OTOLARYNGOLOGY RESEARCH
UPDATE

FALL 2019

DEPARTMENT OF OTOLARYNGOLOGY

Inside This Edition

Expanding the Treatment Landscape for Nasal Polyps

From lab to bedside, **Stella Lee, MD**, is at the forefront of treatment for nasal polyps. Working primarily in chronic rhinosinusitis, she and her colleagues study novel immunotherapy drugs in clinical trials and investigate underlying disease drivers, environmental factors, and new technologies that could lead to improved treatment strategies.

Chronic rhinosinusitis affects five to 12 percent of people worldwide and is characterized by persistent inflammation of the sinonasal cavities. "My patients have difficulty breathing, smelling, tasting, and sleeping," says Dr. Lee. "Given its prevalence and quality-of-life burden, this is an underappreciated condition with causes that are still poorly understood."

Dr. Lee completed her residency in otolaryngology and head and neck surgery at Yale University, followed by a fellowship in rhinology and skull base surgery at Johns Hopkins University. She then joined the University of Pittsburgh Department of Otolaryngology as an assistant professor.

Treatment for chronic rhinosinusitis, which can occur with or without nasal polyps, typically includes topical steroids, oral steroids, or endoscopic sinus surgery — one of the most common surgeries performed in the United States. Many patients experience postoperative recurrence of nasal polyps and may undergo multiple surgeries with no lasting relief. In recent years, however, promising immunotherapy approaches have emerged.

"The University of Pittsburgh was one of the first U.S. sites to participate in international multicenter clinical trials to provide novel immunomodulators for chronic rhinosinusitis," says Dr. Lee. "We realized that if we could block the drivers of immunologic dysfunction, we would discover a more precise, less invasive way to treat our patients."

First Immunotherapy Drug for Chronic Rhinosinusitis With Nasal Polyps

On the basis of clinical trial results from Pittsburgh and beyond, the U.S. Food and Drug Administration approved the first immunotherapy drug for chronic rhinosinusitis with nasal polyps in June of 2019. The drug, Dupixent (dupilumab), can produce dramatic results in some patients with severe disease. "Within two weeks some patients can smell again, they can taste again. Their polyps just melt away, the sinuses are clear, and the mucosa normalizes," says Dr. Lee.

Dupixent targets interleukin (IL)-4 and IL-13, inhibiting the type-2 immune response thought to underlie many cases of chronic rhinosinusitis with nasal polyps. Dr. Lee is currently involved in clinical investigations of additional type-2-targeting drugs, such as omalizumab and benralizumab. Still, not all patients respond

(Continued on Page 2)

Nasal Polyps *(Continued from Page 1)*

to these drugs, symptoms recur after treatment is discontinued, and biomarkers are needed to identify which patients are good candidates for which drugs.

"It is still undefined how these therapies will fit into the current armamentarium" says Dr. Lee. "Now having this experience with clinical trials for drugs developed elsewhere, we now have the bandwidth and capability to do our own clinical trials, with our own drug targets and our own methodology."

Exploring the Potential of 15LO1 as a New Drug Target

For example, in collaboration with Sally Wenzel, MD, from the Division of Pulmonology, Allergy, and Critical Care Medicine at the University of Pittsburgh, and others, Dr. Lee currently is exploring the potential of 15-Lipoxygenase 1 (15LO1) as a new drug target. 15LO1 is a protein that acts downstream from IL-4 and IL-13 in the type-2 inflammatory cascade. In July of 2019, Dr. Lee, Dr. Wenzel, and colleagues reported in the *Journal of Allergy and Clinical Immunology* that 15LO1 is upregulated in nasal polyp cells sampled from patients with chronic rhinosinusitis. Inhibiting 15LO1 in these cells resulted in downstream inhibition of the inflammatory cascade.

"Our findings suggest that 15LO1 could be an even more specific drug target than IL-4 and IL-13. Now, we are using animal models to explore targeting 15LO1 with a small-molecule inhibitor," says Dr. Lee. The new findings earned recognition as the best Basic Science Manuscript at the Rhinoworld conference in June 2019, an international meeting that is held every 10 years.

Meanwhile, Dr. Lee is examining the molecular underpinnings of chronic rhinosinusitis to tease apart the many mechanisms that are likely at play. These insights could reveal new biomarkers that could aid treatment decisions, and they could open up new therapeutic possibilities.

In this vein, she and her colleagues recently reported that a higher load of mast cells in surgically removed nasal polyp cells could predict a more recalcitrant postoperative disease course. Elevated mast cells could thus serve as a biomarker associated with disease severity. This report — recognized as one of the Top 10 Clinical Abstracts at Rhinoworld 2019 — also suggests that mast cells may play an important underlying role in CRS pathogenesis.

Another recent project explored how to define subtypes of chronic rhinosinusitis with nasal polyps. "Not all nasal polyps are the same," says Dr. Lee. Among several dozen patients who underwent endoscopic sinus surgery, she and her collaborators found that levels of several different cytokines in different nasal tissues correlated with different clinical outcomes. The findings point to distinct inflammation-driving mechanisms in different patients that could enable targeted treatment strategies that are individualized to the patient.

Connections Between Environmental Pollutants and Chronic Rhinosinusitis

In addition to the molecular facets of chronic rhinosinusitis, Dr. Lee is actively investigating environmental exposures that may drive or exacerbate the condition.

In an ongoing project, she and her collaborators are combining clinical and residential data with spatial data on air pollution in the Pittsburgh region to examine links between chronic rhinosinusitis and exposure to pollutants, such as black carbon and fine particulate matter (PM 2.5). These efforts have already resulted in several published papers showing connections between the disease and certain pollutants.

"Many of my patients also are exposed to fumes and dust in their jobs at factories, hydraulic fracturing operations, hair salons, restaurants, or other workplaces," says Dr. Lee. "It's hard to prove a causal connection, and much more research is needed, but we are seeing associations between chronic rhinosinusitis and poor workplace air quality."

Breakthroughs in Cystic Fibrosis Research

Patients' microbiomes also may play an important role in driving or exacerbating chronic rhinosinusitis. Currently, Dr. Lee is studying connections between the microbiome and chronic rhinosinusitis in patients with cystic fibrosis. "This form of the disease does not have that type-2 inflammatory connection, but these patients do have polyps and they suffer tremendously," she says.

For this project, she is collaborating with Jennifer Bomberger, PhD, from the Department of Immunology at the University of Pittsburgh, to examine how the microbiomes of patients with cystic fibrosis evolve over time, and how those changes correlate with viral infections and nasal polyps. "We're using a variety of advanced techniques, incorporating machine learning, genome sequencing, and proteomics, and hopefully our findings will eventually translate to improved clinical care," says Dr. Lee. "Now with advanced therapeutics such as TRIKAFTA™ (elexacaftor/tezacaftor/ivacaftor and ivacaftor) we have a multi-institutional grant to study smell, microbiome, lung function, radiographic, and quality-of-life outcomes measures in patients with cystic fibrosis before and after starting the therapeutic. This study will help us better understand the inflammatory, functional, and microbial abnormalities in the disease process in relation to clinical measures and, hopefully, how recovery occurs."

A Device for Objectively Assessing a Patient's Sense of Smell

Dr. Lee also is using advanced technologies to develop new, more precise ways to monitor symptoms of chronic rhinosinusitis and other sinus conditions. Specifically, she is developing an "olfactometer," a device for assessing a patient's sense of smell much more objectively than is possible with current clinical methods.

The olfactometer delivers different odors to a patient's nose in a highly quantifiable, programmable manner. Meanwhile, the patient's brain activity is measured via magnetoencephalography (MEG). Dr. Lee says the sense-assessing technology is now at a patentable stage.

"Smell is often taken for granted, but it can be devastating not to be able to taste your food, and it is dangerous not to be able to smell smoke from a fire or spoiled food," says Dr. Lee. "With the olfactometer, we can hopefully deepen our understanding of loss of smell and develop better ways to diagnose it, first of all, and then treat it, too."

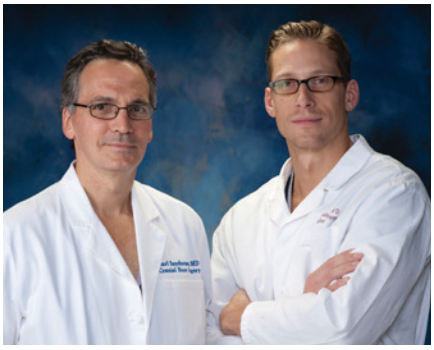
(Continued on Page 4)

Reaching the Apex: A New Surgical Approach to the Petrous Apex

The UPMC Departments of Otolaryngology and Neurological Surgery have been pioneering developers and proponents of the endoscopic endonasal approach (EEA) to skull base surgery for more than 30 years. In that time, the faculty and the skull base surgery program have become internationally sought for their surgical skills, research, and educational programs designed to teach aspects of EEA to new generations of surgeons around the world.

Carl Snyderman, MD, MBA, a professor in the Department of Otolaryngology, with a secondary appointment as professor in the Department of Neurological Surgery, has been with UPMC and the University of Pittsburgh since completing his residency in Otolaryngology in 1987. Dr. Snyderman and **Paul Gardner, MD**, (associate professor in the Department of Neurological Surgery), are co-directors of the UPMC Center for Skull Base Surgery, the first of its kind in North America. Dr. Snyderman was the first fellow to complete the cranial base surgery fellowship at UPMC in 1989. Since then, he has been at the forefront of cranial base surgery, exploring new applications of the endoscopic endonasal approach and driving advances in research and education. Dr. Snyderman is a past president (2015) of the North American Skull Base Society (NASBS) and is a current member of its board of advisors.

The last several years have seen the advent of new technological advances, new surgical procedures, and new training programs from



Carl Snyderman, MD, MBA, and Paul Gardner, MD

Dr. Snyderman and his colleagues, continuing the mission and expanding the legacy of Pittsburgh as a pioneer and leader in skull base surgery across the world.

Accessing the Petrous Apex: The Contralateral Transmaxillary Approach

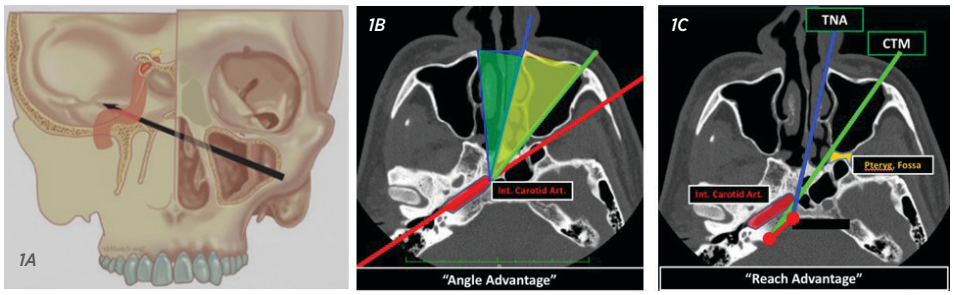
Published in the *Journal of Neurosurgery* in October 2018, Dr. Snyderman and colleagues outlined a new surgical technique they have developed called the contralateral transmaxillary (CTM) approach.

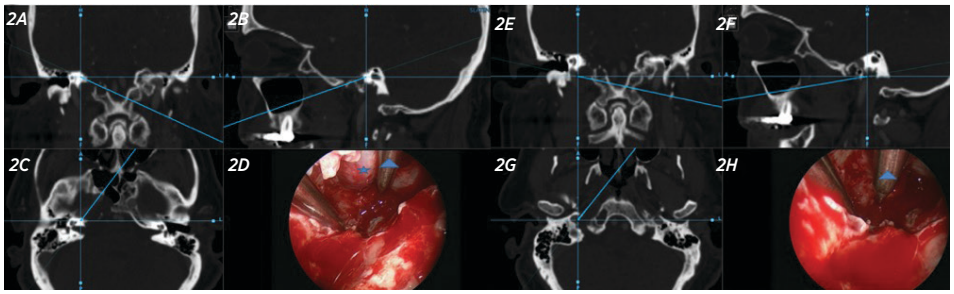
The CTM approach allows surgeons to access the difficult-to-reach region of the petrous apex (PA) with an improved angle of approach of approximately 25 degrees, versus what would typically be required through an endoscopic endonasal approach.

"This region of the skull base is a very challenging area to access; removing large tumors from it with other techniques is difficult and dangerous because of the vasculature and nerves. CTM allows us to access this region by coming at it from the opposite side via the sinuses. This approach allows us to work behind the internal carotid artery (ICA) (generally the paraclival segment of the ICA), greatly diminishing the risk of iatrogenic injury inherent with operating in that area," says Dr. Snyderman.

Their initial study and characterization of the technique, performed on a cadaveric model,

(Continued on Page 4)





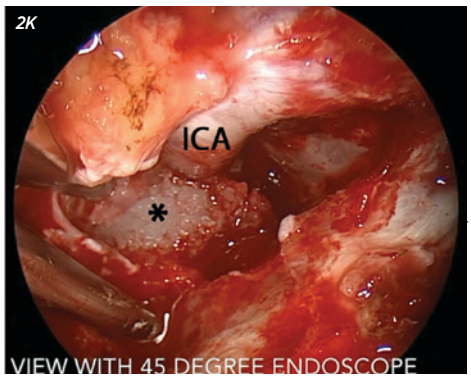


Figure 1. A: *The CTM approach provides access to the contralateral PA.* ***B:*** *The CTM approach improves the angle of approach relative to the petrous ICA by 25 degrees.* ***C:*** *The CTM approach also provides a "reach advantage," improving access to the PA.*

Figure 2: *Chondrosarcoma.* ***A-D:*** *Intraoperative navigation showing superolateral extent of dissection to IAC.* ***E-H:*** *Intraoperative navigation showing inferolateral extent of dissection to parapharyngeal ICA.* ***I:*** *Pre-treatment MRI.* ***J:*** *Posttreatment MRI showing total resection of a lesion.* ***K:*** *Intraoperative view of horizontal petrous segment of ICA with dissection of tumor (asterisk) at entrance of carotid canal (view is rotated 90 degrees).*

Nasal Polyps *(Continued from Page 2)*

Reflecting on the scope of her research, Dr. Lee identifies collaboration as a powerful underlying theme. Because of its translational nature, her work depends on partnerships with scientific collaborators like Dr. Bomberger and clinical collaborators from other fields, like Dr. Wenzel.

"For me, basic to translational research is not only a means to bring mechanistic findings to solve clinical problems but the reverse is true and important. It is an ongoing cycle in which clinical research informs basic science, and that interaction is very exciting and could not be possible without collaboration," she says.

References

1 Ahmed OH, Moore JA, Bruno R, Velazquez N, Poplawsky AJ, Lavigne P, Gardner PA, Lee SE. Neuromapping Olfactory Stimulation Using Encephalography (Nose) — A Proof of Concept Study. Abstract. Presented at Rhinoworld 2019, Chicago, 2019.

2 Ahmed OH, Moore JA, Bruno R, Velazquez N, Poplawsky AJ, Lavigne P, Gardner PA, Lee SE. Neuromapping Olfactory Stimulation Using Encephalography (Nose) — A Proof of Concept Study.

3 Li Z, Zeng M, Deng Y, Zhao J, Zhou X, Trudeau JB, Goldschmidt E, Moore JA, Chu H, Zhang W, Yin S, Liu Z, Di P, Lee SE, Wenzel SE. 15-Lipoxygenase 1 in Nasal Polyps Promotes CCL26/eotaxin 3 Expression Through Extracellular Signal-regulated Kinase Activation. *J Allergy Clin Immunol.* 2019 [in press].

4 Mady LJ, Schwarzbach HL, Moore JA, Boudreau RM, Willson TJ, Lee SE. Air Pollutants May Be Environmental Risk Factors in Chronic Rhinosinusitis Disease Progression. *Int Forum Allergy Rhinol.* 2018; 8: 377-384.

5 Olonisakin T, Moore JA, Wenzel S, Lee SE. Defining Endotypes Via Analysis of Cytokine Expression and Clinical Outcomes in Chronic Rhinosinusitis With Nasal Polyps. Abstract. Presented at Rhinoworld 2019, Chicago, June 2019.

6 Olonisakin T, Moore JA, Wenzel S, Lee SE. Defining Endotypes Via Analysis of Cytokine Expression and Clinical Outcomes in Chronic Rhinosinusitis With Nasal Polyps. In Press.

7 Velazquez N, Moore J, Mady L, Lee S. The Association of Air Pollutants, Airborne Occupational Exposures and CRS Disease Severity. Abstract. Presented at Rhinoworld 2019, Chicago, June 2019.

Reaching the Apex *(Continued from Page 3)*

compared the CTM approach against the standard EEA for accessing this region.

Clinical experience suggests that there may be a reduction in risk and morbidity with the approach because of the improved lateral trajectory of access to the petrous apex and avoidance of the paraclival segment of the internal carotid artery.

The first group of researchers to describe this procedure and publish on it in a medical journal, Dr. Snyderman and colleagues have since performed more than 25 surgeries using the CTM approach to treat a variety of conditions: chordoma, chondrosarcoma, meningioma, schwannoma, petrous apicitis, and metastasis. This experience represents the world's largest series of patients at present treated with the CTM approach.

During these first procedures, the CTM approach has been shown to greatly expand endonasal access to the PA with limited morbidity and without compromising nasoseptal flap reconstruction. Access was improved for lesions with posterolateral PA extension, allowing access as inferior as the jugular bulb and first genu of the ICA and as superior as the internal auditory canal. The ability to achieve gross total resection for chondroid neoplasms of the clivus and PA is greatly improved with the CTM approach.

"In developing the approach, I had the idea that what we needed was a better trajectory and improved angle of approach. Theorizing that if we opened up the cheek sinus, an already well-established historical technique, by making an incision inside the mouth through the front wall of the maxillary sinus, it would provide a nice corridor and alignment with the position of the ICA. Instead of moving the artery out of the way, which is very high risk, now we have a direct path to the recesses of the petrous apex and can follow the tumor for complete resection. Developing the CTM was really about rediscovering an old approach but applying it in a new way to access this area of the skull base," says Dr. Snyderman.

Upcoming Presentations and Publications in the CTM Approach

Dr. Snyderman is currently working on a manuscript for publication of their latest experience. This is in addition to teaching aspects of the CTM approach at the Complex Endoscopic Endonasal Surgery course, which was held November 13-16, 2019, in Pittsburgh, Pennsylvania.

In August, Dr. Snyderman and Dr. Gardner traveled to Israel to perform a demonstration surgery using the CTM approach as part of their global teaching efforts in skull base surgery and endoscopic techniques.

In September, Dr. Snyderman presented on his team's work with the CTM approach at the annual conference of the American Academy of Otolaryngology Head and Neck Surgery (AAO-HNSF) in a presentation titled "Reaching the Impossible: Endoscopic Surgery of the Clivus and Petrous Apex."

References and Further Reading

Patel CR, Wang EW, Fernandez-Miranda JC, Gardner PA, Snyderman CH. Contralateral Transmaxillary Corridor: An Augmented Endoscopic Approach to the Petrous Apex. *J Neurosurg.* 2018; 129: 211-219.

Poster Presentation at the 2018 North American Skull Base Society Annual Meeting: P012: Contralateral Transmaxillary Approach Vs. Purely Transnasal Approach to the Petroclival Region: An Anatomical and Radiological Study. Joao Mangussi-Gomes, MD[1], Gustavo F Nogueira, MD[2], Eric W Wang, MD[3], Juan C Fernandez-Miranda, MD[4], Carl H Snyderman, MD, MBA[3], Paul A Gardner, MD[4]. [1]Surgical Neuroanatomy Lab, UPMC Center for Cranial Base Surgery; [2]Neurological Institute of Curitiba; [3]Department of Otolaryngology, University of Pittsburgh School of Medicine; [4]Department of Neurological Surgery, University of Pittsburgh School of Medicine.

Poster Presentation at the 2018 North American Skull Base Society Annual Meeting: P111: Utilization of the Contralateral Transmaxillary Approach for Chordoma and Chondrosarcoma of the Petrous Apex. Daniel L Faden, MD, Philippe F Lavigne, MD, Juan C Fernandez-Miranda, MD, Paul A Gardner, MD, Eric W Wang, MD, Carl H Snyderman, MD, MBA. UPMC.

Scientific Session of the 2018 North American Skull Base Society Annual Meeting. 068: Contralateral Transmaxillary Corridor: Surgical Planning and Pathway Analytics. Rajeev Sen, MD[1], Rajeev C. Saxena, MD, MBA[1], Nava Aghdasi, PhD[1], Yangming Li, PhD[1], Randall Bly, MD[1], Paul Gardner, MD[2], Carl Snyderman, MD[2], Kris S Moe, MD[1]. [1]University of Washington; [2]University of Pittsburgh.

At the American Academy of Otolaryngology — Head and Neck Surgery 2019

UPMC and the Department of Otolaryngology, a part of UPMC Presbyterian Shadyside, were well-represented at the American Academy of Otolaryngology — Head and Neck Surgery (AAO-HNSF) 2019 Annual Meeting & OTO Experience, held on September 15-18 in New Orleans, Louisiana.

This annual event brings together otolaryngologist–head and neck surgeons from around the globe and all subspecialties to one location for cutting-edge education, as well as to explore the future of otolaryngology. The theme of AAO-HNSF 2019 was "Where Experts and Science Converge" and gave attendees an opportunity to learn from a multitude of perspectives, discuss key challenges and propose solutions, broaden the collective outlook of the field, and inspire new thinking. UPMC and the Department of Otolaryngology faculty gave numerous presentations during the event, and two faculty members were presented with awards this year. **Jeffrey Simons, MD**, was presented with the 2019 Committee Excellence Award, and the AAO-HNS Resident Leadership Award went to **Nathalia Velasquez, MD**. Other presentations, seminars, posters, and panel discussions included:

Presentations

David Chi, MD
Impact of Middle Ear Effusion in Pediatric Tympanostomy Tubes over 10 Years

Long-Term Otitis Media Outcomes in Children with Early Tympanostomy Tubes

Contralateral Hearing in Pediatric Severe to Profound Sensorineural Hearing Loss

Leila J. Mady, MD, PhD, MPH
Biodegradeable Magnesium Stents: Treatment for Pediatric Laryngotracheal Stenosis. This study was one of 19 selected by the Program Committee to highlight outstanding scientific merit and innovation and was part of the "Best of Orals" special session during the meeting.

Joseph Dohar, MD
All That Is Sore Is Not Strep Throat: Beyond the Guidelines of T&A Disease

Pediatric Chronic Otorrhea: Pearls from 30 Years of Clinical Practice & Research

Pearls for Your Practice: A Case-oriented Update in Pediatric Voice Disorders — Part 1 & 2

Thomas Kaffenberger, MD
Influence of Middle Ear Effusion Type in Pediatric Tympanostomy Tube Surgery after 10 Years

Marci Nilsen, PhD, RN
Neck Disability & Swallowing Dysfunction Related in Head & Neck Cancer Survivors

Viran Ranasinghe, MD
Glossotonsillar Sulcus as a Distinct Sub Site in Treatment of Oropharynx Cancer

Ryan Soose, MD
Update 2019: Palatal Surgery for Obstructive Sleep Apnea — Part 1 & 2

Drug-Induced Sleep Endoscopy and Upper Airway Stimulation Outcomes Palate Surgery Course

Jeffrey Simons, MD
Future of Otolaryngology Education, AAO-HNS Section for Residents and Fellows

Scientific Oral Abstract:
Cuneyt Alper, MD
Eustachian Tube Dysfunction Phenotypes: New Paradigm for Diagnosis and Treatment

Instruction Courses

Uma Duvvuri, MD, PhD
Fellows Course: Transoral Surgery for Head & Neck Cancer

Instructional Course: Management of the (Un)known Primary Cancer Patient: Role of HPV — Part 1 & 2

Grant S. Gillman, MD, FRCS
The Nasal Valve Primer: Everything You Need to Know (Simplified)

Improving Outcomes in Septal Surgery

Barry Hirsch, MD
Surgical Decision-making in Cholesteatoma — Part 1 & 2

Meetings

Jeffrey Simons, MD
Coordinator-Elect for Education
Chair of Pediatric Otolaryngology Education Committee
Chair-Elect, Education Steering Committee

Jeffrey Simons, MD
Judge: SIM Tank (Simulation Competition)

Carl Snyderman, MD, MBA
Guest of Honor at Korean American International Symposium

Carl Snyderman, MD, MBA, and Eric Wang, MD
Expert Series: Reaching the Impossible — Endoscopic Surgery of the Clivus and Petrous Apex

Mini Seminars

Libby Smith, DO
Not Just Blowing Wind: Tracheotomy Best Care Practices 2019

Panel Presentations

David Chi, MD
Opioid Sparing Strategies in Otolaryngology: Approaches to Eliminate Opioids

Measure of a Surgeon: Perspectives on Evaluating Surgical Competency

Dennis Kitsko, DO
Prophylactic Perioperative Antibiotics: Treating Patients or Surgeons?

Stella Lee, MD
The Age of Antibodies: No Sinus Surgeon Required?

Jeffrey Simons, MD
Clinical Consensus Statement: Ankyloglossia (Tongue-Tie) in Children

Controversies in the Evaluation and Management of Ankyloglossia in Children

Ryan Soose, MD
An Update on Testing for OSA: What the Otolaryngologist Should Know

Building a Successful Sleep Practice: Fellowship and Career Opportunities

Hypoglossal Nerve Stimulation Surgery: When It Is Not Like the Textbook

Posters

Lindsey Goyal, MD
Assessing Public Interest in Nasal and Sinus Surgery: A Five-Year Analysis

Carotid Blowout Syndrome: Predictors of Hemorrhage and Management Options

Ryan Soose, MD
Phenotypic Predictors of Neurostimulation Outcomes in the ADHERE Registry

Nathalia Velasquez, MD
Predictors of Readmission after Major Head and Neck Cancer Surgery: The UPMC Experience

Head and Neck Cancer Survivorship Update: New Research Into Treatment Financial Toxicity

Head and neck cancers (HNC), even if cured from a primary disease standpoint, can leave lasting and severe morbidities and quality-of-life issues for patients. HNCs constitute the sixth leading cause of cancer worldwide, and there are approximately 60,000 new cases diagnosed annually in the United States. The majority of new cases are diagnosed as late-stage disease and typically have been associated with older adults — over the age of 50. However, with the rising rate of human papillomavirus-associated HNC, the overall trends are leading to an increase in cases and more cases diagnosed in younger individuals.

Jonas Johnson, MD, FACS
Chair, Department of Otolaryngology

Marci Nilsen, PhD, RN
Researcher, University of Pittsburgh School of Nursing

Leila J. Mady, MD, PhD, MPH
T32 Postdoctoral Scholar and PGY6 Department of Otolaryngology Resident

Helping to prepare patients for these potentials before treatment and working with them to help them cope with the post-treatment management of their condition after the fact is the domain of the UPMC Head and Neck Cancer Survivorship Clinic in the Department of Otolaryngology.

Encompassing a range of disciplines and services, the Survivorship Clinic tackles all aspects of HNC patient care prior to and after treatment. Physical therapy, dental health, swallowing therapy, and audiology are combined alongside other disciplines to create a cohesive, individualized program of care designed to deal with the biopsychosocial complexities of HNC patients. Launched in December 2016, the Survivorship Clinic has surpassed the 1,000-patient mark in its first years of operation, a statistic that highlights the need for such a clinic and also reinforces the significant challenges and ongoing care HNC survivors need.

Beyond and behind the Clinic's multidisciplinary care structure is an active research program that is investigating crucial aspects of HNC patient care — some of which receive little attention in the field but are nonetheless critical to long-term outcomes, patient satisfaction, and quality-of-life measures, and the oft-burdensome continuing costs of care and financial impacts associated with HNC.

New Research in HNC Treatment Financial Toxicity

The burdens thrust upon HNC patients and survivors are significant and life-altering, from diagnosis through treatment to post-treatment survivorship. Traditionally, most attention has been paid to the physical, emotional, and psychological tolls HNC inflicts on its victims.

However, a fourth treatment toxicity domain has garnered increasing attention from Department researchers: financial toxicity (FT). As new research is uncovering, the financial implications of a diagnosis of HNC tend to be overwhelming for many, and they can persist long after the diagnosis and initial therapies have been provided.

A new study[1] published this year by Survivorship Clinic members **Jonas Johnson, MD, FACS**, chair of the Department of Otolaryngology; **Marci Nilsen, PhD, RN**; and lead author **Leila J. Mady, MD, PhD, MPH**, and colleagues examined data collected on patients from the Clinic to begin to understand the true nature and implications of the financial strains placed on patients recovering and living after HNC.

Published in the journal *Oral Oncology,* the new study describes the type and levels of FT in HNC survivors, its characteristics and impact on quality-of-life measures, how patients manage or cope with the financial burden of care, and other measures.

The study was conducted on a cohort of 104 HNC patients whose primary disease was located in either the oral cavity, larynx/hypopharynx, or oropharynx. This is the first study to examine FT in HNC patients by the site of the disease with several findings of the impact of cancer site on FT.

Across the entire patient cohort, a significant percentage of patients (40.5%) were shown to exhibit a high level of FT. Those with a larynx/hypopharynx cancer experienced FT at higher levels than those with oral cavity or oropharynx disease.

Factors such as age, marital status, income level, and education level also correlated with worse FT. The younger a patient was at the time of diagnosis was a factor in higher FT. Unmarried individuals and those with lower education levels also suffered higher levels of FT. The majority of patients, 60%, indicated that they needed to use portions of their income savings or take out loans in order to pay for their care.

"Patients with higher levels of financial stress will adapt to the situation, sometimes by exhausting their savings and accruing burdensome loans, but they also will postpone or forgo treatments entirely. Alternatively, as we learned, they may try to compensate by other means by working more or finding additional sources of income," says Dr. Mady.

Solutions to the general problem that patients — some even with what would be considered good or adequate health insurance — cannot afford their treatments will not be easily addressed. However, one mechanism that may begin to address the problem is the ability to screen patients upfront for potential FT and work to address the issue before beginning treatment.

While not exhaustive in nature, this study points to the need for larger investigations to further explore the risk factors and consequences of FT in HNC patients, and to examine the effects of other ways patients may adapt to their care situation that may have even more influence over their long-term treatment and health than the factors identified in this study. Currently, Dr. Mady is the Principal Investigator of a prospective investigation supported by an American Academy of Otolaryngology — Head and Neck Surgery Foundation Health Services Research Grant which is examining FT longitudinally over time.

References

1 Mady LJ, Lyu L, Owoc MS, Peddada SD, Thomas TH, Sabik LM, Johnson JT, Nilsen ML. Understanding Financial Toxicity in Head and Neck Cancer Survivors. *Oral Oncology.* 2019; 95: 187-193.

Further Reading

Nilsen ML, Lyu L, Belsky MA, Mady LJ, Zandberg DP, Clump DA 2nd, Skinner HD, Peddada SD, George S, Johnson JT. Impact of Neck Disability on Health-Related Quality of Life among Head and Neck Cancer Survivors. *Otolaryngol Head Neck Surg.* 2019 Oct 15:194599819883295.

Thomas T, Hughes T, Mady L, Belcher SM. Financial Toxicity: A Review of the Literature and Nursing Opportunities. *Clin J Oncol Nurs.* 2019 Oct 1; 23(5): 5013.

Nilsen ML, Mady LJ, Hodges J, Wasserman-Wincko T, Johnson JT. Burden of Treatment: Reported Outcomes in a Head and Neck Cancer Survivorship Clinic. *Laryngoscope.* 2019 Jan 15. doi: 10.1002/lary.27801. Epub ahead of print.

Cramer JD, Johnson JT, Nilsen ML. Pain in Head and Neck Cancer Survivors: Prevalence, Predictors, and Quality-of-Life Impact. *Otolaryngol Head Neck Surg.* 2018 Nov; 159(5): 853-858.

Mady LJ, Nilsen ML, Johnson JT. Head and Neck Cancer in the Elderly: Frailty, Shared Decisions, and Avoidance of Low Value Care. *Clin Geriatr Med.* 2018 May; 34(2): 233-244.

UPMC
LIFE CHANGING MEDICINE
200 Lothrop St.
Pittsburgh, PA 15213-2582

ABOUT OUR PROGRAM

The Department of Otolaryngology continues to be a national leader in the exploration of otolaryngology and human communication disorders. The Department is highly ranked in research dollars awarded, and continues to provide faculty, residents, and students with the resources and support to generate new health care knowledge related to direct clinical practice and public health policy.

The Department has more than 40 full-time faculty members, representing all the subspecialties of otolaryngology. While the primary mission continues to be providing high-quality patient care, we also are dedicated to advancing education and research within the field of otolaryngology.

To learn more about the UPMC Department of Otolaryngology, please visit **UPMCPhysicianResources.com/ENT**.

UPMC PHYSICIAN RESOURCES

Jonas T. Johnson, MD, FACS
Chairman, Department of Otolaryngology

ADDRESS CORRESPONDENCE TO:
Department of Otolaryngology
Eye & Ear Institute, Suite 500
203 Lothrop St.
Pittsburgh, PA 15213
412-647-2100

For consults and referrals, please call UPMC's 24-hour physician OnDemand service at **1-866-884-8579.**

USNW513092 AS/MP 12/19