repair integrity.

Endoscopic repair has been described for laryngeal cleft types I-III [9]. While type I and type II laryngeal clefts are now commonly repaired endoscopically there are some important patient factors to consider. Endoscopic exposure must be sufficient in order to visualize the bottom of the cleft and the patient should ideally have a cardiopulmonary status that allows them to be maintained under anesthesia with spontaneous ventilation as intubation may compromise the repair. These two considerations are particularly important for attempted repair of type III clefts [9]. Cleft patients depending on the timing of diagnosis, may have poor pulmonary status as a result of ongoing aspiration.

Open repair should be performed for type 4 clefts and strongly considered in patients who have other airway anomalies, such as subglottic stenosis. Children with a laryngeal cleft and another syndrome such as Opitz Frias can be treated endoscopically or with an open procedure depending on the length of the cleft, however, it should

be noted that in our experience these patients have a higher rate of breakdown with either approach. One benefit of open repair is that it allows for the possible placement of an interposition graft of sternal periosteum creating a 3-layer closure.

Tracheoesophageal fistula

Tracheoesophageal fistula (TEF) is a relatively common congenital anomaly, most commonly associated with esophageal atresia (EA). These two anomalies can occur independent of other defects or in conjunction as part of a syndrome such as VACTERL or CHARGE.1 Many patients with TEFs are diagnosed at birth due to associated esophageal atresia, however, the H-type TEF representing 4% of congenital cases may go unrecognized in early childhood. Diagnosis of TEF may be made prenatally on ultrasound by identification of a small or absent stomach bubble in addition to polyhydramnios [10]. Diagnosis is typically confirmed via endoscopy. TEFs may also occur from iatrogenic injury, as a result of caustic ingestion, or button battery ingestion. Repair techniques are variable including both endoscopic and open approaches.

Endoscopic repairs are ideal for long narrow fistula tracts and recurrences after open repair. The techniques described for this involve bugbee cautery, laser, mechanical abrasion, or chemical cautery to create circumferential injury and scar to close off the tract. Submucosal injection of the fistula tract with hyaluronic acid may also be used to help narrow the tract and approximate the cauterized edges of the tract. Endoscopic repair has a significantly shorter operative time, however, repeat procedures may be needed to obtain complete closure [10]. This technique is not typically amenable to a large fistula; however, this can be used as a salvage operation for fistulas that do not completely close after an open approach.

Open repair should be utilized in patients with large TEFs and for those with cartilage involvement. Most congenital TEFs are repaired as part of the esophageal atresia repair through a thoracotomy or thoracosopic approach. TEFs above the third thoracic vertebrae can be accessed via a transcervical approach, while fistula inferior to this level have typically been approached via thoracotomy or thoracoscopic approach [10]. One open technique used for large defects uses trachea overlying the defect as a pedicled flap to close the esophagus and a slide tracheoplasty is then performed over the defect with the proximal and distal ends (Figure 3). Sternal periosteum may also be interposed between the esophagus and trachea for an additional barrier [11]. Complications from open repair include recurrent fistula, (3-10%), and vocal cord paresis/paralysis [10].

If the patient requires ventilation, care should be taken regarding positioning of the endotracheal tube. While it is ideal to position the endotracheal tube distal to the location of the fistula, frequently the TEF is located near carina. If the pouch is large enough advancement of the endotracheal tube may cause the endotracheal tube to enter the pouch causing recanalization of the fistula and or respiratory arrest. Care must also be taken post-extubation with regard to the use of positive pressure, however, there is limited data to suggest that CPAP in the immediate post-extubation period is safe [12].

Figure 3. Use of tracheal cartilage to close a TEF prior to slide tracheoplasty anastomosis.

Neonatal vocal cord paralysis

Vocal cord paralysis (VCP) is the second most common congenital anomaly of the larynx. Both unilateral and bilateral vocal cord paralysis can be a cause of stridor in the neonate. Bilateral vocal cord paralysis requires further work-up to differentiate congenital paralysis from other causes of bilateral vocal fold immobility, including, Arnold-Chiari malformation, hydrocephalus, or acquired posterior glottic stenosis. The decision making can be difficult in this scenario because non-iatrogenic unilateral and bilateral vocal cord paralysis resolve spontaneously in 70% and up to 65% of cases respectively. Most instances of recovery take place within 24 to 36 months. Determining both the timing of intervention and the type of intervention can be difficult for families who are anticipating possible spontaneous recovery. In this chapter we will focus on bilateral vocal fold paralysis, since many children with unilateral vocal fold paralysis are able to compensate with contralateral motion.

Endoscopic intervention for bilateral vocal fold paralysis in the pediatric population has moved away from procedures that are destructive to the endolaryngeal structures as the initial therapy in attempt to preserve these structures in anticipation of possible recovery. Endoscopic interventions commonly used in this scenario include anterior-posterior cricoid split (AP split) and endoscopic vocal cord lateralization. A recent study across four institutions looking at 19 patients with bilateral vocal fold immobility treated with AP split demonstrated a 74% rate of avoiding tracheostomy placement [13]. Vocal cord lateralization has also been described in the neonatal population. A study of 3 neonates with bilateral VCP demonstrated that the lateralization of the vocal cord was stable beyond 3 years in the setting of a rapidly growing larynx and that swallowing and phonation remained intact. Two of the 3 patients in this study had functional vocal cord recovery [14]. Endoscopic posterior costal cartilage grafting has also been described as a means for avoiding tracheostomy tube placement. Although somewhat more technically changing in younger patients, this can be performed in children as young as 3 weeks old [15]. Caveats to this procedure include the risk of aspiration of the graft and risk for post-operative aspiration.

The alternative to endoscopic intervention for bilateral vocal cord paralysis is tracheostomy. Tracheostomy is a safe procedure and allows for observation of the larynx without risk of injury to the vocal cords or endolarynx. Risks post-operatively include accidental decannulation and the very rare risk of trachea-innominate fistula. Post-tracheostomy care requires resources including supplies, suction, and family who are capable and willing to learn trach care for their child. Additionally, in children whose endoscopic exposure is not adequate for graft placement open posterior graft via an anterior tracheotomy remains an option. While this requires an anterior tracheotomy, the improved exposure makes operative time comparable to an endoscopic approach.

Laryngotracheal stenosis

A variety of techniques are described for the management of laryngotracheal stenosis including both endoscopic and open surgery. Typically, endoscopic techniques are reserved for Cotton-Myer grade I and II stenoses while open laryngotracheoplasty (LTP) is typically required to achieve decannulation in grade III and IV stenosis. The mainstay of endoscopic treatment for subglottic stenosis is balloon dilation. In a study comparing endoscopic balloon dilation to LTP, endoscopic balloon dilation was much more successful in the treatment of grade I and II stenosis. Seventy-six percent of patients with grade 3 stenosis who underwent initial dilation required subsequent LTP [16]. This study also found that 11% of patients that were initially treated with balloon dilation

had worsening of their stenosis. While no direct cause and effect relationship should be assumed, this risk should be considered when evaluating a patient for balloon dilation, which is often considered to be a safe and conservative approach. Evaluation of the stenosis itself is important to determine the likely response to balloon dilation. Thin scars which have formed relatively recently to examination are the most likely to respond well to balloon dilation. Acute subglottic stenosis (diagnosed up to 30 days after extubation/tracheostomy) was successfully treated with balloon dilation in 100% of patients in one study, while chronic subglottic stenosis had only a 39% success rate [17]. Scar division and steroid injection can be helpful adjunctive therapies in the setting of a chronic subglottic stenosis to achieve improved results.

One predictor of success when considering endoscopic intervention is the status of the cartilaginous framework. When the cartilage framework is intact and providing enough support, both endoscopic and open interventions are available because the rigidity of the skeleton of the airway allows for change and manipulation of the soft tissue. However, if cartilage support is missing or deteriorated, open surgery is required to restore the framework. All open airway surgery can be categorized as one of the 3 types of operations: augmentation grafting (LTP), cricotracheal resection (CTR), or slide tracheoplasty. The success of open airway surgery for subglottic stenosis is well established. Decannulation rates are reported as high as 100% for single stage LTP and 93% for double stage LTP [18]. Decannulation rates are reported exceeding 90% for cricotracheal resection as well [18]. CTR is ideally used for short segment stenosis 3 mm below the vocal cords. Injury to the recurrent laryngeal nerves is a higher risk in this procedure. Slide tracheoplasty is typically utilized in cases of long segment stenosis, tracheal stenosis and complete tracheal rings and is typically performed as a single stage procedure.

As technology has advanced and pushed surgical innovation forward, we have generated new solutions and techniques to treat airway pathology while minimizing morbidity. Endoscopic techniques offer an excellent alternative to open procedures with generally faster operative time and shorter inpatient hospitalization. However, assessment of risk and surgeon experience should be considered prior to proceeding. Complications following airway intervention can lead to respiratory arrest and death. Tracheostomy and conservative management in any patient with airway obstruction should always remain on the list of management options.

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Why every boy and girl should have HPV vaccination

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Introduction

Perhaps the greatest global population health advance in the entire history of medicine is the development of vaccines that prevent a myriad of diseases from smallpox to polio. In the USA, almost everyone got measles in the pre-vaccination era and hundreds died each year. In 1921, over 15,000 people died from diphtheria. With widespread vaccination, there were only 2 cases reported from 2004 – 2014. And, in 1964-5, rubella infected 12.5 million Americans with 2,000 infant deaths. After vaccination was introduced in 1966, rubella nearly disappeared within a decade.

Human Papilloma Virus (HPV) is the most common sexually transmitted infection from human to human. Over 14 million new HPV infections occur each year in the United States. Over 50% of American women and men have at least one strain of HPV by 50 years old. HPV subtypes 16 and 18 account for over 70% of cervical cancers, 50% of anal cancers, 40% of vulvar cancers and 40% of penile cancers. Over 10,000 new cervical cancers are diagnosed in the United States each year with over 3,00 deaths. Moreover, the Center for Disease Control (CDC) in 2017 estimated that new HPV-related oropharyngeal cancers due to HPV subtypes 6 and 11 occur annually in men and over 3,200 in women. The CDC notes that HPV related oropharyngeal cancers have risen steadily over the past 15 years.

How vaccines work

Vaccines are like a training course for the immune system. When foreign invaders such as viruses or bacteria enter the body, lymphocytes produce antibodies to fight the foreign invader and protect against future infection. Vaccines induce this response by imitating an infection to produce T-lymphocytes and antibodies. This leaves the body with a supply of memory T-lymphocytes and B-lymphocytes that remember how to fight a potential future infection.

Traditionally, when at least 90 - 95% of the population has been vaccinated, this confers herd immunity with dramatic reduction to the possibility of swift and widespread transmission by one unvaccinated person. HPV transmission differs from many other infectious diseases for which there are vaccines by its direct person-to-person trans-

mission requiring direct mucosal contact rather than airborne transmission. Therefore, herd immunity differs with minimal risk of swift and widespread transmission.

HPV vaccination

The 4-valent vaccination called Gardisil (Merck) first became available in 2006. In addition to covering the 16 and 18 subtypes that cause anogenital cancers, the manufacturer also included subtypes 6 and 11 that prevent recurrent respiratory papillomatosis. The 2-valent vaccine that became available in 2009 called Cervarix (Glaxo Smith Kline) only contained subtypes 16 and 18. Gardisil became more popular and promoted by the CDEC and professional societies for its greater coverage. Subsequently, Cervarix was discontinued in the USA. In 2014, Merck introduced the 9-valent vaccine that also included subtypes 31, 33, 45, 52 and 58. This broadened the preventive coverage. Moreover, the immunization schedule went from a 3 to a 2 shot series with better compliance. The vaccine is FDA approved for both females and males ages 9 – 26 years old. The reported adverse effects are minimal with reported syncope, local pain and redness, dizziness, nausea and headache. There are 2 total reports of amyotrophic lateral sclerosis (ALS) that has been attributed to the HPV vaccine.

Parental vaccine reluctance and misinformation by anti-vaccine groups have lessened the anticipated vaccine rates with the CDC reporting only 51% of adolescents ages 13 – 17 fully vaccinated in 2018. Over 68% received at least one dose. State and regional vaccine rates vary widely with immunization rates ranging from 21% in New Jersey to 78% in Rhode Island. States legislate their own vaccination requirements and vary on their medical and religious vaccination exemption laws (Figure 1).

The experience in other countries is also widely divergent. Australia developed a mandatory vaccination program for girls 12 – 13 years old in 2001 and boys similarly in 2013. They achieved over 85% immunization rates. The results so far demonstrate an unqualified success with identifiable genital warts in females decreasing from 22.7% in 2005 to 1.1% in 2015. Precancerous cervical abnormalities decreased 34% in the same time period in females 20 – 24 years old. The Australian initiative serves as a highly successful population health model for mother nations to emulate.

In contrast, Japan has a very different experience with HPV vaccination. Initial rates were high with a 70% vaccination rate by 2013. However, unsubstantiated reports by anti-vaccination groups of adverse effects led to Health Ministry reluctance to promote vaccination. Subsequent vaccination rates plummeted to <1%.

In 2011, the Argentina developed a national HPV immunization program for all girls 11 years old. By 2013, 87.9% received at least 1 dose and 52.2% received all 3 doses.

So, why are parents reluctant to have their children immunized? In multiple parental surveys the most common negative responses include:
– not needed
– lack of knowledge
– safety concerns
– not recommended by pediatrician
– child not yet sexually active

Advocates counter that all children, boys and girls should receive the HPV vaccination to prevent sexually transmitted warts that lead to cancer of the cervix, vulva, penis, anus, and the oropharynx. Physicians and all health care professionals should advocate for HPV vaccination. The general public needs to better understand the health

benefits of vaccination and most certainly the benefits of a vaccination that prevents cancer.

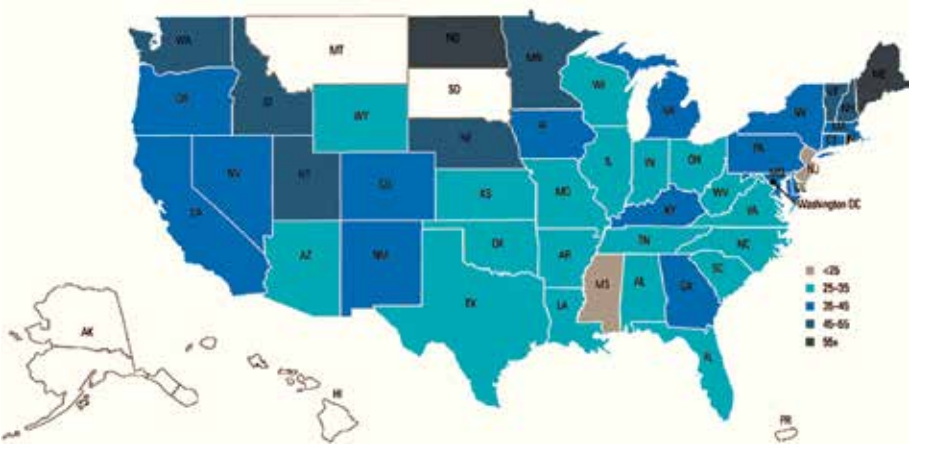

Figure 1. Percent of all adolescents who completed the first dose of the HPV vaccine before their 13th birthday by state (completion year -2016).

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Dysphonia in children and professional singers

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Various case studies representing a variety of voice disorders in children as well as singers will be considered, including a review of potential evaluation and treatment approaches.

Endoscopic evaluation of voice

Voice assessment protocol of children with voice disorders consists of many components, including rigid and flexible endoscopic examinations. Various factors are considered in selecting the optimal assessment tool including the patient's age and coopera-

tion for completing the examination. A pediatric rigid endoscope can be completed on many younger, compliant children and this produces high quality images. If a patient is very young or unable to complete rigid endoscopy, flexible fiberoptic endoscopy can be completed using smaller size diameter scope for younger children, if better tolerated. New smaller size distal chip videoscopes (2.6 mm) have improved image quality compared to fiberoptic instruments and can also be performed on younger patients. Some older children can complete both rigid and flexible stroboscopic examinations.

Vocal fold lesions

A 5-year-old female presented for evaluation of dysphonia. She was referred by her pediatrician due to chronic rough sounding voice which had been noted since birth. There was no history of vocal abuse or voice loss. The family reported they have assumed what they hear is just "her voice" and therefore did not have specific voice concern. Without the pediatrician's recommendation for comprehensive voice evaluation, her family would not have pursued assessment. Perceptually, she demonstrated moderate dysphonia characterized by strain and roughness. Flexible stroboscopy revealed presence of bilateral vocal fold lesions and mild vocal fold edema.

An initial approach to management could include completion of voice therapy. If improved perceptual voice quality is achieved, further treatment or surgical intervention may not be indicated. Completion of voice therapy can establish healthy vocal hygiene habits and reduce vocally abusive ones, to maximize and improve overall perceptual voice quality. Previous research has indicated improved lesion resolution rate after incorporating a vocal hygiene education program (Hosoya et al., 2018). Phonotraumatic behaviors such as yelling, loud talking, and vocal play sounds can negatively impact voice. If reduction of these behaviors is not demonstrated during voice therapy and surgery is considered in the future, the lesions could recur postoperatively. A variety of direct voice therapy exercises could be incorporated, in addition general vocal hygiene education. Examples of direct voice therapy programs that could be incorporated include resonant voice, semi-occluded voice therapy techniques, flow phonation, and vocal function exercises. If vocal fold edema is present at diagnostic examination and there are limitations with establishing a definite diagnosis (i.e., whether differential diagnosis includes vocal fold nodules versus cyst), a clearer diagnosis can be established post-therapy when edema is often reduced.

Surgical treatment for surgical excision of lesions could be considered when the patient is older, around 7 years of age, if there has been limited response to voice therapy and no perceptual voice improvement despite adequate patient participation. Receiving voice therapy prior to surgical intervention can positively impact surgical outcomes. Preoperative voice therapy is also associated with improved vocal hygiene habits and reduced phonotraumatic behaviors that could impact healing postoperatively (LeBorgne & Donahue, 2019). If resolution of the lesions post-therapy is not achieved, overall responsiveness and ability to incorporate behavioral change can be assessed with successful completion of voice therapy. This helps determine if surgical intervention could be considered. Future surgical intervention is warranted if the patient is determined to be a good surgical candidate and there has been no improvement in perceptual voice quality. The patient and family's perception of the severity of the voice disorder, desire for surgical intervention, and discussion of the "right time" to proceed with surgical treatment are important considerations.

Professional singers

An 18-year-old female complained of limitations in the high range of her singing voice and reported chronic voice strain following completion of recent musical theater

performances. The patient reported a history of singing in school and church choirs for several years prior to performing in musical theater productions. Vocal demands had increased significantly during her recent performances. She noted plans to be a musical theater major in college with aspirations to pursue singing professionally as a career. Pertinent information to gather during the voice assessment case history of singers includes onset of current symptoms in addition to the patient's previous singing training, any previous formal instruction such as singing lessons or having a vocal coach, the singer's current voice part (soprano, alto, tenor, bass), and singing style (i.e., classical, pop, jazz, musical theater). Previous research has demonstrated improvements in singing voice from receiving formal instruction (Teachey, Dominguez, & Simpson, 1991). Additional pertinent information to obtain can include whether the current symptoms impact singing and speaking voice, vocal hygiene habits, participation in other school-based activities, and any periods of voice loss. Some singers may not pursue formal voice evaluation until they become symptomatic with suspected vocal pathology, due to the increased performance demands and schedules of many professional singers and artists.

The patient's laryngeal imaging findings included presence of left vocal fold cyst and right reactionary lesion. Vocal hyperfunction and decreased bilateral vocal fold vibratory characteristics were noted specifically with sustaining the high pitches in her singing voice. Common vocal pathology of singers can include vocal fold lesions (nodules or cyst), vocal hyperfunction, and muscle tension dysphonia. These can be caused by voice misuse and over-use. The patient was not interested in initial surgical management, as she reported concern regarding the possible impact of cyst removal on the unique element of her singing voice. She noted concern as to whether this may also affect her ability to obtain the parts she desired at musical theater auditions.

Initial recommendations for the patient can include voice therapy, prior to considering surgical intervention. It is beneficial for singers to receive voice therapy with a speech-language pathologist who has specific expertise in working with singers, as a singing voice specialist. Young singers and performers are vocal athletes and have been compared to physical athletes. It is imperative that they receive instruction on proper technique and healthy voice habits as a physical athlete would (Donahue et al., 2013). Improper singing technique, lack of voice rest or vocal warm-up, increased frequency of vocal performances, and voice overuse can potentially lead to vocal pathology.

During the patient's course of voice therapy, direct voice therapy exercises can be incorporated in addition to indirect therapy including vocal hygiene education. Specific voice therapy techniques for singers can be chosen based on symptoms and diagnosis. Voice therapy goals can also include establishing correct singing part and vocal range. A singer may have always sung soprano part, but the voice may be more suited for alto range. Following completion of voice therapy, overall therapy responsiveness can be determined during the patient's post-therapy voice evaluation. A decision as to whether sufficient voice improvement has been achieved during therapy can be made by the patient and voice treatment team. If further voice improvement is desired and the patient's singing voice continues to be impacted, surgical removal of the cyst can be considered. Vocal fold cysts have been found to be less responsive to voice therapy as compared to vocal fold nodules, and this should be taken into consideration as treatment plan is established (Tibbetts, Dominguez, & Simpson, 2018).

Unilateral vocal fold paralysis

A 10-year-old female with cardiac surgical history of patent ductus arteriosus ligation presented for voice evaluation. She reported long-standing breathy voice quality and difficulty with increasing her voice volume. There were limitations with projecting her voice when background noise was present. Her family described her as having a quiet personality. There were no breathing complaints. Perceptual assessment of voice included a significantly decreased maximum phonation time of 7 seconds and mean intensity measurement of 63 dB SPL. Flexible stroboscopic examination revealed left vocal fold paralysis in paramedian position and large posterior glottic gap. Initial temporary treatment options could include injection laryngoplasty and voice therapy. Shorter term injectibles such as Radiesse voice gel or Restylane can initially be administered to determine if adequate voice improvement is achieved. Injection laryngoplasty alone or in conjunction with post-injection laryngoplasty voice therapy can improve glottic closure and perceptual voice quality, prior to considering other permanent surgical options.

A current permanent surgical mainstay for treatment of pediatric unilateral vocal fold paralysis is recurrent laryngeal nerve reinnervation. This is performed in conjunction with injection laryngoplasty. This can result in both improved tone and positioning of the vocal fold during phonation, but it does not restore vocal fold mobility. Voice therapy post-laryngeal nerve reinnervation can maximize voice improvement. Perceptual voice characteristics post-therapy or surgical intervention for unilateral vocal fold paralysis can include decreased breathiness and strain, increased volume, and improved ability to project voice. Other possible procedures for treatment of unilateral vocal cord paralysis can include medialization laryngoplasty, arytenoid adduction or arytenopexy.

Post-airway reconstruction dysphonia

A 12-year-old female complained of chronic dysphonia for many years. Medical history included premature birth at 27 weeks, tracheostomy, and laryngotracheoplasty with posterior cartilage graft that she underwent at age two. Primary airway management was successful, and there were no breathing concerns. She demonstrated breathy vocal quality, significantly reduced voice volume during sustained vowels and connected speech, and an intermittent lower-pitch voice. She reported frustration that she often has to repeat herself, particularly in noisy environments. Due to persistent voice concerns, she presented for voice evaluation. She and her family were interested in secondary management of voice.

Voice evaluation in patients demonstrating post-airway reconstruction dysphonia includes obtaining instrumental voice assessment measures (acoustic and aerodynamic analysis), perceptual evaluation, and laryngeal imaging for examination of anatomy and identification of phonation sources. The patient completed flexible stroboscopic examination which revealed bilateral arytenoid fixation, suspected posterior glottic incompetence, and large posterior gap during phonation. The primary phonation source was glottic, however occasional supraglottic phonation as an alternative phonation source via the false vocal folds was visible when increasing voice volume. Supraglottic phonation and compression limited the visualization of the posterior glottis. Voice outcomes following airway reconstruction often include dysphonia, which may result from posterior glottic diastasis, posterior glottic gap, and vocal fold immobility. Common perceptual voice characteristics include roughness, breathiness, low pitch for age and gender, periods of aphonia, utilization of supraglottic phonation to compensate for glottic incompetence, presence of two phonation sources (glottic and/or supraglot-

tic), and inhalation phonation. A dynamic voice CT can be completed to further evaluate the posterior glottis in patients with post-airway reconstruction dysphonia. This new laryngeal imaging technique can also verify glottal gap and examine vocal cord mobility, as supraglottic phonation may prevent adequate visualization of posterior glottis during rigid or flexible stroboscopy (de Alarcon et al., 2019).

Management of post-airway reconstruction dysphonia can be a complex process and is tailored to each patient's unique presentation. The specific voice concerns of the patient and family in addition to the timing of when the patient chooses to pursue treatment are all important factors to consider. Successful airway management and decannulation are the primary focus when patients are younger, typically between ages 1-5. As children become older, approximately 11 years and up, voice often becomes more of a concern as social interaction and others' perceptions of their voice can play a greater role. This patient's concern included limitations with social interaction and insufficient voice volume, which impacted her communication across many environments including at school and home.

Initial surgical procedures for secondary management of post-airway reconstruction dysphonia can include injection laryngoplasty. This can effectively increase volume and decrease strain during voice production, specifically with supraglottic phonation. Increased strain and effort are often noted if there is glottic incompetence, especially with supraglottic phonation (Weinrich et al., 2007). More improvement with supraglottic phonation is often noted as compared to glottic phonation, as injection aids with bulking supraglottic structures for improving approximation and closure (Kelchner et al., 2014).

Further framework surgical intervention could also be considered for the patient. Endoscopic posterior cricoid reduction is a surgical procedure for improving post-airway reconstruction dysphonia or postintubation dysphonia, for treatment of posterior glottic diastasis. This involves reduction of the posterior glottic region. Recent research has shown this procedure can effectively reduce posterior glottal gap and improve voice. Postoperative voice assessment findings have demonstrated increased volume and improved voice efficiency with significant increase in maximum phonation times (de Alarcon et al., 2019).

Voice therapy alone or in conjunction with secondary surgical management of voice can maximize voice outcomes in patients with post-airway reconstruction dysphonia. Incorporating therapy techniques such as resonant voice therapy or semi-occluded techniques can help decrease strain and effort during phonation and elicit more efficient voice production (Titze, 2006; Kelchner et al., 2014). If there are two phonation sources, a decision is often made as to which voice to target during therapy. Typically, this is dependent on which voice is more functional and can include which voice is louder, more intelligible, and which is more age and gender appropriate. Supraglottic voice production can sometimes be a better option for primary voice production as compared to glottic phonation. Supraglottic phonation is often louder despite the notable elements of roughness and low pitch. A patient may be unaware they are capable of two voice productions. A first step in therapy can include identifying the presence of two voice productions and producing each separately. An advantage of completing endoscopy/stroboscopy in patients demonstrating two phonation sources is that it can serve as a diagnostic auditory feedback technique, to trial if the patient can identify and produce each of the voices (glottic and supraglottic).

Designation of "old voice" and "new voice" are terms that can be assigned to distinguish, identify, elicit, and increase generalization of the preferred voice. As voice is tied closely to identity, others' perception of the new voice can be a concern of the

patient. There is generally more peer acceptance of voice when patients are younger. Generalization of the targeted voice across environments can be the most challenging task in voice therapy. It is a hierarchical process of incorporating practice trials using the new voice with various communication partners. Practice trials with the new voice can be incorporated during therapy and can progress to trials with family members at home, friends, and peers in other environments such as school and in the community.

Puberphonia

A 16-year-old male presented for evaluation with voice concern for two years, including persistent high-pitch voice, roughness, and pitch breaks. There were a few symptoms suggestive of reflux. He was placed on a course of anti-reflux medication with no improvement. Due to his inability to project his voice, he was unable to referee soccer anymore. Acoustic and aerodynamic data revealed a habitual pitch of 207.55 Hz and mean intensity of 66.6 dB SPL. Perceptually, he demonstrated moderate dysphonia characterized by high pitch, breathiness, strain, and decreased volume. His CAPE-V rating score was 51 (moderate). The CAPE-V is a visual-analog voice perceptual rating scale, from 0 to 100. A rating of 0 would be no voice disturbance with 100 being the most severe. Ratings are classified along the scale from mild, moderate to severe (Kempster et al., 2009). During connected speech and trial voice therapy tasks, he demonstrated the ability to produce lower-pitch voice during laughing and throat clearing, although he was unaware of this production. There was also noted musculoskeletal tension during speech.

Puberphonia is the inability of a pre-adolescent higher-pitch voice to transition to lower-pitch following puberty. Perceptual voice characteristics include high-pitch, breathy, strained, weak, diplophonic, and child-like voice. A course of treatment includes voice therapy, and voice therapy techniques and manual laryngeal reposturing can be incorporated. The patient was able to identify between the higher pitch and new, lower pitch voice productions and was eventually able to produce each separately. Manual laryngeal reposturing and circumlaryngeal approaches can be administered by the speech pathologist and can later be incorporated by the patient repositioning his own larynx as needed. Therapy tasks include progressing through a hierarchy of producing vowels, phrases, and sentences using the lower-pitch voice. Manual laryngeal reposturing has been found to be an effective primary treatment approach for puberphonia (Roy et al., 2017). Negative practice techniques can also be incorporated to increase awareness of both the sound and feel of the separate voice productions, and how to maintain the new, lower-pitch voice. Carry-over of the new voice in patients with puberphonia is also a hierarchical process. It can initially be more challenging to utilize the voice with peers and friends compared to familiar family members. After three therapy sessions, the patient was able to generalize the new, age-appropriate lower-pitch voice to connected speech across all environments. The patient reported maintenance of this voice several months following completion of voice therapy.

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Esophageal foreign bodies in pediatrics: The otorhinolaryngologist's performance

Edio J. Cavallaro Magalhães, MD, and **Janaína Bentivi**, MD, PhD.

Introduction

Esophageal foreign bodies (FB) are common among children. It is especially observed between 6 months and 3 years old and most of ingested foreign objects passes spontaneously without any complication (80%), while 10 to 20% require removal.

Recent studies have shown that the occurrence of accidents by ingestion of foreign bodies increased more than 90% in the last two decades (in the United States), highlighting the importance of further knowledge of the management of such cases by health professionals nowadays.

Traditionally, in some referral hospitals, the peroral endoscopist otorhinolaryngologist is the responsible for the management of esophageal FB. Therefore, a training program of this specialist is essential for better understand the problem and act safely in each case (respecting local limitations).

Epidemiological data and diagnosis

A recent retrospective study that considered children under 6 years-old who were attended due to FB ingestion in the United States, from 1995 to 2015, have showed that the annual rate of this problem increased 91.5% (rate per 10 000 children from 9.5, in 1995, to 18, in 2015).

An analysis of the 10 years' experience at the Department of ENT emergencies of Hospital Municipal Souza Aguiar, Rio de Janeiro (from 2005 to 2014), regarding children of 0 to 12 years-old with esophageal foreign bodies have showed the main features summarized in Table 1 below. As seen, approximately 90% of cases of pediatric esophageal foreign bodies were metallic objects.

Gender		Type of foreign body					TOTAL
Male	Female	Coin	Button battery	Other metallic objects	Bone	Other	
777	758	1.251	36	94	30	124	1535
(50,62%)	(49,38%)	(81,49%)	(2,34%)	(6,12%)	(1,95%)	8,07%)	

Table 1. Some characteristics of cases of esophageal foreign bodies attended at the Department of ENT emergencies of Hospital Municipal Souza Aguiar, Rio de Janeiro (from 2005 to 2014).

The clinical presentation is variable. In our experience, the most common symptom is sialorhea. Other symptoms like dysphagia, sore throat, and vomiting or respiratory symptoms (such as cough and dyspnea) may occur. However, approximately 20% of cases are asymptomatic. In these cases, relatives witness the foreign body ingestion or are alerted by the child.

The characteristics of the ingested object (perforating?, circular?, potentially corrosive?), previous health conditions, and time elapsed between ingestion and medical care are important to management. But sometimes the ingestion is not witnessed by parents or caregivers what makes diagnosis difficult.

In our region, as mentioned, metallic objects predominate. Thus, plain radiographies (neck and chest at posterior to anterior and lateral views) are sufficient for diagnosis at the most of cases (Figure 1). Button batteries are coin-shaped metallic objects with great potential for complications and must be identified as soon as possible. In these cases, the presence of signs of slight corrosion and, mainly, the presence of the double halo signal (Figure 2) allow their identification. Sometimes it is easy to confuse with two overlapping coins impactation. In these cases, a diagnostic and therapeutic esophagoscopy is indicated. Also, it is important to note that "all that glitters is not gold". Sometimes we identify small metallic images on radiographs that, in fact, represent only a part of a foreign body composed mostly of plastic (Figure 3).

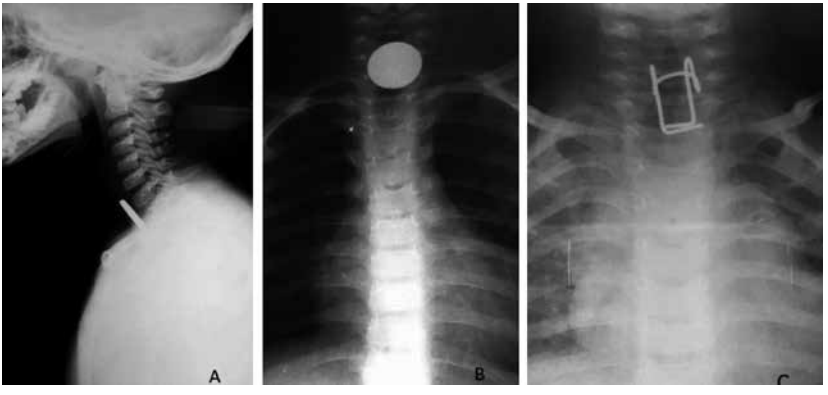

Figure 1. A: Plain film - Coin in upper cervical esophagus - lateral view. B: Plain film - Coin in upper cervical esophagus - PA view. C: Clothespin metal - PA view.

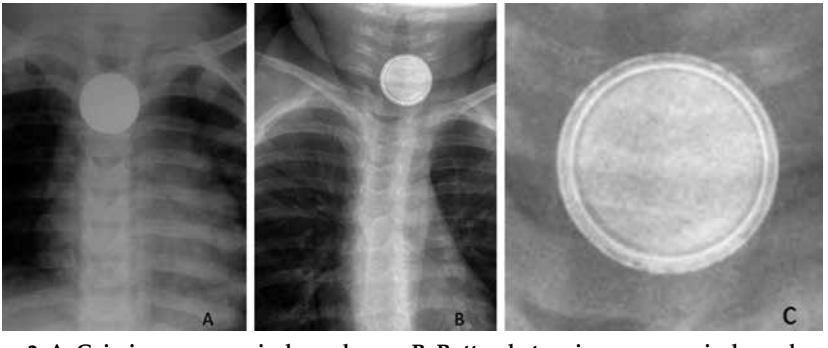

Figure 2. A: Coin in upper cervical esophagus. B: Button batery in upper cervical esophagus. C: Button battery: double halo signal.

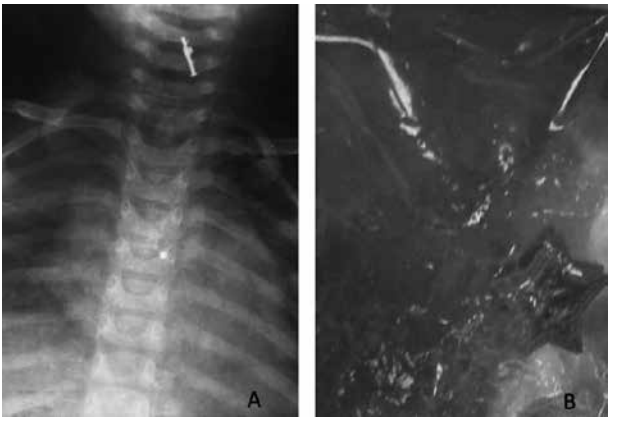

Figure 3. A: Spring-shaped metallic object. B: Real shape of the object: plastic hair pin with metal shaft and spring.

The swallowing of a small piece of cotton soaked in oral barium sulfate contrast is useful to diagnosis little radiopaque or radiotransparent foreign bodies. When history and symptoms are compatible, the identification of contrast stucked in the esophageal pathway greatly increases the possibility of a esophageal foreign body, indicating exploratory esophagoscopy under general anesthesia. On the other hand, even if imaging tests (with or without contrast) are negative for FB, a witnessed ingestion and the presence of symptoms (mainly sialorrhea and dysphagia) must be considered and the exploratory esophagoscopy under general anesthesia is indicated.

Long duration of impaction, button-batteries and perforating FB are more prone to lead to complication, such as esophageal perforations, mediastinitis, pleural effusion, fistulas, diverticula, and others. In the case of organ perforation and its complications, the main symptoms are cervical subcutaneous crepitation, fever, dyspnea, and worsening in general condition. In these cases, a multidisciplinary team with Pediatrician, Pediatric Surgeon and Thoracic Surgeon is prepared. The computed tomography of the neck and chest must be performed and the administration of oral barium sulfate contrast is contraindicated. Iodinated contrast agents are one option.

Treatment

There are several management options available: pharmacological therapy with conservative approach, flexible endoscopy, rigid endoscopy, Foley catheter removal, esophageal bougienage, forceps extraction, surgery and pushing the FB to the stomach. The treatment choice depends on several factors as follow: age and clinical conditions of the patient, shape, size, type, localization e number of FB, and personal experience and preference of the physician. The safety of performance and costs must be considered too.

The conservative approach with inpatient or outpatient observation reduces complications and costs but must be accompanied by sequential radiographic study and we often do not identify the object's progression, indicating its removal at a later time.

In our Hospital, the Foley catheter removal is our elected method for coins located in up to the middle third of the thoracic esophagus, less than 36 hours of impaction and no history of previous disease or esophageal surgery. This procedure can also be per-

formed if the duration of impaction is no longer than 72 hours, but the chance of success decrease 50%. Also, the hospital must provide pediatric direct laryngoscope, rigid esophagoscope and bronchoscope, laryngeal and bronchial forceps, suction apparatus and oxygen supply; it all kept ready.

In summary, we use the following technique (Figure 4): (1) The balloon of the Foley catheter number 08 or 10 is first tested to make sure it inflates symmetrically. (2) With the child sitting on caregiver's lap, the catheter is inserted transorally, advancing it inferiorly while the child swallow it, until it pass about 20-25 cm from the dental arch, passing distally to the ingested FB. (3) Then the balloon is inflated with 8 mL air. (4) Before the catheter is withdrawn, the child is placed in a prone oblique position with mild cervical extension. (5) With moderate traction, the inflated balloon pulls the foreign body out from the esophagus. No child is sedated and he/she is kept in seated position, restrained by one of his/her caregiver. If the child is not cooperative, a tongue depressor may be used to prevent the child from biting the catheter. After a successful try, the child is monitored for 30 minutes before be discharged. The parents are instructed to feed the child with a soft diet and to return immediately if the child has symptoms of chest pain, fever, dysphagia, bloody saliva, respiratory difficulty or abdominal pain. If three attempts fail, this technique is suspended and the child must be referred to a new radiographic study and forwarded to the rigid esophagoscopy or removal with Magill forceps under general anesthesia. In our series, the success in removing coins from the esophagus with this technique was 95.3%, which represents the removal of 77.66% of all esophageal foreign bodies in children with a simple, effective and safe technique (when carefully followed its indications). About costs, the literature estimates that the removal of esophageal FB by Foley catheter is 20 to 50 times cheaper than esophagoscopy under general anesthesia.

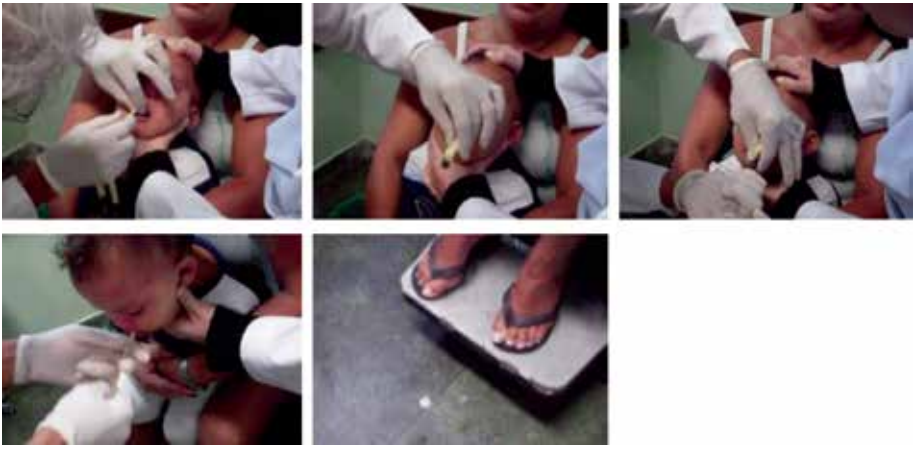

Figure 4. Technique removing coin from the esophagus with Foley probe.

Currently, all cases of non-coin esophageal foreign bodies (and those that are but have not been successfully removed with the Foley catheter) are taken to the operating room for exploration and removal by esophagoscopy under general anesthesia. Magill forceps under laryngoscopy can be used to remove esophageal FB as long as it is lodged at or immediately below the level of the cricopharyngeus muscle (upper esophagus) and better if it is a safety pin. This procedure is a minimally invasive method compared to rigid esophagoscopy.

We used the following technique to perform rigid esophagoscopy in children under general anesthesia: (1) Supine position placement with the neck in neutral position. (2) Dental protection with gauze. (3) Endoscope held between the first and second fingers of the non-dominant hand. The third finger is used to open the mouth and support the endoscope on the incisor teeth. (4) Introducing the esophagoscope into the oral cavity and advancing on the tongue to the posterior pharyngeal wall. (5) Slip the tip of the device through the hypopharynx, changing the angle of entry (from 90° to an angle parallel to the pharyngoesophageal tract). (6) Careful advancement of the instrument under direct vision with the thumb of the non-dominant hand. The other hand is used to change the angle of entry, avoiding unnecessary pressure on the esophagus. (7) Aspiration of esophageal lumen if necessary. (8) Examination of the walls and lumen of the organ and removal of the foreign body. (9) Revision of the esophageal mucosa, mainly during the slow and gradual removal of the esophagoscope, gently rotating it on its axis. The Figure 5 shows a sequential endoscopic view of the procedure.

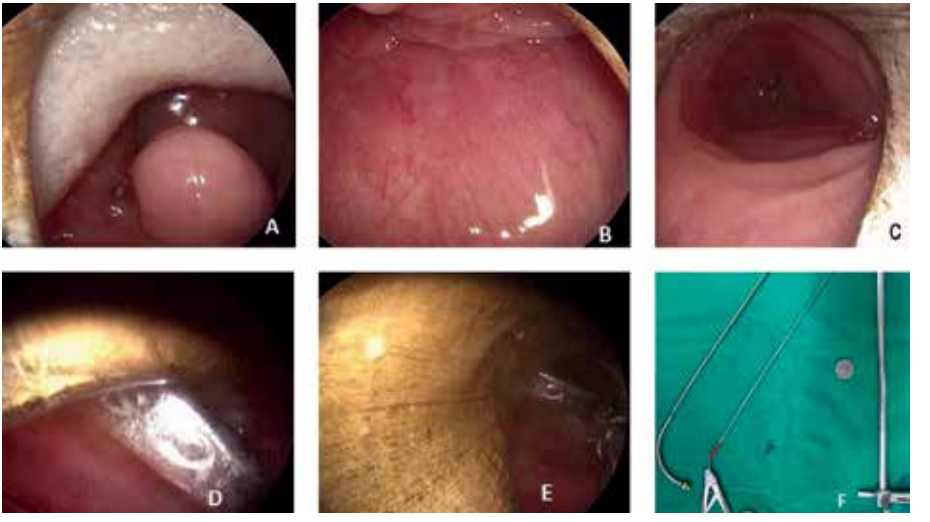

Figure 5. A: Uvula. B: Upper esophageal sphincter. C: Esophageal lumen. D to F: Removing a coin.

If esophageal perforation is suspected during the procedure, a nasoenteral tube is inserted at the same time, under general anesthesia, in order to guarantee nutrition and protect the esophageal mucosa until a confirmation after contrast imaging tests. The same approach is taken in cases of great local tissue damage due to button batteries.

Button batteries deserve special attention in our Hospital. The aim is to remove then within two hours after the child's admission (ideally within two hours after ingesting the object), as we know that after this period the amount of caustic material released can cause more serious injuries. In these cases, we have recently adopted the approach of irrigating the affected mucosa with 0.25% acetic acid, after removing the battery, in order to neutralize the process of mucosal damage caused by the alkaline substance released at the site.

Conclusions

Accidents with foreign bodies in children, including esophageal, are common in emergencies, and otolaryngologists must be able to manage the problem. The diagnosis is easy most of the time because, in our experience, radiopaque foreign bodies account for more than 90% of pediatric cases (especially coins). The Foley catheter removal is a high success rate and safety procedure widely used in our Hospital.

The otolaryngologist must have a multidisciplinary team, with surgeons and radiologists, and also proper hospital facilities (with procedure room, operating room, bronchoscopy, esophagoscopy and emergency support) to provide fast, safety and effective treatment to children with esophageal foreign body and its complication.

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Animal simulation for airway foreign body and open airway surgery

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Foreign bodies within the trachea, emergent tracheotomy, and open airway reconstruction are potentially life-threatening situations that ENT physicians may confront during their career. Management of pediatric airway foreign bodies requires swift, precise endoscopic skills that cannot be "practiced" with a patient in the operating room. However, Residents training in the United States (US) only experience approximately 1.3 aerodigestive foreign body cases per year [(1)]. Although tracheotomy case log numbers in Otolaryngology residencies have declined over time, the Otolaryngologist must learn and maintain the skill set and confidence to obtain a surgical airway in an

emergency situation [2,3]. In addition, as more pediatric airways are able to be managed endoscopically, trainees may only see a small number of open airway surgical reconstructions during a 5 year Otolaryngology residency. This is a skill set that needs to be taught, refined, and reinforced as these same skills are used in basic neck and airway surgery.

Simulation is an integral part of successfully training future physicians, particularly for complex and low-frequency procedures. Various simulation models have been used for airway management and airway surgery including low and high-fidelity mannequins, task-trainers with feedback, virtual reality, simulated scenarios in an "OR" or "ER" environment, three-dimensional printing as well as animal models: ex-vivo and in-vivo [4]. Face validity (realism/anatomical accuracy) and feasibility of an ex-vivo ovine head and neck tissue model for use in simulation of tracheostomy, cricothyroidotomy, laryngofissure, tracheal resection with slide tracheoplasty, laryngotracheoplasty, and laryngectomy have been reported [5]. However, the closer the simulation is to a "real life" situation, the better the skillset and preparation the physician will have when faced with those challenges in practice.

A recent prospective observational study evaluated the validity of an in-vivo, live porcine model for trainees learning pediatric tracheotomy and laryngotracheoplasty and found high face validity (realism/anatomical accuracy) and content validity (perceived effectiveness) for tracheotomy and laryngotracheoplasty using anterior costal cartilage and thyroid ala cartilage [6]. The live porcine model provides realistic tissue haptic feedback as well as an opportunity to practice dynamic airway management and hemostasis [6]. There are some important anatomical differences including relative positions of the thyroid and cricoid cartilages to the trachea, which are more anterior in the porcine model, and the thyroid gland, which is more superiorly located in the porcine model. This necessitates small adaptations in the surgery including removing the thyroid gland to access the cricoid cartilage. These are detailed in the Airway Reconstruction Dissection Manual by Propst et al., which also details modifications required for rib harvest [7]. Although this model has not been specifically studied for evaluation of surgical competence, other tools have been developed to assess trainees during simulation and further investigation is ongoing [8-10].

At the University of Texas Southwestern Medical Center in Dallas, we have created an airway foreign body simulation and open airway reconstruction course for our Otolaryngology residents and Pediatric Otolaryngology fellow. As described by Dr. Propst, we use a porcine model for our simulation due to its realistic nature and size which approximates the pediatric airway [7]. Our project was approved by our institution's animal research center (ARC) and Institutional Animal Care and Use Committee (IACUC). The IACUC is a committee of scientists, non-scientists, veterinarians and community members who oversee the welfare and humane treatment of animal research subjects in accordance with Public Health Service (PHS) and the Animal Welfare Act. We have a veterinary team from our animal research center who prepare the pig before the course, maintain total intravenous anesthesia during the course, and euthanize the pigs after simulation procedures have concluded.

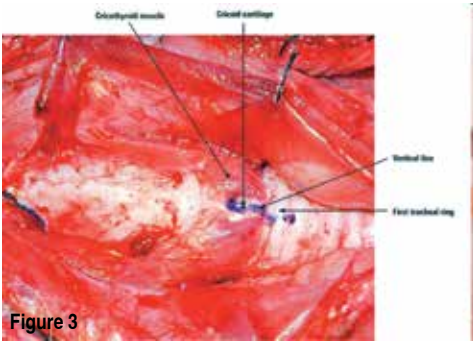
The airway foreign body simulation includes diagnostic rigid bronchoscopy and foreign body removal on anesthetized pigs. We use a 10-20 kilogram pig for which a size 3.5 or 4.0 bronchoscope is used to evaluate the airway. We have a camera, light source and tower with a screen for visualization. Endoscopic instruments including optical forceps (alligator, peanut graspers) are available. The pig is intubated and anesthetized in the anesthesia suite and then brought into the operating room (OR) and placed on

the OR table where heart rate and oxygen saturation are monitored. Prior to placing the bronchoscope, all participants perform direct laryngoscopy on the intubated pig given that the pig larynx is slightly different than the human larynx with larger and more anteverted arytenoids, more anterior larynx and long soft palate. Next, the participant performs direct laryngoscopy, obtains a view of the larynx, removes the endotracheal tube and performs the bronchoscopy, evaluating the airway down to each main bronchus. Once the bronchoscope is removed, the pig is bag and mask ventilated by the trainee. If the saturation drops or the pig is not able to be ventilated, direct laryngoscopy and intubation are performed (Figure 1). Participants also monitor clinical signs such as cyanosis, chest rise, and condensation in the endotracheal tube or mask during ventilation.

After diagnostic bronchoscopy is performed by all participants, the airway foreign body removal task is started. The participant who is going to remove the foreign body is asked to leave the room. Using direct laryngoscopy, a foreign body (for example peanut (though the oil can be irritating to the lungs), carrot, bead, eraser bits, push pins, small spherical magnets) is placed through the vocal cords into the airway under direct visualization using an alligator or peanut forceps; optical forceps can be used as well to confirm placement. The pig is either reintubated or maintained using bag mask ventilation. The participant who is to remove the foreign body is asked to come back into the room. She/he begins with a diagnostic bronchoscopy, finds the foreign body, and determines which forceps she/he would like to use and then attempts removal (Figure 2). As more and more procedures are performed, the airway becomes swollen, pulmonary reserve may decrease and the simulated intensity of airway bronchoscopy and foreign body removal heightens.

Once all members of the simulation team have gained satisfactory practice with foreign body extraction, the pig is intubated and the team proceeds to open airway surgery. Dissection is guided by the Airway Reconstruction Surgical Dissection Manual by Propst et al. Participants first perform a tracheotomy. Next the neck is opened to expose the airway from hyoid bone down to the 5-8th tracheal rings. An anterior cricoid split is performed, thyroid ala cartilage is harvested and sutured into the cricoid

Figure 1. Participant performing bronchoscopy on anesthetized pig. Note the mask for ventilation and pulse oximetry monitor.
Figure 2. Participant performing airway foreign body removal with an optical grasper on anesthetized pig.



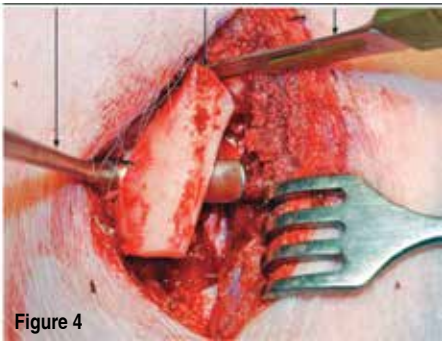
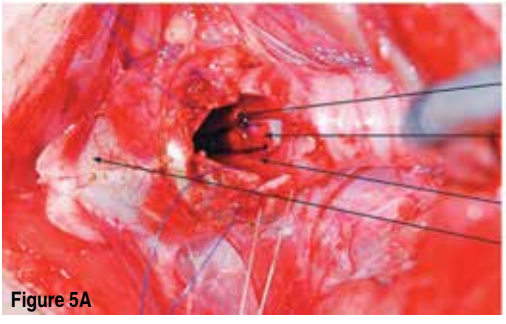


Figure 3. Vertical line drawn over cricoid cartilage and first tracheal ring marking anterior cricoid split [7].
Figure 4. Seine retractor elevating medial aspect of posterior perichondrium to harvest costal cartilage rib graft [7].



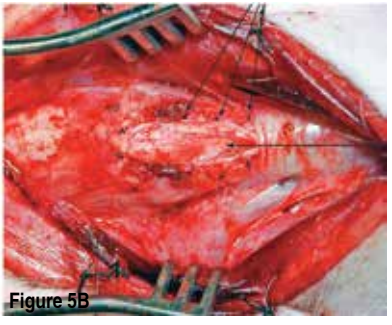
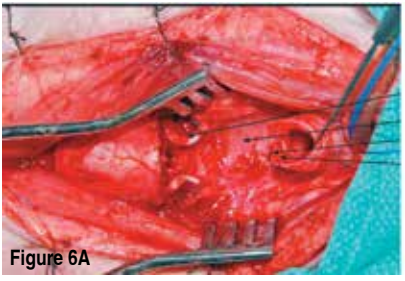


Figure 5A. Graft is placed into the posterior cricoid split [7].
Figure 5B. Graft is sutured to the anterior cricoid defect [7].

defect (Figure 3). In preparation for an anterior-posterior laryngotracheoplasty (LTP), a rib graft is harvested. The chest wall anatomy of the pig is somewhat different from human anatomy, but principles such as preventing pneumothorax still apply, and technical skills such as exposing the relevant portion of the rib, distinguishing between bony and cartilaginous segments, and harvesting the rib while protecting the pleura and underlying lung parenchyma are similar (Figure 4). Once the cartilage is harvested, participants learn to carve anterior and posterior cartilage grafts. Then the participants perform the LTP with anterior-posterior cricoid split and can place the posterior graft and suture in the anterior graft (Figure 5A and 5B). They may then practice performing cricotracheal resection (CTR) by removing the segment of the trachea that was recently "reconstructed" during the LTP (Figure 6A and 6B) and conclude with a slice tracheoplasty more distally (Figure 7A and 7B). Other procedures such as airway stent placement (i.e. Montgomery T tube) and single stage and double stage airway surgery can be explored. The open airway portion can be performed on an anesthetized or euthanized pig.

The airway foreign body and open airway reconstruction course is coordinated on a quarterly basis for our Residents and Pediatric Otolaryngology fellow. This allows the fellow to take the course 4 times in a 12 month fellowship year and each resident to



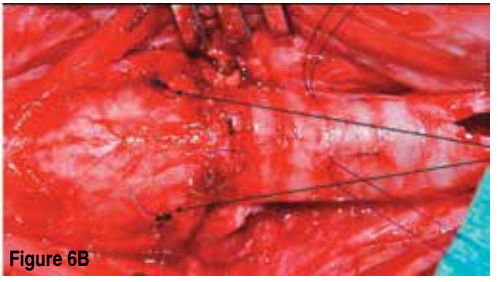
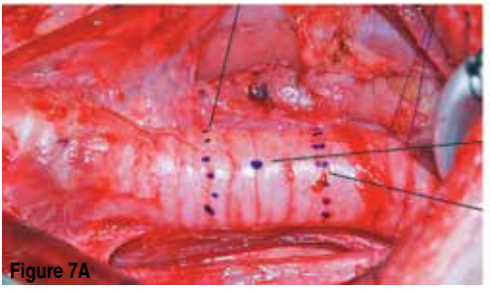


Figure 6A. Cuts for cricotracheal resection are made through anterior cricoid ring, and the stenotic tracheal rings are removed. The posterior cricoid plate is thinned [7].
Figure 6B. Distal trachea is pulled in superiorly and posteriorly into the thyroid cartilage [7].



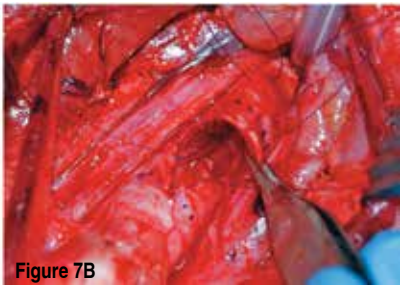


Figure 7A. To prepare for slide tracheoplasty, the superior and inferior limits as well as the middle of the simulated stenosis is marked out [7].
Figure 7B. The trachea is divided at the midpoint on a bevel. The triangularly shaped edges are removed from the distal posterior tracheal division and the proximal anterior tracheal division, and the trachea is reapproximated [7].

participate at least 4 times in their 5 year residency training program. The frequency and repetition of the course increases exposure and hands-on training in airway foreign body and open airway surgery and has become integrated into our residency curriculum for airway surgery. The participants feel more comfortable when performing bronchoscopy, airway foreign body removal and open airway surgery on patients as they go through training due to having the pig lab available on a yearly and quarterly basis.

An Objective Structured Assessment of Technical Skills (OSAT) may be used during the course for evaluation of pediatric direct laryngoscopy and rigid bronchoscopy [8-11]. However, there is no validated evaluation tool for open airway surgery. Other limitations include access to an animal lab, availability of a veterinarian and veterinary medicine technologists, cost of the pigs, and cost of endoscopic instruments, camera and tower.

In conclusion, airway foreign body and open airway surgery are not high volume cases in ENT residency training but require skills and expertise from practicing Otolaryngologists. Animal simulation provides highly realistic and accurate practice for these potentially life threatening surgeries. Integrating the course into the ENT training curriculum allow for frequent practice and repetition. The main limitations include cost and access to an animal facility. Development of an evaluation tool for performance of tracheotomy and open airway surgery is required.

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Head and neck mass in children

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Summary

Head and neck masses in children are very common and in most cases benign. Differential diagnosis of head and neck mass in children includes **inflammatory diseases** (viral and bacterial lymphadenitis), **lymphadenopathies** (chronic inflammation, Rosai Dorfman syndrome), **congenital anomalies** (thyroglossal, branchiogenic and dermoid cysts, fistulae), **vascular anomalies** (lymphangiomas and hemagiomas), **tumors** (benign and malignant), as well as **salivary gland** and **thyroid diseases**.

Diagnosis of inflammatory disease is usually based on the medical history and the clinical examination. The diagnostic procedures involve laboratory investigations, microbiological assessment, ultrasound, cytology, CT, MRI, and histopathology. After obtaining the patient history and performing a clinical examination, an ultrasound examination is done. Ultrasound plays a major role in the diagnosis of thyroglossal and branchiogenic cysts, lymph nodes, as well as head and neck tumors. Depending on the results of the ultrasound exam, cytological puncture may also be indicated. In acute inflammation (abscess) the aspirateis sent for microbiological and cytological assessment. All children presenting with a fast-growing neck mass or long-term lymphadenopathy should undergo ultrasound of the neck and cytological puncture to distinguish benign from malignant growths. In the presence of a large cyst or a vascular malformation (lymphangioma or hemangioma), and in cases where there is the possibility of compression or complications during surgery due to the localization of the mass, further radiological imaging (MRI or CT) is indicated, in addition to fistulography in cases of fistulae.

All malignant tumors are extirpated and the removed tissue is sent for histopathological assessment. Depending on the results, further disease staging is indicated, as

well as treatment by a team involving a pediatrician, oncologist, and hematologist, in addition to radiotherapy.

Treatment of acute viral inflammation is symptomatic. In acute bacterial infections incision and drainage is performed with concomitant antibiotic treatment.

Cysts, fistulae, and benign tumors are treated surgically.

Key words: mass, head and neck, children, congenital anomalies, tumors, lymphadenopathies.

Introduction

Head and neck masses occur very frequently. Fifty percent of children aged two years have enlarged lymph nodes, which are mostly benign; only 5% are malignant tumors.

Head and neck masses include inflammatory diseases, congenital anomalies, and tumors. A patient history and clinical examination, as well as the child's age, are key factors in the diagnosis. The most common presentations are inflamed lymph nodes due to acute viral or bacterial throat, nose, and ear infections [(1)].

Newborns and infants usually present with congenital anomalies [(1)]. In addition to the clinical picture, knowledge of anatomy and embryology are necessary to reach the correct diagnosis. Ultrasound and cytology are also a very important part of the diagnostic protocol [(2)].

Lymphomas are the most frequent malignant tumors [(8)].

Medical history

The personal and family history, duration of symptoms, as well as the child's age are all very important [(1)]. Congenital anomalies are present at birth, and other benign formations can occur at a very young age as well. Slow growth and absence of acute symptoms suggest congenital anomalies [(2)].Some congenital anomalies (thyroglossal and branchiogenic cysts) typically occur later, sometimes only in the presence of inflammation. Fast growth always indicates either inflammation or a malignant neoplasm. Lymphadenopathies are a common occurrence in children prone to bacterial or viral throat infections.Fever, weight loss, and sweating always indicate malignancies. Joint and muscle pain suggest a systemic disease (infectious mononucleosis) [(9)].

Clinical examination

A complete ear, nose, and throat (ENT) examination (oropharyngoscopy, rhinoscopy, fiberendoscopy, and otoscopy) in addition to a bimanual palpatory neck exam are of almost importance [(1)]. Node consistency, localization, tenderness, erythema, and fluctuation are always an indication of inflammation. Firm or immovable nodes suggest a suspected malignancy. Difficulty swallowing, torticollis, trismus, or voice changes point to deep inflammatory changes (abscess) in the neck [(2)]. Bilateral lymph node enlargement usually has an inflammatory etiology. Epistaxis, nasal obstruction, and bilateral lymphadenopathy, as well as impaired hearing, are suspicious for nasopharyngeal carcinoma [(2)]. Medial edema is usually caused by medial cysts (thyroglossal, dermoid) and thyroid disease [(6)]. The nodes may also be localized in the parotid and submandibular regions, and in such cases salivary gland disorders (inflammation and tumors) must be ruled out by differential diagnosis [(3)].

Investigations

Laboratory

A complete blood count is routinely done in cases of acute inflammation complications of phlegmons and neck abscesses. In cases of suspected infectious mononucleosis, a complete blood count as well as biochemistry and serology for Epstein-Barr virus (EBV) and cytomegalovirus (CMV) is necessary.If there is clinical suspicion of cat scratch disease, serology for toxoplasmosis and Bartonellahenselae is done as well [1].

A microbiological analysis of node samples obtained by puncture as well as nasopharyngeal and pharyngeal swabs is done in cases of acute inflammation, and sometimes also in the presence of persistent neck lymphadenopathy (most frequently caused by Streptococcus pyogenes and Staphylococcus aureus) [9].

Ultrasound and cytology

In the last 30 years, ultrasound examination of the neck in children has been the primary diagnostic procedure [2].Indications for ultrasound of the neck are pathologically enlarged lymph nodes in the neck, other pathological masses (cysts, tumors), salivary gland diseases, and thyroid diseases [2].

The size, number, localization, margins, and echostructure of the enlarged nodes are assessed.

Ultrasound is cheap and simple; it does not expose the patient to radiation and is very useful in deciding whether cytological puncture is necessary or not. In acute inflammation (abscess) a heterogeneous echostructure with hypogenicechos is shown, and purulent content may be extracted by ultrasound guidance. If ultrasound is performed concomitant with cytological puncture, diagnosis precision amounts to approximately 99%. Cysts in the neck are visualized as hypoechgenic, sharply delimited zones. Ultrasound is also very useful in the follow-up of children with congenital malformations (cysts) and vascular tumors/malformations, in addition to aiding in decisions on performing surgical procedures in children [2].

It is important that the ultrasound examination is performed by an ENT specialist.

Cytology is a simple, non-traumatic, and reliable procedure which prevents unnecessary lymph node extirpation in children, and which may help in distinguishing benign from malignant lesions. If done concomitantly with ultrasound, its accuracy amounts to 95% in comparison with histological assessment [4]. In cases when the cytology results point to a malignant tumor, further radiological workup is necessary in the form of MRI and CT to enable the planning of surgical treatment. In vascular malformations (lymphangiomas, hemangiomas) Doppler ultrasound and MRI as well as MRI angiography are indicated [5].

Classification

I: Inflammatory diseases

Acute inflammation is caused by viruses and bacteria.

Acute suppurative lymphadenitis is most frequently caused by Staphylococci and Streptococci. Children with throat, nose, and ear infections usually present with bilaterally enlarged lymph nodesin the neck. Antibiotic treatment is indicated.

Abscesses in the neck are caused by infectious pathogens that enter the neck through rhagadeson the tongue and the oral mucosa.The clinical presentation involves difficulty swallowing, fever, erythema, and painful, usually unilateral, neck edema. Treatment

is surgical and includes incision and drainage accompanied by parenteral antibiotic therapy [9].

Infectious mononucleosis is a lymhoproliferative diseasecaused by the Epstein-Barrvirus (EBV). The clinical picture is characterized by generalized lymphadenopathy, fever, throat inflammation, and splenomegaly. The differential diagnosis also includes other types of lymphadenitis caused by cytomegalovirus (CMV), toxoplasmosis, malignant lymphoma, and nasopharyngeal carcinoma metastasis. An accurate diagnosis requires a complete blood count, biochemistry, and serology. In 90% of the affected children bilateral neck lymphadenopathy is present. The tonsils are hypertrophic with pseudomembranes and plaques. The treatment is mostly symptomatic, and corticosteroids are administered in more serious cases [2].

Chronic inflammation or nodes which persist for longer than a month require a detailed ENT and hematological evaluation. Depending on the localization, ultrasound and cytological puncture are done, as well as nasopharyngeal and pharyngeal swabs, ASTO, ASTA, and, depending on the patient history, serological assessment. A regular ultrasound follow-up is necessary (node size, number, and echogenicity). The treatment depends on the cause, size, localization, and number of affected lymph nodes, as well as on the complete ENT status [2].

Cat scratch disease (CSD) is characterized by regional necrotizing lymphadenitis, fever, and chills which occur two to three weeks following a skin injury caused by a cat scratch. A history involving the fact that the child was in contact with a cat is of utmost importance. In 43% of the affected children there is neck lymph node involvement (submental, periauricular, anterior and posterior cervical). Differential diagnosis should exclude tuberculosis, tularemia, and other types of lymphadenitis with focal necrosis. Antibiotic treatment is indicated, and in cases which do not respond to antibiotic therapy, incision or complete extirpation of the lymph node is performed [1,2].

Toxoplasmosis is a specific lymphadenitis caused by Toxoplasma gondii. The typicallocations are in the postauricular, occipital, or parotid regions. The infection is usually transmitted by cats. Diagnosis is based on the clinical presentation, cytology, and serology. The differential diagnosis includes all granulomatous inflammations (TBC, sarcoidosis) and Hodgkin disease. Recently, azithromycin and clarithromycin treatment has been recommended [1,9].

Mucocutaneous lymph node syndrome (Kawasaki disease) is an acute systemic type of vasculitis that occurs in infants and young children, typically between the first and second years of life. The symptoms include high temperature, bilateral conjunctivitis, erythema, oropharyngeal fissures, lymphadenitis in 75%, and myocardial involvement in 50% of the affected children. Differential diagnosis involves tuberculosis, leptospirosis, systemic lupus, thrombocytic purpura, and infantile nodular periarthritis. Treatment includes high-dose immunoglobulin and aspirin [2].

Rosai-Dorfman syndrome (sinus histiocytosis with massive lymphadenopathy) presents with enlarged lymph nodes in the neck accompanied by fever and leukocytosis. The etiology and pathogenesis of the disease are unknown, and male children are affected twice as often. In 94% of the children the first symptom is massive lymphadenopathy in the neck. The nodes are large, painless, and usually localized bilaterally. If the cytological findings point to Rosai Dorfman syndrome, extirpation is performed with subsequent histopathological confirmation of the diagnosis. Differential diagnosis requires a careful distinction from ML, NHL, Hodgkin disease, and histiocytosis. The syndrome is treated with corticosteroids [2].

Granulomatous lymphadenitis with necrosis (tuberculosis) usually occurs unilaterally, affecting one or more lymph nodes in the angular and submandibular region. The nodes are soft, mobile, and sometimes fistulate. All puncture samples are sent for biochemistry analysis, and the patient must undergo radiological evaluation of the lungs as well as pediatric assessment. The treatment is conducted by a pediatrician [10].

Granulomatous lymphadenitis without necrosis (sarcoidosis) is a multisystem disorder which affects the hilar lymph nodes, lungs, and skin, as well as the cervical lymph nodes, tonsils, nose, and salivary glands. In children it is very rare.

II. Congenital malformations

1. Vascular malformations

Hemangiomas usually affect the skin and mucosa, but may also occur in deeper regions of the neck. Approximately 10% of children are born with a hemangioma, most often localized on the head or, in approximately 30%, on the neck [2]. Initially the hemangiomas are characterized by fast growth, but they usually regress by the end of the first year of life. In the last 20 years, propranolol has been used in the treatment. If spontaneous regression does not occur, surgical or laser treatment is also used, depending on the localization [1].

Lymphangiomas (hygromas) are usually diagnosed immediately after birth or in infancy. In 80% of the affected children they present on the neck and the parotid in the form of a soft, painless, multilocular cystic mass. They are normally diagnosed by ultrasound, except for cases of fast growth and compression of the surrounding structures, which may cause dyspnea and dysphagia, requiring MRI. Surgical treatment is demanding due to the child's age and localization of the tumor [1,2].

2. Cysts and fistulae

Thyroglossal cysts most commonly occur in the medial line and make up approximately 70% of all congenital anomalies in children, following benign neck lymphadenopathies.

Branchiogenic cysts make up approximately 30% of all anomalies. They commonly occur in the upper third of the neck, but parotid location is also possible.

Dermoid cysts are very common and occur in various subcutaneous locations (submental, sublingual, etc.) in the head and neck region. They are painless and sized 1-2 cm.

Fistulae are abnormal openings in the neck,running in front of and along the sternocleidomastoid muscle, which produce secretions. They may be complete or incomplete.

Cysts and fistulae are treated surgically.

III. Tumors

1. Benign tumors

Teratomas are usually located in the midline of the nose, nasopharynx, orbit, and oral cavity.

Neurofibromas are benign tumorswhich may be solitary, multiple, and plexiform. The clinical presentation depends on the localization.

Pilomatrixomas are benign tumors usually occurring in the head and neck region (retroauricular, nuchal, preauricular). Surgical treatment is indicated [7].

2. Malignant tumors

Nasopharyngeal carcinoma ischaracterized by the occurrence of nodes in the neck, nasal obstruction, nasal bleeding, and impaired hearing. Fiberendoscopy of the nasopharynx, cytological puncture of the cervical nodes, and audiological workup are performed. Epipharyngeal curettage and histopathologcal assessment are mandatory, as well as immunohistochemistry and serology for EBV, in addition to MSCT for disease staging. Treatment includes radiotherapy and chemotherapy [(2)].

Hodgkin disease occurs in the neck in 60-80% of the cases. The nodes are firm and painless; the most common symptoms are fever, night sweats, weight loss, and itching. Ultrasound and cytological puncture play an important role in the diagnostic process. Extirpation followed by histopathological confirmation is mandatory for staging and treatment initiation [(8)].

Non-Hodgkin lymphoma presents as painless neck node enlargement in 60% of the cases. Other possible localizations are the tonsils and the epipharynx. Diagnosis is based on the cytology; the node is extirpated and undergoes histopathological confirmation. Immunophenotypization and staging of the lymphoma are mandatory [(8)].

Neuroblastoma is the most common extracranial malignant tumor in children under one year of age [(2)].

Rhabdomyosarcoma is a malignant childhood tumor, in second place after malignant lymphoma. In 91% of the cases it presents as a primary tumor of the head and neck. In addition to the primary tumor, metastases in the neck may also occur [(2)].

Depending on the disease stage, all malignant tumors are treated according to appropriate protocols (chemotherapy and radiotherapy) by pediatricians, hematologists, and oncologists.

Conclusion and recommendations

The objective of this review paper is to present the diagnostic and treatment procedures applied in the most common types of head and neck masses.

A detailed patient history accompanied by a clinical examination is key. Ultrasound and cytological puncture play an important role in the diagnostic process. Early diagnosis of tumors enables timely treatment, involves fewer complications, and prevents further disease spread. Cysts,fistulae, and benign tumors require surgical treatment. If nocomplications (difficulty breathing, compression) are present, it is possible to delay the surgery until the age of 2 years. All procedures are conducted under general anesthesia, which also makes cooperation with an anesthesiologist very important. In cases of persistent nodes without progression and with negative cytology, 3-month ultrasound follow-ups are necessary. There is always the dilemma whether to prescribe an antibiotic to children who present only with an enlarged lymph node. Antibiotic treatment is not indicated in cases of viral, reactive inflammation, but 75% of the children referred to ENT specialists already are on antibiotic therapy. Also, there is the issue of follow-up in cases of reactive hyperplasia. For nodes occurring unilaterally, or in the parotid or submandibular gland regions, concomitant ultrasound and cytological puncture are mandatory. The treatment must be decided on by a team involving a pediatrician, ENT specialist, cytologist, specialist for infectious diseases, and family practitioner. Diseases of the salivary glands and the thyroid are not described.

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Diagnosis and management of pediatric differentiated thyroid malignancies

Erin Wynings, MD and **Christopher Liu**, MD.

Introduction

Thyroid cancer is rare in children and accounts for 3% of all pediatric malignancies. The prevalence of pediatric differentiated thyroid cancer (DTC) in the United States is 10 per 10,000 and the incidence appears to be rising. This increase may be secondary to increased surveillance and enhanced detection. Papillary thyroid carcinoma (PTC) is by far the most common type of DTC and accounts for over 90% of cases, followed by follicular carcinoma (FTC) [1].

The pathophysiology, clinical presentation, and long-term outcomes of pediatric DTC are very different when compared to adults [2]. Exposure to radiation is the biggest risk factor for pediatric DTC [1]. Other risk factors for DTC are listed in Table 1.

The most common clinical presentation for DTC in children is a thyroid nodule [1]. Unlike adults, a pediatric thyroid nodule is more likely to be malignant. Children are more likely to present with advanced disease including large tumor volume, extrathyroidal extension, locoregional metastases, and distant metastases. Over two-thirds of children with thyroid cancer have regional lymph node metastasis and up to 20% will have distant metastases [3]. Despite the increased incidence of these aggressive features in pediatric thyroid cancer, long-term disease specific mortality in children is less than 2% [2].

Risk Factors for Pediatric Thyroid Cancer
Radiation exposure (especially age < 5 years)
Autoimmune thyroid disease
Grave's Disease, Hashimoto Thyroiditis
Family history of benign thyroid disease
Family history of differentiated thyroid cancer
Cancer predisposition syndrome
PTEN Hamartoma, DICER1, Werner Syndrome, Carney Syndrome

Table 1. Risk factors for pediatric thyroid cancer.

Management of pediatric thyroid nodules

Unlike adult thyroid nodules that are common and usually benign, thyroid nodules are relatively rare in children and over a quarter of nodules malignant [1]. The initial

workup of a pediatric thyroid nodule should include thyroid function studies and ultrasound of the neck. Sonographic features that are predictive of malignancy are listed in Table 2 [4]. If the clinical suspicion for differentiated thyroid cancer is high, a complete ultrasound of the neck should be performed to assess for regional lymphadenopathy in the lateral neck.

Fine needle aspiration (FNA) of thyroid nodules with ultrasound guidance is recommended in pediatric patients. The use of ultrasound increases diagnostic accuracy and is important in children given the higher likelihood of malignancy and the technical difficulty in performing repeat biopsies in pediatric patients [1].

The Bethesda Classification System is used to categorize FNA cytopathology in both adults and children [5]. In instances where repeat FNA is recommended such as nodules with nondiagnostic pathology, sampling should be delayed for at least 3 months to avoid detection of atypical cells that are associated with the reparative process from the previous biopsy [6]. Molecular testing on FNA samples is not standard practice in the pediatric population, however Monaco et al. demonstrated that all pediatric FNA nodules with Bethesda Category III pathology and above that were also positive for RAS, BRAF, RET-PTC or PAX-8 mutations were papillary thyroid cancer on resection [7]. Unlike in adults, nodules that result as atypia of undetermined significance or follicular lesion of undetermined significance should undergo surgical resection including lobectomy and isthmusectomy instead of repeat FNA given the higher probability of malignancy in children [1].

In the case of benign nodules, ultrasound should be performed every 6 to 12 months. If the nodule is stable, ultrasound can be repeated every 1 to 2 years. Repeat FNA should be performed if the nodule increases in total volume by greater than 50%, increases in two dimensions by greater than 20%, or if there is development of suspicious features (Table 2). Lobectomy should be considered for benign nodules greater than 4 cm given the high false negative rate due to sampling error and to simplify long term follow up. Other considerations for surgical resection of benign thyroid nodules include patient or parent preference, cosmesis, and the presence of compressive symptoms [1].

Ultrasound Features of Nodules Predictive for Malignancy
Hyperechoic
Irregular margins
Intranodular blood flow
Speckled microcalcifications
Taller than wide morphology
Lymphadenopathy

Table 2. Thyroid nodule ultrasound features predictive for malignancy [4].

Surgical management of pediatric differentiated thyroid malignancies

Pediatric thyroid cancer is primarily treated surgically. Preoperative evaluation should include a complete neck ultrasound to identify locoregional metastatic disease [1]. Further imaging with computed topography (CT) or magnetic resonance imaging (MRI) should be considered for bulky disease or if there is suspected aerodigestive involvement. Keep in mind that radioactive iodine (RAI) ablation need to be delayed for up to three months after administration of an iodinated contrast load. However, the time from evaluation to surgery and final staging generally allows sufficient time for the total body iodine burden to decrease after contrast administration.

Total thyroidectomy is recommended for PTC given the higher incidence of bilateral and multifocal disease in children. Total thyroidectomy also optimizes RAI for imaging, surveillance, and treatment and allows thyroglobulin (Tg) to be used as a surveillance marker.

Therapeutic central neck dissection (CND) is performed if there is evidence of central or lateral neck metastases or if gross extrathyroidal extension is present. CND in this population is associated with a decreased risk of persistent and recurrent disease and can increase the efficiency of RAI [1]. On the other hand, prophylactic CND is controversial. Some argue to perform prophylactic neck dissection routinely because children with PTC have a higher risk of locoregional disease and the presence of locoregional disease is associated with lower disease-free survival. However, there is insufficient data to decide which patients will have the highest risk of metastases and recurrence. For example, tumor size has been demonstrated to correlate with risk of metastases. Larger tumors (>4 cm) have an increased risk, but up to 36% of tumors less than 4 cm also have metastases [1]. The risk of leaving microscopic persistent disease that could potentially be treated with RAI, should be weighed against the increased risk of recurrent laryngeal nerve (RLN) injury and postoperative hypoparathyroidism when considering prophylactic CND.

Lateral neck dissection (LND) is indicated when there is histologic confirmation of metastatic disease in the lateral neck. Lymph node features suspicious for metastases include increased size, rounded shape, loss of the central hilum, cystic appearance, peripheral vascularity, and microcalcifications. Tg washout may be performed if FNA diagnosis is equivocal. All LNDs should be compartmental dissections and include levels II, III, IV and anterior level V. Compartmental dissection allows for higher lymph node yields and a lower risk of recurrence. "Berry-picking" or "node-plucking" is discouraged. Adequate lymph node yields may help risk stratify patients by ruling out occult metastasis. For T1b, T2, and T3 stage disease [6,9,18] lymph nodes, respectively, must be examined to rule out occult disease with 90% confidence [8,9]. Routine prophylactic LND is not recommended in children.

Compared to PTC, FTC is typically encapsulated, less advanced, has fewer locoregional metastases, spreads by vascular invasion, has an increased rate of distant metastases without locoregional disease, and has a lower rate of recurrence. A hallmark of this type of tumor is distant metastasis in the absence of locoregional disease. Total thyroidectomy should be performed for FTC with greater than 3 vessel invasion or large tumors (>4cm). Lobectomy for FTC may be considered on a case by case basis. CND for FTC is only recommended if there is clinical evidence of locoregional disease.

Complications of surgical management

Compared to adults, pediatric patients undergoing surgical intervention for thyroid disease have an increased risk of complications. Pediatric thyroid surgery performed by high volume surgeons, defined as those performing over 30 cervical endocrine procedures per year, is associated with fewer complications, shorter hospital stays, and lower overall costs [1,10].

Complications of thyroid surgery can be classified as either endocrine or non-endocrine. Endocrine complications are more common. Postoperative hypoparathyroidism is the most common complication and is related to the extent of surgery. Intraoperative manipulation of the parathyroid glands can lead to transient or permanent hypoparathyroidism. In high volume centers, the risk of transient hypoparathyroidism ranges from 5% to 37% and the risk of permanent hypoparathyroidism is <2.5% [1,10]. If there

is concern for parathyroid devitalization intraoperatively. Tissue auto-transplantation should be performed after frozen-section confirmation.

To decrease the risk of postoperative hypocalcemia, testing of Vitamin D levels and cholecalciferol supplementation if low should be performed one month prior to surgery. Generally, postoperative hypocalcemia is managed either with calcium supplementation given to all patients or patients are stratified by risk with supplementation as needed. At our institution we have adopted a protocol published by Patel et al. [11]. Patients are stratified into high or low risk groups based on their intraoperative parathyroid hormone level (PTH). Prior to incision, calcium, albumin, magnesium, phosphorus, and parathyroid hormone (PTH) labs should be collected in the operating room. The short half-life of PTH allows for parathyroid function to be monitored intraoperatively to identify patients at risk for hypocalcemia. PTH and calcium levels are collected 25 minutes after removal of the thyroid. If CND is being performed, calcium and PTH should also be collected 25 minutes after dissection completion as the parathyroid glands are at an increased risk of devascularization during CND. The PTH level is then used to stratify patients as high risk (PTH $\leq$ 16 pg/mL) or low risk (PTH $\geq$ 17 pg/mL) for hypocalcemia which then determines whether postoperative calcium monitoring and supplementation are indicated.

Patients should be monitored closely postoperatively for symptoms of hypocalcemia.

Mild symptoms of hypocalcemia include perioral numbness, paresthesias of the hands and feet, muscle cramps, and fatigue. Severe symptoms include tetany, laryngospasm, focal or generalized seizures, and cardiac arrhythmias including prolonged QRS or QT intervals. Any symptomatic patient should have calcium and magnesium levels drawn immediately and supplemented. Pediatric intensive care unit admission should be considered for patients with severe symptoms or calcium levels less 7.0 after to two doses of intravenous calcium gluconate.

Non-endocrine complications of thyroid surgery are less common and include recurrent laryngeal nerve (RNL) injury with vocal cord paralysis, Horner's syndrome, and spinal accessory nerve injury. Rates of non-endocrine complications average 1% to 6% in pediatric patients [10]. Of note, intraoperative RLN monitoring is commonly used but has not been shown to reduce the rate of nerve injury [12].

Postoperative staging and management

The risk of persistent and recurrence PTC is correlated with several risk factors, so patients should be staged within 12 weeks of surgery to determine if additional therapy is indicated. Patients with PTC are staged according to the American Joint Commission on Cancer TNM Classification System [13]. Patients are then classified as low, intermediate, or high risk of recurrence as outlined by the American Thyroid Association guidelines [1]. Low risk patients can be initially staged with thyroid stimulating hormone (TSH)-suppressed Thyroglobulin (Tg). Patients with evidence of extrathyroidal invasion or metastasis are categorized as intermediate or high risk. In these patients TSH-stimulated Tg and diagnostic I123 whole body scan (DxWBS) are recommended to further stratify them and determine if additional imaging or treatment is needed.

RAI eliminates iodine-avid thyroid tissue and residual tumor. The goal of therapy is to reduce risk of recurrence and simplify follow-up (by monitoring thyroglobulin). Indications for RAI include patients with unresectable iodine-avid persistent locoregional disease and in those with presumed iodine-avid distant metastasis. Some

advocate for the routine use of RAI in children with advanced tumors or extensive regional nodal involvement [1]. Prior to RAI therapy, elevated TSH levels are necessary to maximize iodine uptake. Thus, levothyroxine should be withdrawn for 14 days with a goal TSH greater than 30 mIU/L. In patients who cannot tolerate withdrawal, use of recombinant human TSH (rhTSH) should be considered. Side effects of RAI include sialadenitis, xerostomia, dental caries, stomatitis, dry eyes, gonadal damage, bone marrow suppression, and pulmonary fibrosis.

Long-term surveillance for DTC according to risk category is outlined in the 2015 ATA guidelines [1]. Patients in the low risk category should have surveillance ultrasound every 6 months for the first year followed by yearly ultrasound for a total of 5 years. Thyroglobulin while on levothyroxine should be monitored every 3-6 months for 2 years and then annually. Surveillance for intermediate and high-risk patients are similar. They should have surveillance ultrasound every 6-12 months for 5 years. Thyroglobulin while on levothyroxine should be monitored every 3-6 months for 3 years and then annually. Compared to low risk patients, intermediate and high-risk patients should have TSH-stimulated thyroglobulin checked 1-2 years postoperatively. Consider a diagnostic whole-body scan if the patient was treated with radioactive iodine previously. TSH suppression goals vary by risk category: Low risk – 0.5 to 1.0 mIU/L, Intermediate risk – 0.1-0.5 mIU/L, and High risk <0.1 mIU/L. Tg antibody levels should be collected as well because up to 25% of patients will have Tg antibodies. Any rise in Tg or thyroglobulin antibody should prompt a workup for recurrence.

Role of molecular targeted therapies in pediatric differentiated thyroid cancer

Identification of several signaling pathways and genetic mutations central to thyroid cancer pathogenesis has led to the approval of targeted molecular therapy such as tyrosine kinase inhibitors as treatment for thyroid cancer [14]. The majority of research on these molecular therapies, however, has focused on adult thyroid cancer. Pediatric thyroid carcinoma, on the other hand, has an increased incidence of gene fusions compared to adult disease (50 to 60% and 15% respectively) with RET fusions and BRAF mutations being the most common [2,14]. When used on tumors with the appropriate mutation, targeted molecular therapies have a high response rate and lead to a rapid reduction in tumor size within weeks to months [15,16]. Case reports have described the use induction TKIs in advanced or unresectable PTC to decrease tumor burden and allow for surgical resection and RAI therapy [17-19]. Currently these therapies do not replace the standard of care treatment but can be considered in cases of recurrent, RAI-resistant, or metastatic disease [20].

Several clinical trials are currently investigating the role of targeted molecular therapy in pediatric DTC. Response to sorafenib has been reported in pediatric patients with RAI refractory PTC, diffusely metastatic PTC not amenable to upfront RAI, and in patients who could not receive RAI in a timely manner [2,21-24]. The use of neoadjuvant TKI therapy to downstage tumors and reduce surgical morbidity in pediatric patients is also being investigated. Targeted molecular therapy is a promising therapeutic option for pediatric DTC, but more research is needed to determine when and how these therapies should be utilized.

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Management of airway obstruction at the tracheostomy site

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Introduction

A common indication for tracheostomy placement is the prevention of airway complications due to prolonged intubation. However, tracheal stenosis or obstruction secondary to prior tracheostomy placement is not an uncommon occurrence, and incidence estimates for this range widely from 6 to 21% [1,2]. The current paper will briefly discuss various airway sequelae resulting from prior tracheostomy tube placement and the wide-range of management options for these problems. For the purpose of this review and as a general approach, we divide these post-tracheostomy complications

into endoluminal soft tissue versus framework problems. As a general rule, soft tissue problems requiring surgical intervention tend to be more amenable to endoscopic or minimally invasive approaches, whereas framework problems requiring operative management may require a more aggressive approach.

Evaluation

Imaging studies may provide some information with regards to tracheal complications from prior tracheostomy, the appropriate work up requires endoscopic evaluation of the airway. Although chest and/or neck x-rays have historically been used in the acutely distressed patient, the tracheal air column on x-ray provides only limited low-resolution information on airway caliber, morphology, extent and degree of narrowing, and does not provide information on the integrity of the tracheal cartilaginous framework as well as soft tissues. Computed tomographic scans provide significantly more information and some ability to document airway collapse when performed both during inspiration and expiration, and multiplanar reconstructions (virtual bronchoscopy) can provide further information about morphology and extent of airway obstruction [3-5]. Magnetic resonance imaging has been used in small case series of tracheal stenosis and can provide information on the relationship between trachea and adjacent vascular structures and aid in determining the degree of stenosis without ionizing radiation [3,5]. Benefits notwithstanding, neither CT nor MRI can provide accurate information pertaining to mucosal changes or reliably provide information about the integrity of the cartilaginous framework of the airway [3-5].

Airway evaluation-technique:

It follows, that endoscopic evaluation of the airway remains the gold standard technique to evaluate for the presence and etiology of tracheal abnormalities in the post-tracheostomy patient. At our institution this is frequently performed using a combination of flexible bronchoscopy and rigid telescopic techniques. From a diagnostic perspective, it is important to perform these examinations in the correct order, and to maintain close communication with the anesthesiologist. Under light sedation, a trans-nasal, trans-glottic flexible bronchoscopy should first be performed. This is done in the absence of an endotracheal tube or laryngeal mask airway (LMA), so as to reduce the effects of positive airway pressure on the visible patency of the airway. Under light sedation the patient may be breathing with some degree of force, and the dynamic changes of the airway can be visualized. This may include otherwise elusive peristomal collapse, intrinsic tracheomalacia, or extrinsic vascular influences. If the patient has a tracheostomy in place, it is important that the tracheostomy tube is removed under direct visualization and the evaluation is performed with the stoma gently finger occluded. Some of the less-obvious dynamic peri-stomal collapse can be seen using this technique. Limitations to flexible bronchoscopy include the requirement for impeccable sedation as well as the inability to palpate and accurately size the airway. Rigid endoscopy is performed second, as this requires a deeper level of sedation. Using a rigid Hopkins rod and with or without laryngeal suspension, the airway can be visualized under high-definition, sized, and palpated. Additional dynamics can be seen using this technique which may be blunted due to the increased sedation required for the procedure as well as the ability for the telescope to stent the airway.

In select patients, exercise laryngoscopy has been found to be a useful adjunct in the work up. This technique involves exercising the patient on a treadmill or stationary bike and performing a flexible nasolaryngoscopy at peak exertion. In select patients

and after appropriate topical anesthesia, the scope can be advanced through the true vocal cords to assess subglottis and trachea. This is usually only possible in older children and teenagers, due to procedural stimuli. Exercise laryngoscopy should be considered in patients whose symptoms only present during exercise or exertion or who solely present with reduced exercise tolerance [6].

In the minimally symptomatic patient, as sleep study may be a useful adjunct for obtaining additional information pertaining to the severity of any observed obstruction, and in many institutions is considered an essential investigation prior to decannulation [7]. Nevertheless, this can be a misleading investigation for several reasons. The tracheostomy tube may, as a source of obstruction, lead to false positive results during a capped sleep study. In contrast, in patients with framework abnormalities, the tracheostomy tube may stent the airway open and lead to false negative results that are only identified at the time of decannulation. Thus, a sleep study should not be used in isolation to determine a patient's fitness for decannulation.

Soft tissue problems

a. Intratracheal skin tract

Following tracheostomy abnormal overgrowth of the skin lining the stomal tract into the trachea may occur. Of note, this may be mistaken for other causes of suprastomal collapse or obstruction on endoscopy. Management consists of stoma revision with complete excision of the tract [8,9]. The resulting tracheal defect, if small, can be left to close by secondary intention, or can alternatively be closed with a small muscle advancement flap (e.g. strap muscle), or if larger with a small reinforced cartilage graft [8,9]. Decision-making in this regard should take into consideration the size of the defect to be closed, benefits of closure (lower likelihood of failure to close or incomplete stoma closure) as well as associated risk (surgical emphysema and pneumomediastinum / mediastinitis). Of note, Osborn et al. did not find a significant difference in closure rates between primary closure or healing by secondary intention [9].

b. Suprastomal granuloma and fibroma

Suprastomal granulation tissue often present as friable, pink, inflammatory tissue above or within the stoma. More established suprastomal obstructive growths are often referred to as "fibromas" or "granulomas" and may be paler in appearance and firmer in consistency. These lesions do have some gross anatomic as well as histological differences, although the terms are often used interchangeably, and management is similar. While suprastomal granulomas can be asymptomatic, they may also present with symptoms of airway obstruction or present as the expectoration of blood tinged mucous. In cases of small amounts of granulation tissue, surgical intervention may not be necessary. However, addressing suprastomal granulation becomes important prior to decannulation, or if the suprastomal granulomas are significantly obstructing the suprastomal airway, bleeding, or preventing passage of air for speech. Of note, large suprastomal granulomas should be addressed in children with tracheostomies, as they may place them at risk for significant airway compromise in the setting of accidental decannulation [8,10,11].

Several options exist for the management of suprastomal granulomas. When small, these may be excised entirely endoscopically using microlaryngeal instruments, the microdebrider, endoscopic forceps or the CO2 laser. An alternative approach would be to grasp and resect the granuloma trans-stomally using a sphenoid punch under direct visualization with a rigid endoscope. For larger granulomas, a small incision may be

made above the stoma. This is then followed by eversion of the granulation tissue and resection through the stoma [8,10,11]. In the child with tracheostomy tube in situ, topical ciprofloxacin-dexamethasone combination drops may be effective for small granulomas or as an adjunct to the aforementioned surgical procedure.

Framework problems

a. Suprastomal collapse

Suprastomal collapse is felt to be a result of persistent pressure on the first and second tracheal rings by the tracheostomy tube itself. This induced a chronic chondritis and leads to a weakening of the tracheal cartilage in this area and eventually collapse, or tracheomalacia. In some cases, the severity of the suprastomal collapse can prevent decannulation due to significant airway obstruction. Patients undergoing tracheostomy at a younger age are particularly felt to be at risk in some studies. It is also thought that the removal of cartilage at the time of tracheostomy will also increase the likelihood of suprastomal collapse [12].

When considering treatment, the first goal is to assess whether or not the suprastomal collapse needs to be addressed. Under many circumstances, small segments of collapse, or even larger segments that are minimally intrusive, can be managed expectantly. When operative management is required, a variety of techniques to treat suprastomal collapse have been employed. The two most commonly described techniques, similar to addressing subglottic stenosis, center on resection or augmentation of the affected segment. More specifically, suprastomal collapse repair may consist of either resection of the collapsing segment of trachea with primary anastomosis [8,12,13]. Alternatively, tracheoplasty with an anterior cartilage graft may be performed [8,12,13].

A different approach, with the goal of providing support to the malacic framework, employs bioabsorbable miniplates or absorbable sutures. There are several methods described that employ the use of miniplates, one of which includes molding a miniplate around an endotracheal tube and then securing it to be the patient's trachea with suture, thus providing support to the malacic segment. The miniplate in essence then acts as an external splint to prevent the weakened segment from collapsing into and obstructing the airway [14]. Multiple small case series have reported favorable outcomes with this approach to malacic tracheal segments, and to suprastomal collapse in particular [14,15]. In a similar vein, ongoing efforts are investigating the potential role of external splinting with 3D printed biodegradable polymers such as polycaprolactone [16,17]. This has particularly been investigated for tracheo- or bronchomalacia, but could in principle also apply to suprastomal collapse. Whereas the majority of (encouraging) data so far has been gathered from animal studies [16], a recent publication from a group from Michigan describes their experience of successfully applying this technology to human subjects as well [17].

A similar but different approach to the problem of suprastomal collapse is cricotracheal suspension. This is accomplished by suturing the adherent fibromuscular tissue overlying the cricoid and peristomal trachea to the musculofascial insertions of the cervical strap muscles. These sutures then achieve anterior cricoid and peristomal tracheal elevation through ventral and inferior pull on the airway [18]. Tawfik et al., in a small case series suggest excision of the stomal tract down to trachea and flush with the collapsing anterior wall, followed by closure of the tracheal defect primarily with absorbable sutures [19]. From a more minimally invasive standpoint, bronchoscopic KTP laser excision of the collapsing cartilage has been previously described in a series of six patients [20], and may have some utility in select patients.

b. Tracheal stenosis

Subglottic or tracheal stenosis may occur as sequelae of both tracheostomy as well as the intubation precipitating tracheostomy in children. Prolonged intubation has been well established as risk factor for the development of subglottic stenosis in both adult and pediatric populations. Subglottic stenosis may, however, also result from placement of the tracheostomy itself, particularly when placed too high in the airway. Furthermore, local trauma from a tracheostomy cuff may cause trauma akin to that of an endotracheal tube cuff, inducing local inflammation and circumferential scarring [8,12]. Soft, low-grade stenosis may be amenable to incision and balloon dilation. However, stenoses characterized by higher grades, longer segments, hard scar, or stenoses failing endoscopic treatment may be addressed using augmentation or resection techniques. Augmentation in this case refers to laryngotracheoplasty with cartilage graft insertion in order to increase the diameter of the airway. With regards to resection, depending on the length of the stenotic segment as well as surgeon and institutional preference, tracheal (or cricotracheal) resection with end-to-end anastomosis or slide tracheoplasty are considered options. The latter carries the advantage of greater dilation of the manipulated airway segment, thereby decreasing the possible impact of stenosis at the anastomosis sites [8,21].

c. A-frame deformity

A tracheal A-frame deformity typically occurs at a former tracheostomy site but may also occur (less commonly) at the distal aspect of a prior anterior graft [1,8,12]. In these cases, transection of one or multiple tracheal rings in the context of tracheostomy has led to cartilaginous deficiency of the affected rings anteriorly, in turn causing inward collapse of the lateral tracheal walls. As this area heals, a triangular or A-shaped airway results [1,8,12]. Importantly, symptoms of the A-frame deformity may not become evident until after decannulation. A thorough endoscopic airway evaluation prior to decannulation should be performed anticipating this complication. The significance of A-frame deformities may also be underestimated, as conventional sizing with endotracheal tubes may be normal due to the compliance of the posterior membranous trachea, and the expandability of the A-frame deformity itself. Furthermore, the effect of the A-frame deformity may be exacerbated by posterior tracheomalacia, i.e. by virtue of the trachealis intrusion into tracheal lumen, which at the level of the deformity constitutes the most patent area of the airway [8,12]. There are many accounts of patients who have a normal-sizing airway, and who tolerate capping and capped sleep studies prior to decannulation. Following decannulation, they have progressive airway collapse and respiratory distress that occurs as early as in the postoperative recovery room. Upon more thorough evaluation, the dynamic A-frame deformity is evident. More insidious progression to airway obstruction may also occur when the patient is decannulated and the stoma becomes smaller. This results in increased tracheal airflow and may result in a more dynamic tracheal segment at the level of the A-frame. Under both circumstances, re-cannulation is often required, and management of the A-frame is needed.

Surgical correction of the A-frame deformity should be performed if the patient is symptomatic and requires correction of the framework similar to cases of tracheal stenosis. A thorough evaluation of the A-frame deformity should allow for one to determine if the A-frame is fixed in position with rigid cartilaginous compression, or if it is dynamic with changes in patency dependent on intraluminal airflow. Resection

of the segment containing the A-frame deformity with primary anastomosis is one option, as is slide tracheoplasty [8,21] (Figure 1). Alternatively, using an augmentation strategy requires anteriorly splitting the tracheal segment with the A-frame deformity and inserting a cartilage graft with a deep flange, which is necessary for the graft to stay in place. Relaxing incisions can also be placed posterolaterally in the tracheal cartilage to release tension [8]. If there is excessive tension on the cartilage graft (which may be the case in rigid, fixed deformities), the anterior graft may have progressive reduction, ultimately resulting and failure requiring a revision procedure (Figure 2). Finally, a combination of anterior suture suspension techniques, with or without anterior alar cartilage or miniplate augmentation, have also been utilized. This involves the placement of bilateral suture loops around the collapsible segment of trachea and suspending the A-frame anterolaterally to the strap musculature. For this to withstand the test of time without recurrent collapse, there likely needs to be some degree of scarification to allow for the suspended trachea to maintain the patent position. In other words, the sutures act to temporarily suspend the airway in the desired position, while scar tissue between the straps and trachea or intratracheal incisions are allowed to heal in the desired position. This technique has been used in concert with endoluminal laser incisions and stent placement, anterior thyroid alar graft augmentation, and during primary stomal closure with good anecdotal success (Figures 3 and 4). Suture placement can be performed in an open fashion, or through percutaneous incisions with suture insertion via angiocatheters.

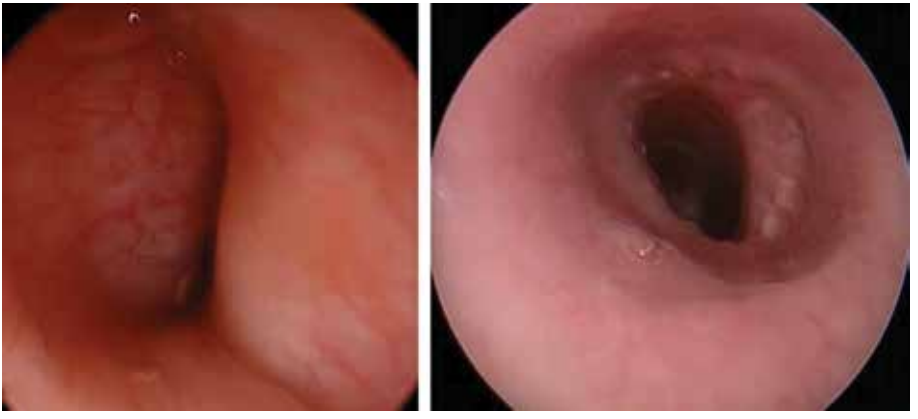

Figure 1. Severe A-frame deformity (left) following resection and primary anastomosis (right).

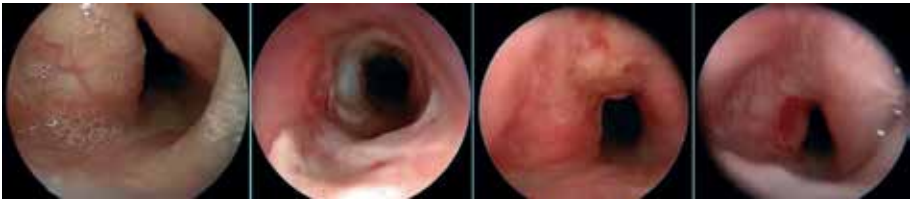

Figure 2. Initial A-frame deformity repaired with laryngotracheoplasty with anterior rib graft. Progression to recurrent obstruction is seen in the figures from left to right. The patient ultimately required resection of the A-frame deformity and primary anastomosis.

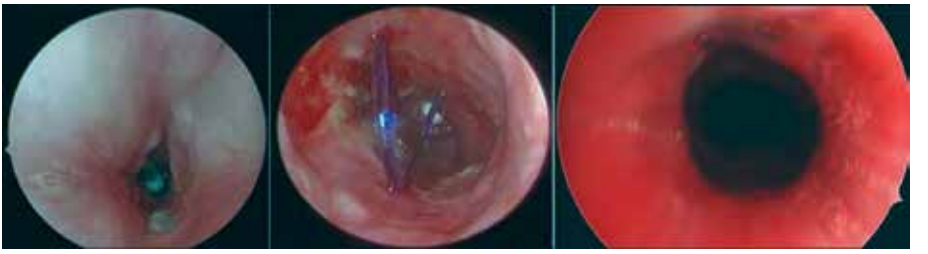

Figure 3. Revision laryngotracheoplasty for A-frame deformity involving anterior suspension sutures. Preoperative, intraoperative and postoperative endoscopic views.

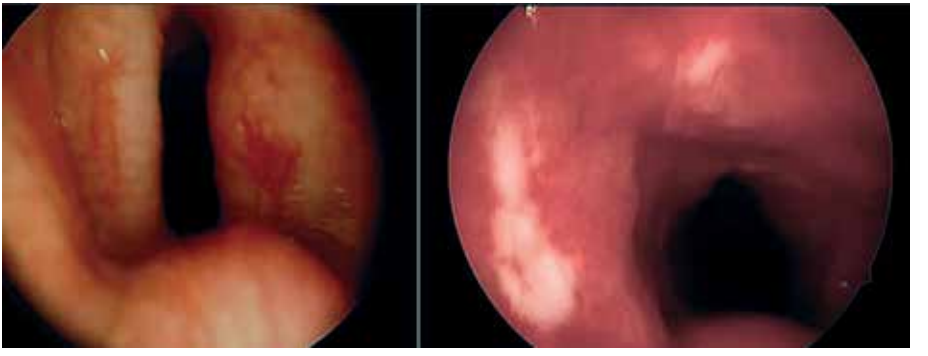

Figure 4. A-frame deformity (left); 3 months following endoscopic laser excision and hollow silastic stent placement. The stent was removed after 3 weeks.

Conclusion

Tracheostomy remains a common and often life-saving procedure. However, despite its utility, several short and long-term complications have been reported pertaining to airway patency and structure. Peristomal complications may become evident before or after decannulation, and often require active management in order to ensure successful decannulation. Diagnosis of these lesions requires appropriate suspicion and work-up, and a thorough endoscopic evaluation of the airway remains the criterion-standard. As discussed in this chapter, peristomal complications can be categorized as a problem of tracheal soft tissue or tracheal framework, the former being more amenable to endoscopic intervention. Importantly, the management of peristomal complications is pathology-specific, and no single method is suitable for all complications.

Finally, it should also be noted that, while this chapter discusses the most common peristomal complications as well as their most common approaches to management, it is not all-inclusive. The field of airway reconstruction is dynamic, with novel techniques and approaches emerging on an ongoing basis. Selection of a management approach for the pathologies described herein should be informed by novel insights from the constantly evolving literature and the airway community. It should employ the skillset that best-suits the practitioner and their patient population.

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The role of posterior tracheopexy for severe tracheomalacia in children

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Key words: Severe tracheomalacia, cough, respiratory infections, tracheopexy.

Tracheopexy is the fixation of the trachea to neighboring structures with the aim to widen the lumen of the trachea and avoid collapse [1].

Tracheomalacia (dynamic collapse of the trachea and bronchi) presents as a wide clinical spectrum ranging from asymptomatic patients with positive findings on bronchoscopy to patients with a life-threatening condition [1,2]. Patients that present with collapse of the posterior wall of the trachea and bronchi due to the loss cartilage-to-soft tissue ratio (normally 4:5) and that have severe symptoms affecting their quality of life, such as cyanotic spells, incapacitating episodes of cough, sleep disturbances, life-threatening brief resolved unexplained events (BRUEs), exercise intolerance, recurrent infections, multiple hospital admissions, apnea, and in some cases death, may benefit from surgical correction [3].

Patients with collapse of the posterior wall are usually those with a history of esophageal atresia but some may have primary tracheobronchomalacia associated with genetic syndromes, such as trisomy 21 [4].

Posterior tracheopexy may be performed all along the trachea; here, we describe cervical and intrathoracic posterior tracheopexy [5].

Intrathoracic posterior tracheopexy consists of a stepwise intervention:

1. Endoscopic assessment of the trachea in three phases.

2. Chest angiotomography to localize the aortic arch and evaluate the presence of vascular rings to determine the appraoch (left or right thoracotomy or via the fourth intercostal space, or sternotomy in case of associated vascular malformations).

3. Transoperative endoscopic view requiring a fibrobronchoscope of an adequate calibre that allows for the ventilation of the patient during the surgery so that external ventilation of the patient is not necessary. Availability of the necessary equipment and a multidisciplinary team in which the anesthesiologists play a fundamental role; ECMO may be used in children in whom mechanical ventilation is not feasible due to lung disease (Romero D, unpublished data).

4. Identification of the longitudinal ligament anterior to the spine and dissection of the thoracic conduct with lateralization towards the aortic arch.

5. Aortopexy of the descending aorta to reduce the space between the carina and the spine: stitches are placed in the anterior wall of the aorta up to the lateral wall of the spine protected with pleural or pericardial pledgets. In this phase of the surgery, hemodynamic monitoring is important. Preductal and a postductal arterial lines are recommended to avoid the risk of obstruction of the blood flow of the aorta. Dissection of the descending aorta and the aortic arch should be done cautiously, avoiding damage to the vertebral arteries and the artery of Adamkiewicz (arteria radicularis magna), a spinal cord artery that arises between T5 and T8 in 15% and between T9 and T12 in 60%, typically on the left side of the aorta. A lesion to the arteria radicularis magna may cause paraplegia.

6. Posterior tracheopexy is performed with vascular prolene stitches and a TF needle, reinforced with autologous pledgets, from the wall of the involved bronchi and the posterior trachea up to the anterior longitudinal ligament of the spine taking care not to ligate vital arteries. If the descending aorta is on the left side, the pexy is initiated from the left bronchus, following the left line of the posterior wall of the trachea, leaving untied sutures in place, then the right line of the posterior wall of the trachea, and finally the right bronchus. The endoscopic view is useful to prevent intraluminal sutures because of the risk of granuloma formation and to check if the pexy is adequate. The suture line should not be too close to the extremes of the cartilages and at the level of the longitudinal ligament the sutures should be placed in a transverse position to fix them to the longitudinal fibers of the ligament.

Both the thoracoscopic and the robotic approach have been described. The latter option has been shown to solve inconveniences of distal movements facilitating some steps in the surgery. Selection of the technique depends on the size of the patient, history of previous surgeries, and the learning curve of the surgeon [4,8,9].

Posterior tracheopexy of the upper (T1) and middle (T2) trachea has been performed via cervicotomy, mainly in patients with a congenital tracheoesophageal fistula without esophageal atresia with posterior wall prolapse [1,5,7]. This technique has been performed endoscopically (unpublished data, Romero D.) through right lateral cervicotomy with an anterior approach to the sternocleidomastoid muscle, careful dissection of the tracheoesophageal groove sparing the recurrent laryngeal nerves, anterior rotation of the trachea, posterolateral mobilization of the esophagus, identification and

resection of the fistula, closure of the trachea and esophagus with interrupted absorbable sutures, identification of the anterior longitudinal ligament of the spine and a double-line pexy with pledgeted prolene sutures from the trachea to the anterior ligament sparing the esophagus. Before performing the dissection, anterior suspension of the trachea can be tested with external splinting with bronchoscopic evaluation to check whether the malacia is hereby repaired or if a posterior cervical pexy or a combination of the techniques is required. Dr Jennings recommends a left-sided approach through cervicotomy as the right recurrent laryngeal nerve is further from the tracheoesophageal groove and the risk of injury is lower in a left-sided approach.

Post-operative management: Depending on the clinical condition of the patient and previous lung involvement, a short hospital stay with a mean of two days in the PICU has been reported. Most patients are extubated immediately after surgery [1,5].

Usually, the effectivity of the tracheopexy is determined based on symptom improvement. A 100% improvement in cyanotic spells and BRUEs, and different degrees of improvement in cough, a change in cough characteristics, a decrease in respiratory infections with marked improvement in the quality of life of the patients is observed [3].

Successful management of these patients is also influenced by concomitant management (at the time of surgery) of associated conditions, such as esophageal stenosis, recurrent tracheoesophageal fistula, and residual esophageal diverticulum in patients with a history of esophageal atresia and/or correction of vascular rings.

Ventilation-dependent patients with tracheobronchomalacia had the worst prognosis as ventilator weaning was achieved in only 50% and a need for complementary airway procedures. Decannulation was possible in a good proportion of children (4/5 and 20/25, respectively) after combined anterior and posterior management [1,5]. In the phase of endoscopic evaluation, prematurity-related malacia of the small airway, bronchopulmonary dysplasia, and other entities should be ruled out [1].

Nasofibrolaryngoscopy is performed on the fifth day postoperatively to assess vocal-fold mobility and compromise of the recurrent laryngeal nerve.

Follow-up endoscopic evaluation depends on the symptoms of the patient postoperatively; Boston recommends at one year after surgery [3,5].

Preventable intraoperative complications may present, such as extubation or tube occlusion due to thick secretions that may require repositioning of the patient for adequate airway management. Surgery-related complications include bleedings, injury to the recurrent laryngeal nerves, injury to the vertebral and spinal cord arteries (which has not been reported but may present), and chylothorax [8]. These surgical risks diminish when the procedures are performed by a multidisciplinary team at specialized centers.

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Airway pearls

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Introduction

"Pearls" are generally items of practical advice, not so much evidence based, but more typically experience based. These may represent diagnostic suggestions, therapeutic suggestions, or may even be more advice based, eg "do not do this, it won't go well". As with most information in this vein, you may not agree with some of these suggestions, or you may actually have a better idea or technique. This serves as a series of ideas and techniques, and if only one or 2 are relevant to you, then this article is still of value. While this will focus on airway problems in children, it will also spill over into other allied pathologies on occasion. Entirely deliberately, there are no references, although some of these techniques have been published.

Overview / concepts

It is useful to consider airway surgery as some basic concepts that can help drive your management decisions.

Concept 1: The larynx, trachea and bronchi may be considered as a cartilaginous exoskeleton. This is useful when considering whether a child with a laryngotracheal stenosis is best managed endoscopically, or with open surgery. If the cartilaginous exoskeleton of the airway is intact, and you are dealing with intraluminal scar tissue, then endoscopic surgery may be a useful management strategy. However, if there is a problem with the exoskeleton of the airway (missing cartilage, complete tracheal rings, an "A" frame deformity at an old trach site, an elliptical cricoid, etc), then open airway surgery may be more appropriate. If it is possible to alter the exoskeleton of the airway endoscopically (eg endoscopic anterior cricoid split, endoscopic laser resection of one side of a tracheal "A" frame deformity) then open surgery may still be avoided for some pathologies.

Concept 2: Open airway surgery for laryngotracheal stenosis superficially appears to have a myriad of possible operations. However almost all operations may be classified under 1 of 3 headings: Expansion procedures, Resection procedures and Slide procedures. Expansion procedures include laryngotracheal reconstruction (LTR), whether with costal cartilage or thyroid alar cartilage, whether anterior grafts or posterior grafts, and whether single staged or double staged. Expansion procedures also may include other operations, including pericardial patches. Resection procedures include tracheal resection and cricotracheal resection (CTR). And the most recent technique is the slide tracheoplasty, first described in 1989.

Concept 3: Evaluate and optimize before you operate. Airway surgery is not necessarily simple, and the consequences of failure are not trivial. Outcomes are less optimal with revision surgery. Pre-operative evaluation and patient optimization prior to surgery are strongly advocated. We prescreen children for MRSA and pseudomonal infections, especially if a tracheotomy is present, and pretreat accordingly. Children with an "active" larynx, with inflammation and edema, have significantly worse outcomes. An "active" larynx may be due to gastroesophageal reflux disease, eosinophilic esophagitis, or may be idiopathic. If the underlying cause is treated, and

the larynx no longer "active" then the risk of failure is greatly diminished. In children with an idiopathic "active" larynx, azithromycin used as an anti-inflammatory drug is effective in 50% of cases – this is using a Monday / Wednesday / Friday dosing regime for weeks or months at a time.

Intubation

Intubation of the retrognathic infant can be extremely challenging. Three suggestions that will assist in intubation in most (but not necessarily all) retrognathic infants are as follows:

- Place your laryngoscope blade to the right of the midline (so close to the canine tooth area than the incisor tooth area) – this flattens the angle of attack.
- With your left hand holding the base of the laryngoscope blade and handle, leaving your little finger free to place laryngeal pressure, rather than having an assistant do so.
- Intubate with a styletted endotracheal tube, with the tip of the bevel of the tube being anterior, and with a 30 degree bend in the stylet 1-1.5cm from the tip – that way if you can visualize the back of the arytenoids only, the tube will tend to deflect anteriorly into the glottis if the bevel tip is anterior.

Note: if you are struggling to intubate, most neonates can still maintain oxygenation while being bag and mask ventilated – it is better to abandon your first attempt if the oxygenation is dropping, and bag the baby till oxygenation recovers, and then have a second attempt, rather than persist in the face of falling saturations and a dropping heart rate.

Novel off-label uses of quinolone / steroid topical drops

In many countries, a commonly used eardrop is Ciprodex. This contains a quinolone antibiotic (ciprofloxacin) and a steroid (dexamethasone, 1mg/ml). Where not available, there are often similar drops available, or mixing bottles of dexamethasone eye drops with a quinolone eye drop will achieve the same result. The high topical quinolone antibiotic and steroid concentration provide excellent Staphlococcal and Pseudomonal coverage, making this a useful topical drug in the airway. It is extremely effective on granulation tissue. Typically in a patient with a tracheotomy, 3 drops 3 times a day down a tracheotomy tube for a week is suggested, or in there is not a tracheotomy, a typical dose is 1 ml of Ciprodex mixed with 1 ml or saline and nebulized twice a day for a week. This useful in treating granulation tissue, tracheitis, and episodes of bloody secretions.

Ciprodex may also be useful in the nose (eg for a week following choanal atresia repair, or sinus surgery). It is effective on stomal granulation tissue (1 drop on the outside of the shaft of a trach tube 3 times a day for week). It is useful following stent removal to promote the resolution of granulation tissue.

Endoscopic surgery

There are many techniques for performing supraglottoplasty for laryngomalacia in children under a year. Our preferred technique is to perform an initial microlaryngoscopy and bronchoscopy (MLB), and then nasally intubate the child with a relatively small cuffed endotracheal tube, suspend the child on an appropriate laryngoscope, and perform the supraglottoplasty with microlaryngeal instruments. This has the advantages of being simple for the anesthetist, and if microlaryngeal instruments are used (as opposed to a laser), then intubation is permissible. It is relatively easy to work around the endotracheal tube. We typically extubate at the end of the procedure, observe overnight, and discharge the following day.

In children with a laryngeal cleft, endoscopic repair is often achievable. This is our preferred technique in child with a deep interarytenoid notch, a type 1 or type 2 cleft, and in selected type 3 clefts. Retrognathia may hinder endoscopic repair. Our preferred technique is single layer mass closure, where we remove a strip of mucosa on either side of the cleft, from 2 mm above vocal cord level, to the apex of the cleft. This may be done with microscissors, or with a laser. Suturing is done with a monofilament thread, with the needle initially entering on the esophageal side of the repair, very close to the cut mucosal edge, and exiting on the same side very close to the tracheal cut mucosal edge. The needle is them passed on the opposite side, tracheal side to esophageal side, and the suture tied with at least 6 throws of the monofilament suture. Once the proximal suture is tied, the aryepiglottic folds are then divided, to minimize the risk of inducing laryngomalacia. In an infant a 6.0 PDS on BV-1 needles is suggested, and if there is a longer cleft, it is useful to bend the BV-1 needle to resemble a P-2 needle. In older children a 4.0 PDS on a P-2 needle or even an RB-2 needle is effective. While this is typically a fairly rapid procedure, if it is taking over an hour, we suggest taking the patient out of suspension for 5 minutes each hour to minimize the risk of tongue ischemia.

Traditionally upper esophageal foreign bodies, usually coins, are removed with an esophagoscope and appropriate forceps. Often the lens of the endoscope will have secretions distorting the view, and often a suction is required to clear secretions. We have found that in an intubated child, a long straight anesthetic laryngoscope blade (eg a Phillips 2), may be passed behind the larynx, and through cricopharyngeus, and provide excellent visualization of an upper esophageal foreign body, and permit the use of endoscopically guided forceps to easily and rapidly remove the foreign body without the need for an esophagoscope.

The use of stents in the airway in a child without a tracheostomy, should be considered only with great caution. However rarely it may be appropriate. With expandable metal stents (eg Palmaz deployed with a balloon dilator), we suggest relatively underinflating the stent. Ideally it needs to be big enough to prevent collapse of the lumen, and to "grip" the walls of the trachea (to prevent migration), but small enough to not integrate into the walls of the trachea, or cause granulation or scar formation. Ideally a stent should be considered a temporary solution, and if possible, removed within weeks or months. The removal technique is to endoscopically grasp the proximal end of the stent, and bend it into the lumen so that a firm grip can then be obtained. If this is an endoscopically guided forcep, the camera and light cord are then detached, and the forcep is spun 360 degrees, at least 4-5 times, to wrap the stent around the forcep, disengaging it from the tracheal walls, and it is then removed. It is advisable to have pre-oxygenated the patient, to have sprayed Afrin or a similar decongestant into the airway, to have back up forceps and most importantly, to have a tolerant anesthetist. Nebulized Ciprodex should be used for the week after stent deployment and stent removal.

Balloon dilation

A key consideration is that the size of the balloon is more important than the pressure placed within it. For example, a 4-year-old should take a 5.0 mm endotracheal tube with an outer diameter of 6.8 mm. So typically we would select an 8mm balloon to dilate the larynx and a 9mm balloon to dilate the trachea, usually inflating to the rated burst pressure of the balloon (typically 17 Atmospheres [Atm]). However, if you selected a 6mm balloon, even if you inflated it to 100 Atm, it would slide in and out without achieving any useful dilation. Meanwhile a 12 mm balloon in the larynx, even at only 5 Atm, could risk significant damage to the larynx. Balloon size recommenda-

tions may be found in the "Airway Card" app available for free for both iPhones and Androids.

As a guideline, most cases of acquired stenosis requiring balloon dilation, ideally require repeated balloon dilation. The concept is that as scar tissue reforms, repeated dilation will maintain an adequate lumen. While animal studies are now underway, until those results are known, we recommend dilation on 3-5 occasions, with 7-10 day intervals between dilations. On the first or second dilation, consideration may also be given to steroid injection (Kenalog), and scar division (whether with a laser or a sickle knife). However if, after 5 dilations, the problem persists, then consideration should be given to other options, such as open airway reconstruction. It is worth noting that a guideline is indeed a guideline, not a mandate, and that in individual circumstances, continued dilation may be appropriate.

There are certain conditions where repeated dilation is not necessary. Balloon dilation and steroid injection in cases of subglottic stenosis (SGS) associated with Wegener's Granulomatosis (granulomatosis with polyangiitis) is extremely effective, and a single dilation may provide years of benefit, till symptoms recur, and repeated dilation is required. A similar situation is seen with idiopathic SGS (typically Caucasian women in their 40s, give or take a decade).

While airway balloons are primarily designed for use in the larynx, trachea and bronchi, there are many useful and novel uses for them in other areas:

– Balloon dilation of the nasal passages to out fracture the inferior turbinate in a child with narrow nasal passages – typically use a balloon 2-3mm bigger than would be used in the trachea of a child of the same age. A turbinate reduction (eg cautery) may be combined with this if deemed appropriate.
– Balloon dilation of the choanae – this may be very useful a week after choanal atresia repair, and typically, in a term infant, and 8mm or 9mm balloon would be selected.
– Balloon dilation of the pharynx or esophageal inlet – here select the diameter you wish to dilate to, and then select 2 balloons of half that size, and inflate them simultaneously side by side – this is a more anatomical configuration. For example, in a teenager, if you wanted to achieve 32mm of dilation, we recommend placing 2 x 16mm balloons side by side and inflating at the same time.
– In a child with a small tracheocutaneous fistula (TCF), who is requires tracheotomy tube replacement for whatever reason, placing a balloon dilator through the TCF may rapidly allow tracheotomy tube replacement. Use a balloon that is 2mm larger than the outer diameter of the desired tracheotomy tube.

Open surgery

While LTR with costal cartilage grafts is not necessarily simple or straightforward, outcomes are primarily influenced by the grade of stenosis, whether the larynx is inflamed, whether the stenosis is multilevel, and whether it is a revision procedure. The surgeon is also a factor, but as with most surgeries, not necessarily the critical factor. And if complications arise, typically a tracheotomy will salvage the situation, at least in the short term. Meanwhile CTR and Slide Tracheoplasty are operations where the training, experience and ability of the surgeon are more relevant. And any operation where the trachea is transected carries the innate risk of dehiscence. As with all operations, a surgeon should be not only capable of performing the procedure but should ideally be capable of managing the consequences of complications should they occur.

In a double stage airway surgery utilizing a suprastomal stent, we suggest "Quad" therapy at the time of stent removal. "Quad" therapy comprises the 4 following me-

dications: a proton pump inhibitor; an antibiotic that covers staphylococcus (eg Augmentin); a steroid (decadron, 4mg/kg up to 20mg, given every 48 hours); and Ciprodex down the tracheotomy tube. The "Quad" therapy should start 3 days prior to stent removal and continue for 7 days after, usually coinciding with a second look MLB. The Ciprodex is best given as 3 drops tid, with a speaking valve being placed over the tracheostomy tube for 5 minutes immediately after the drops are instilled.

Operations to expand the glottis (whether for stenosis, paralysis, or cricoarytenoid joint fixation), risk exacerbating any aspiration tendencies the child may have. If a child is not aspirating pre-operatively, they are at far lower risk of aspirating post-operatively. In a child with a tracheotomy tube, the simplest test for aspiration is food dye testing – a drop of green food dye in what the child eats or drinks, or in the GT feeds, or placed on the tongue – if green is suctioned from the tracheotomy tube after, then the child is aspirating. This is a cheap physiological test that can be done by the family in their home, and can be done on multiple days with multiple consistencies. It is not a useful test in a child with a grade 4 SGS, in which case a functional endoscopic evaluation of swallowing (FEES) would be recommended.

In children with congenital tracheal stenosis, usually due to complete tracheal rings, initial evaluation with bronchoscopy should be performed with caution as you do not want to transform a compromised airway into a critical airway. The smallest available telescopes are used, and it is better to note a stenosis, than to force an inappropriately large telescope through a stenosis and induce edema in an already narrowed airway. Rarely are the first 2 tracheal rings complete, and therefore, if circumstances demand, shallow intubation may be tolerated. In an intubated child with distal tracheal stenosis, a long inspiratory time (I-time), and more importantly a long expiratory time (E-time) may assist with ventilation, and high peak pressures may be toleratred (as the stenosis relatively protects the alveoli from the consequences high proximal pressures). High humidity is strongly recommended as mucous plugging is potentially catastrophic, and often preceded but slowly rising CO2 levels, even when oxygenation is adequate. In a crisis, 1 ml of 1:10,000 epinephrine down the endotracheal tube may be life-saving. If the child is successfully extubated, high humidity is still required, and regular nebulized saline is recommended. Tracheotomy is rarely helpful when dealing with distal tracheal stenosis, and is more likely to induce a crisis than alleviate one. The operation of choice for congenital tracheal stenosis is the Slide Tracheoplasty. Our current recommendations are to estimate the central point of the stenosis, dividing the trachea on a bevel over 2 rings, proximal anterior to distal posterior, with the distal margin of the transection being at the midpoint of the stenosis. The distal half of the tracheal is then split in the midline posteriorly to normal trachea, or to carina, or even down a bronchus if required. The proximal trachea is split anteriorly to just beyond the stenosis. In a child under 1 year we perform the anastomosis with a 6.0 PDS with double armed BV-1 sutures, and do a running repair, tightening with nerve hooks as we progress, and with a single proximal know completing the anastomosis.

Tracheotomy care

In a ventilated child, an extended collar tracheotomy tube will place less pressure on the skin from the flanges of the tracheotomy tube, and will lower the risk of skin breakdown.

In some children, use of a speaking valve may be challenging, due to either a large tracheotomy tube, a suprastomal narrowing or a subglottic stenosis. Our protocol when trialing a Passy Muir Valve is to place an in-line oxygen adaptor on the tracheo-

tomy tube, with the tubing from the oxygen adaptor going to a pressure manometer, and the Passy Muir valve then placed on the oxygen adaptor. If the pressure is over 10cm of water pressure during quiet exhalation, then the valve is modified with a hole drilled in the side (this needs to be a small hole – a 1/16th of an inch drill bit, or a 1mm drill bit). If the pressure is still over 10cm of water pressure, a second hole may be drilled. If the pressure is still over 10cm of water pressure breathing quietly, despite 2 holes drilled with a 1/16th inch drill bit, then a Passy Muir Valve should not be used.

Another occasional problem with tracheotomy tubes is that they may become affected by bacterial biofilms, usually due to pseudomonas. This is usually seen in a child who initially did not have secretion problems, and now has recurrent tracheitis, often with a pseudomonal odor, and a tendency to mucus plugging. This will improve for a few days after tracheotomy changes, but then recur. Our protocol is to take 3 brand new tracheotomy tubes, and then start daily tracheotomy tube changes for a 2-week period. On any given day, one of then tubes is in the patient, another is soaking in a gentamycin solution (an 80mg ampoule of IV gentamycin is placed in a beaker with just enough water to cover the tracheotomy tube, with the water being replaced weekly), and the third tube is drying. At the same time, the child is using Ciprodex, 3 drops tid, down the tracheotomy tube.

When it is felt that a child is approaching decannulation, our protocol is to perform an MLB, and then downsize the tracheotomy tube, and when the child is fully awake, place a cap on the tube to plug it. We watch the child in the hospital for 2 nights, and then let the child return home capping day and night (assuming there is nighttime monitoring of the child). It is useful if the child has an upper respiratory tract infection over this time to be sure that they do not need to be unplugged. A sleep study is also an option. If a child has done well, then weeks or months later (depending on individual circumstances), the child returns for a further MLB, and decannulation, with a further 2 nights of monitoring. They return 6-8 weeks later for a further MLB (to ensure that there is not tracheal granulation tissue at the old tracheotomy site), and is there is still a tracheocutaneous fistula, the removal is planned in another few weeks, so that the hole may shrink as much as possible.

Our technique for tracheocutaneous fistula closure is to "apple-core" out the skin tract, insert a very small tracheotomy tube, and once the child is fully awake an hour later, remove that tube and let the fistula heal by secondary intention. The closure rate is very high, and the complication rate (especially subcutaneous emphysema) is extremely low.

Skin / stoma care

The skin around a tracheotomy stoma may get quite inflamed, moist, and at risk of ulcer formation. A simple and effective skin protectant is Chapstick lip balm. This is a wax, and so durable. It is not possible to overdose, it is readily available and cheap. This may be placed around a stoma, under tracheotomy ties, multiple times a day if desired, and allow skin to recover. It is also effective around other ostomies, such as gastrostomy tube sites, and is also useful on the chin in children with chronic drooling. If granulation tissue is also present, then topical Ciprodex for a few days may of value.

Conclusions

While evidence-based medicine has much to recommend it, not all ideas are amenable to an evidence-based approach. There is still a place or opinion, experience and expertise. I appreciate the opportunity to contribute an entirely non evidence-based article.

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