Establishing a Data-Driven Approach to Voice Care

The care of voice disorders is often based on received wisdom — information and clinical practices that may or may not be effective, but have been legitimized by tradition. “While that’s not a rare phenomenon in medicine in general,” says Lucian Sulica, MD, a nationally recognized laryngologist in the Department of Otolaryngology – Head and Neck Surgery at NewYork-Presbyterian/Weill Cornell Medical Center, “it’s important that we pursue the data where it exists, and test our practice against it.”

Dr. Sulica, Director of the Sean Parker Institute for the Voice at Weill Cornell Medical College, has a particular interest in medical and surgical treatment of voice disorders resulting from phonotrauma — or the physical stresses on the vocal folds (“folds” and “cords” are synonymous terms) resulting from voice use. Phonotrauma, notes Dr. Sulica, is a complex event and generates a wide spectrum of injury. “With phonotrauma, there are a lot of changes in the tissue,” he says. “Some of it is amenable to behavioral change, some of it requires surgical excision and reconstruction, and then some of it culminates in permanent scar.”

One of the more alarming types of phonotraumatic injuries is a vocal fold hemorrhage, or bleed. This occurs when one of the small blood vessels of the larynx tears and releases blood into the vibratory tissues of the vocal folds. Not only is it dramatic in appearance, but the voice change is usually sudden and pronounced. Conventional wisdom holds that it is a grave event, with potential career-ending consequences in vocal performers.

Cleft Lip and Palate: High Incidence in Honduras Leads to Search for Genetic Origin

Each year, hundreds of children are born with cleft lip and cleft palate in Honduras, a country that has among the highest incidence of these conditions in the world. While cleft lip and cleft palate can be related to nutritional factors, there is potentially a genetic basis as well, though this is not yet well defined.

In an effort to uncover the reasons for these birth defects, the Doris Duke Clinical Research Fellowship at Columbia University, in collaboration with the Honduran Medical Institute, has embarked on a research effort to elucidate the genetic basis of non-syndromic cleft lip and cleft palate in the Honduran population. The study, which involves families with more than one affected member, is under the direction of Joseph Haddad, Jr., MD, Chief of Otolaryngology, NewYork-Presbyterian/Morgan Stanley Children’s Hospital, along with Wendy K. Chung, MD, PhD, Director of the Clinical Genetics Program at NewYork-Presbyterian/Morgan Stanley Children’s Hospital. Dr. Haddad has long had ties to Honduras, North coast, Peru, Portrait Vessel of a Man with a Cleft Lip and Tattoos, 100 B.C./A.D. 500, Ceramic and pigment, 21.3 x 14.9 x 21.6 cm (8 3/8 x 5 7/8 x 8 1/2 in.), Gift of Nathan Cummings, 1957.607, The Art Institute of Chicago
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“Despite vocal fold hemorrhage turning up reasonably frequently in the clinic,” says Dr. Sulica, “we didn’t know basic information. For example, a patient with a hemorrhage always wants to know how likely it is to happen again – a perfectly reasonable and important question for which the answer does not exist. We set out to address this.”

The goal of their investigation – the results of which were published in the January 2014 issue of The Laryngoscope – was to examine patients with vocal fold hemorrhage to determine how many experienced a second one, and to identify factors which might lead to such an event.

Their method included a review of 47 patients presenting with a new vocal fold hemorrhage. Of these, they found that 12, or 26 percent, hemorrhaged again. The researchers then studied four features of the examination to see if they correlated with recurrence, as well as outcomes after the hemorrhage. Their findings showed that recurring hemorrhage was significantly more likely – about twice as likely – in patients with enlarged blood vessels, or varices, on the vocal folds. Just as importantly, they discovered that all patients were able to return to performance after appropriate treatment.

“Beyond establishing the rate of recurrence, we concluded that a surgical intervention to address varices was appropriate in patients who had had a hemorrhage to minimize the risk of another,” says Dr. Sulica. “Just as importantly, we showed that patients with hemorrhage – many of whom are performers – are almost always able to return to their prior level of voice use. This serves to allay the anxiety about this type of injury and change the prevailing notion of hemorrhage. It is almost never a catastrophic event.”

Dr. Sulica and his colleagues have also examined other types of phonotraumatic damage in a similar way. Pseudocysts are lesions that affect voice quality in a more chronic way than hemorrhage. “Pseudocysts are frequently treated like polyps, with a uniform recommendation for surgery, although their appearance and clinical behavior are clearly different,” observes Dr. Sulica. A study of 46 cases, which appeared in the May 2014 issue of The Laryngoscope, revealed that in three patients – again, many of whom are performers – do not need surgery to continue in the level of voice use their profession demands. Voice therapy by itself appears to be sufficient. A follow-up study of surgical outcomes in the one-third of patients who chose to undergo surgery is in progress.

Many unresolved clinical issues in voice disorders lend themselves to this type of study, notes Dr. Sulica. “Finding the data helps us take a more effective approach for the benefit of our patients,” he says. “It also helps us to dispel some of the clinical misconceptions and accompanying anxieties, so that patients can understand their choices in a rational way, and allows us to show them that in the vast majority of cases, these injuries can be repaired.”

Reference Articles

For More Information
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Sean Parker Institute for the Voice: A Bench-to-Bedside Approach to Voice Care

In September 2013, the Sean Parker Institute for the Voice made its debut at Weill Cornell Medical College thanks to funding by new-media entrepreneur and philanthropist Sean Parker. “The Parker Institute represents an approach to voice care in which excellent clinical care is married to research and innovation,” says Lucian Sulica, MD, Director of the Institute, whose clinical expertise lies in the treatment of voice disorders, including care of the performing voice.

“Sean Parker made a very generous donation to establish the Parker Institute for the Voice out of an appreciation first, for the importance of the voice and voice health, and second, for the fact that this is really an underfunded field,” notes Dr. Sulica. “People tend to take the voice for granted, until they themselves have a voice problem. When their ability to communicate is impaired, they realize what a tremendous problem it is. In an information-based economy, communication is currency. If you don’t have your voice, you’re simply handicapped. And Mr. Parker really understands that.”

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to Honduras, having traveled there twice each year since the early 1990s with Howard Smith, MD, Professor Emeritus at Columbia, to provide surgical and medical care for children with cleft lip and cleft palate. “These children were not getting appropriate medical care at a young age when it could make a significant improvement in their childhood and adulthood,” says Dr. Haddad.

Their medical missions ultimately led to the development of a program in which he and his NewYork-Presbyterian colleagues began to train Honduran doctors in the delicate surgical techniques of repairing cleft lips and cleft palates. Working with the Honduras Ministry of Health, the University of Honduras School of Medicine, and the Hospital Escuela Department of Plastic Surgery, they established a three-year residency training program specifically to deal with congenital abnormalities in children. “That was really the beginning of our very strong commitment to the country,” says Dr. Haddad, who today serves as President of the Honduran Medical Institute, the foundation established in 1995 that helps to support this work.

The Genetic Connection

Gaining significant experience in the care and treatment of children with cleft lip and cleft palate, Dr. Haddad began to recognize that many of the children had multiple members of their family who were also affected with clefts. “Knowing that there was a possible genetic component to the problem and having a research interest in this area, I decided to investigate how many of our patients had other relatives affected,” he says. “About one-third of the patients we saw had relatives with cleft lip and cleft palate, be they a cousin, a parent, an aunt or uncle, or a grandparent.”

Dr. Haddad points to further evidence of a likely genetic component in the Honduran population that has been passed along to generations of families. “The manifestation of clefting goes back centuries,” he says. “We know this because many of the early cultures made realistic pottery and some of the pottery depicts individuals with cleft lip.”

Examining all the possible causes of cleft lip and cleft palate, Dr. Haddad notes that in addition to genetics, poor hygiene, diet, alcohol use during pregnancy, and the environment can also play a role. “Now whether it’s somebody who has a genetic predisposition and then has the additive factor of having a nutritional problem, or whether it’s purely nutritional or purely genetic in some individuals, that’s where a lot of the questions remain,” he says.

Looking for Answers

To begin to find some answers, Dr. Haddad started recruiting families having other affected family members. “We put together pedigrees of families that showed all of their relatives – who was affected and who wasn’t,” he says. “Then we got blood samples in order to obtain DNA from as many family members as we could. When we reached a critical number of over 100 families and many hundreds of individuals, we started to look at the genetics behind it.”

The researchers conducted their analysis by first studying the candidate genes. “We reviewed what other investigators had thought were important genes related to clefting and we started by looking at those,” he says. “We zeroed in on certain segments of the DNA with an SNP [single nucleotide polymorphism] evaluation.”

The results led them to apply and be accepted in a study funded by the National Institutes of Health that would examine the Mendelian genetics – the different ways that genetic information can be transmitted in families, some of them following a dominant gene model and some a recessive gene. “As part of the University of Washington arm of the study, the Center for Mendelian Genomics evaluated many of the family pedigrees that we sent to them,” says Dr. Haddad. “They decided that just by looking at the family pedigrees that there was some support for the idea that there could be a genetic mode of inheritance following Mendelian patterns for some of the families that we were seeing. Their analysis involves taking a step away from the really focused SNP testing and doing whole exome analysis – looking at all of the DNA data.”

Dr. Haddad and his team are now evaluating information sent back to them, seeking to determine if certain families have genes that appear to be playing a role in causing the cleft. “We’re essentially trying to find our own candidate genes,” says Andrew Lee, a medical student at Columbia University College of Physicians and Surgeons and a research fellow in ENT. “One of the biggest challenges is to find the best techniques to prioritize what genes could be related to clefting.”

“For 90 percent of the population in Honduras has the same genetic variation, then clearly that’s not going to be meaningful because 90 percent of the population doesn’t have clefts. But if a much smaller number has that variation and we’re noticing that it’s following a pattern in the families that we’re looking at, then that’s the sort of thing that gets us more excited. If it happens to be in a gene with a known function that might relate to this problem, it takes on even greater meaning.”

According to Dr. Haddad, the gene mutation that seems to be implicated can be created in mice that have the same genetic mutation. “We’re at a point in our research where we suddenly have this wealth of important information that’s specific to our families,” he says. “This is the dawn of a whole new age as we understand the human genome. We are fortunate in a sense to be doing the work in a country that is so right for this kind of study.”
According to Dr. Sulica, the clinical mission of the Parker Institute is to treat patients positively with an eye towards rehabilitation, and he says, “throw out the catastrophe/career-ender model of vocal fold injury.”

Says Dr. Sulica, “During voicing, vocal cords get injured repetitively, over and over again. This cumulative injury leads to very subtle abnormalities in performers’ vocal folds that impact their voice performance. And these artists are often poorly served. They get patted on the back, they are given steroids, they are told that nothing’s wrong and that they are anxious. They themselves have an inclination to blame themselves and question their technique. And there’s nothing more frustrating than seeing someone who’s been second-guessing themselves on technique when they’ve got a scar on the vocal cord that’s been the problem all along.”

Understanding the physiological problems they are having with their voice and receiving accurate information, explains Dr. Sulica, is tremendously empowering for any patient, but especially performers. “It’s very steadying for them,” he says. “They’re excellent to work with because they have much more self-awareness of their voice than most people.”

A specific goal of the Parker Institute is to address the problem of scar, which is central to anyone who uses his or her voice. In the context of voice problems, scar refers to a loss of tissue properties that permits the high-speed vibration necessary to voice production. It can result from disease or injury, and there currently exists no satisfactory treatment.

“It is explicit in the structure of the Institute that it is a bench-to-bedside translational enterprise,” says Dr. Sulica. “We’re currently recruiting for a basic scientist to focus specifically on vocal fold regeneration, and it will involve all of the advances related to tissue engineering – potentially stem cells, tissue scaffolds, biomodulators – all of that. There have been some great laboratory efforts in scar and there are great clinicians. We want to put all the resources in one place for the entire spectrum – for the science and for the patients, and especially for those who are performing artists, because they are the patients who really push us to do our best.”