Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/understanding-nasal-polyposis/12389/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Understanding Nasal Polyps

Chapter 1: Understanding Nasal Polyposis

Dr. Tara F. Carr:
Hi, my name is Tara Carr. I run the Allergy Immunology Program at the University of Arizona, and I'm happy to be talking to you today about understanding nasal polyposis.

This program is sponsored by Novartis Pharmaceuticals Corporation, and as presenter. I am being compensated for my time. This presentation is a non-CME event and does not qualify for CME, CE, or MOC credit. This event is not part of the official CHEST Annual Meeting 2020 conference sessions. This event is not an endorsement by CHEST and does not reflect the views or opinions of CHEST.

Nasal polyposis is characterized by chronic inflammation of the nasal mucosa, resulting in multiple, bilateral nasal polyps. Nasal polyps are noncancerous lesions that arise from the lining of the nasal sinuses or the nasal cavity. Patients with nasal polyps may present very commonly with reduction or loss of sense of smell, nasal obstruction or congestion, rhinorrhea, postnasal drip, and headache or facial pain. Nasal polyps can be associated with several different and overlapping conditions, including chronic sinusitis, allergies, asthma, cystic fibrosis, and aspirin sensitivity.

One of the most frequently associated conditions is chronic rhinosinusitis, which is more commonly called CRS. CRS is a significant health concern, impacting 5% to 12% of the population worldwide. CRS is defined as the inflammation of the nose and paranasal sinuses with at least 2 of the following symptoms, one of which should be nasal blockage, which may be described as obstruction or congestion, or nasal discharge, anterior or posterior nasal drip lasting for more than 12 weeks. Other symptoms may include facial pain or pressure or reduced or loss of sense of smell. Historically, 2 forms of CRS are defined based on their phenotype: CRS without nasal polyps or CRS with nasal polyps. CRS with nasal polyps is observed in about 25% to 30% of CRS patients.

From a quality-of-life standpoint, nasal polyps is associated with a substantial negative impact on multiple aspects of daily life, including both work and social settings. Patients find themselves constantly preparing for and dealing with symptoms, and they can struggle with sleep disruption and fatigue, as well as feelings of depression, sadness, and embarrassment, all of which ultimately lead to reduced social enjoyment. There is also an element of stress related to constant health care needs and costs. Ultimately, patients live with the new normal of trying to manage this disease. From an economic standpoint, symptoms can impact concentration and productivity at work, as well as impact a person's ability to effectively fulfill certain work-related goals and can contribute to absenteeism. There is, therefore, a significant economic cost burden in the medical and surgical management of these patients.

It is important to note that the various comorbid conditions frequently associated with nasal polyps can significantly impact the pathophysiology of nasal polyps, can add to the symptomatic burden that patients experience, and can pose a challenge for providing optimal treatment for these patients. Interestingly, there is a biologic connection between nasal polyps and the most common comorbid conditions, which tend to be respiratory-related conditions, and that is an underlying shared inflammatory process. We'll explore this inflammatory process in more detail in the coming slides.

Ongoing research into the pathophysiology of nasal polyps resulted in the realization that clinical phenotypes alone are not reflective of the underlying inflammatory mechanisms of this disease. This led to the categorization of disease endotypes, which are categories based on their most prominent cellular responses. These endotypes are broadly defined as type 1, type 2, and type 3 inflammation, as shown here. Each endotype is characterized by several key immune cell types and inflammatory mediators that characterize that type of inflammation. Today, we will focus on type 2 inflammation, which is associated with increased disease severity disease, disease

recurrence, and risk of comorbid asthma.

Here, we have a simple schematic of an intact upper airway epithelial barrier, wherein various exogenous factors can be introduced and trigger immunologic response. It is important to note that an immune response can be triggered by exposure to an allergen, such as in an atopic response, or an antigen, such as in a nonatopic response, or even an autoimmune trigger. Colonization with Staph aureus is a common occurrence, and Staph aureus is known to produce enterotoxins that act as superantigens to trigger a type 2 inflammatory response. Pathogenic challenge and epithelial injury in the upper airways can result in the secretion of epithelial-derived cytokines, termed “alarmins.” These include thymic stromal lymphopoietin (or TSLP), interleukin (IL)-33, and IL-25. These alarms signal a breakdown in epithelial integrity and trigger the activation of different immune cells that drive a type 2 inflammatory response. One of the cell types stimulated by these alarmins is the dendritic cell, which is a key component of the adaptive immune response, facilitating sensitization to allergens or antigens, such as those enterotoxins. Sensitization occurs when new antigens are captured by antigen-presenting cells, such as dendritic cells, and are subsequently presented to T cells. Antigen binding to T cells results in the release of various type 2 cytokines. In addition to the adaptive immune response, epithelial-derived cytokines also stimulate the innate immune response through activation of group 2 innate lymphoid cells (or ILC2) via specific cytokine receptors. ILCs then also produce type 2 cytokines.

Type 2 cytokines play important roles in driving type 2 inflammation via various mechanisms, which you’ll see on these slides. A key role for IL-4 is the stimulation of B-cell activation, which triggers the production and release of polyclonal IgE antibodies, which then bind to the surface of different immune cells, including mast cells. IgE antibody binding to mast cells facilitates a positive feedback loop upon antigen exposure to drive the innate immune response. Antigen binding induces degranulation and production of type 2 cytokines by mast cells. In addition, prostaglandins, like PGD2, and cysteinyl leukotrienes, like LTC4, are produced by mast cells and bind to specific receptors on the ILC2s, further stimulating the production of type 2 cytokines.

IL-5 stimulates eosinophilia, acting on eosinophils at multiple levels and time points. IL-5 stimulates the proliferation, differentiation, and maturation of eosinophils in the bone marrow. It also contributes to eosinophil egress to the intravascular compartment and prolongs eosinophil survival, along with other anti-apoptotic factors. IL-13, as well as IL-4, is also responsible for stimulating various other cellular activities during this type 2 inflammatory response. They both drive cellular recruitment of immune cells, including macrophages, type 2 helper T cells, basophils, and eosinophils, to the site of the inflammatory response; stimulating production of mucus via goblet cells; and stimulating the cross-linking and deposition of fibrin, which leads to tissue remodeling, a key factor in nasal polyps formation.

Finally, as the different types of immune cells, like the dendritic cells, mast cells, basophils, and eosinophils, are being recruited to the site of inflammation, the antigen-specific IgE antibodies are binding to the surface of the cells through IgE receptors. This process primes these different immune cells for subsequent exposure to the antigen and further stimulates the release of immune mediators that then continue to drive the immune response.

So what does all this look like in a developing polyp. We have a simple example of nasal polyp formation here, wherein we start with normal nasal mucosa that has been colonized with microbes. This colonization triggers the activation of immune cells, as discussed in the previous slides, in the production and release of various immune mediators.

An increased abundance of microbes also results in injury to the mucosal barrier, further triggering and driving the inflammatory response.

The recruitment and expansion of inflammatory cells leads not only to tissue inflammation and swelling, but deposition of fibrin and cross-linking of fibrin, which causes the polyps to form.

Chronic inflammation with tissue remodeling due to profound inflammatory cell expansion and loss of submucosa glands ultimately results in the formation of protrusions in the lining of the nasal sinuses or the nasal cavity.

Histologically, nasal polyps are characterized by thickening of the basement membrane; stromal and submucosal edema, which results in extensive clear space between the submucosa connective tissue fibers; and an inflammatory infiltrate, which includes eosinophils and mast cells dispersed throughout the polyp. A range of mucosal alterations in the epithelium may also be observed, including hyperplasia of the goblet cells.

Recommendations for the diagnosis of patients with nasal polyps include assessment for a clinical history; assessment of patient-reported clinical symptoms, severity, and health-related quality of life; and assessment of comorbid conditions, such as asthma. Some examples of scoring systems used in research and clinical practice to assess symptoms and quality of life are shown here. For example, patient-reported symptoms, severity, and impact on daily living can be captured using the Total Nasal Symptoms Score (or TNSS); the 22-item Sino-Nasal Outcome Test (or SNOT-22); and the University of Pennsylvania Smell Identification Test, which is the UPSIT. The

TNSS focuses on nasal symptoms, with the higher score range between 0 and 12, indicating greater severity. The SNOT-22 is used to assess both symptoms and their impact on daily life, with a higher score between 0 and 110 also indicating a greater severity of symptoms and a worse quality of life. The UPSIT is a smell identification test used to assess olfactory dysfunction, and here a higher score ranging between 0 and 40 represents better olfaction. Patient-reported quality of life can be captured using the Euro Quality-of-Life 5-dimension, which is a measure of overall health status across 5 domains: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. A higher score in each domain indicates worse quality of life. In addition to persistent signs and symptoms, a physical examination is performed to look for evidence of nasal polyps.

Various physical assessments are also used to diagnoses the polyps. Anterior rhinoscopy is often used as a first step to identify nasal polyps in the medical care setting; however, a limitation to rhinoscopy is that only larger polyps can be visualized. Nasal endoscopy is the preferred method by the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma, & Immunology, and includes the Nasal Polyp Score to assess severity of disease. Imaging techniques, including CT and MRI, can be used for visualization of the paranasal sinuses and are useful for surgical planning. Nasal biopsy can be used to exclude severe conditions such as cancer.

The general goals for the management of nasal polyps are to provide symptom relief for patients, to improve patient quality of life, reduce polyp size, and to prevent disease recurrence. Of note, management of nasal polyps is based primarily on symptom severity. There are currently no specific guidelines that address the potential for biomarker-driven treatment decisions.

Management begins with an initial therapy consisting of intranasal steroids and saline irrigation, as well as patient education, and compliance related to use of these intranasal treatments. That's critical for their success. In addition, treatment of other known comorbid conditions, such as allergy, is also important. For these patients, antibiotics are generally avoided, and systemic steroids may not be necessary with the exception of severe cases. If no improvement is noted, then referral to secondary or tertiary care, like an Ear, Nose, Throat specialist, is recommended. Following reevaluation of symptoms and severity of disease, including imaging techniques and assessment for possible comorbid infection, further medical therapy is typically recommended. At both the primary care and tertiary care stages, it is always important to consider potential contributing factors and comorbid conditions that a patient may be experiencing and to consult appropriate specialists for management. If symptoms continue to persist, then surgery may be considered.

Surgical intervention is typically reserved for patients who have not achieved benefit from medical therapies. Patients eligible for surgery have objective evidence of disease on CT scan, show persistent symptoms without improvement following recommended courses of intranasal or oral steroids. Sinus surgery aims to remove nasal polyps and improve access for intranasal therapy. Appropriate maintenance medical therapy is recommended after surgery. For patients who experience recurrence of polyps despite having surgery and appropriate medical maintenance therapy, other therapies and modes of delivery should be considered depending on disease characteristics, as well as relevant contributing factors.

Ultimately, the optimal approach to diagnosing and managing nasal polyps involves a multidisciplinary team including primary care physicians, specialists, and the patient themselves. Primary care physicians should understand the full scope of patient symptoms and impact on quality of life, including comorbidities that may require specialist evaluation. They should also be aware of the different types of treatment modalities available for patients who have nasal polyps. The specialists, such as allergists, Ear, Nose, Throat doctors, and pulmonologists, should also understand the full scope of patient symptoms and comorbidities, as well as the different therapies received, and will coordinate care with the PCP and other specialists, ultimately contributing to a holistic treatment approach. Finally, it's important that the patient understands their diagnosis, the available treatment options, and the treatment expectations. The patient should have access to relevant information and support groups to allow them to feel empowered as an active partner in decision-making.

In summary, nasal polyposis is a complex disease, characterized by chronic inflammation that includes multiple types of immune cells and inflammatory mediators that play important roles in nasal polyp pathophysiology and the resultant symptoms. This pathophysiology not only results in local sinonasal symptoms, but it also underlies commonly associated comorbidities that should be considered in our approach to patient diagnosis and management. Optimal diagnosis and management of nasal polyps requires an integrated care approach across primary care physicians, specialists, and patients for shared decision-making.

Chapter 2: Type 2 Inflammatory Cascade in Nasal Polyposis

Narrator:
This video describes the role of the type 2 inflammatory cascade in nasal polyposis.

Nasal polyposis is characterized by chronic inflammation of the nasal mucosa with multiple, bilateral, noncancerous lesions (called nasal polyps) arising from the lining of the nasal sinuses or nasal cavity.

Nasal polyposis may be associated with several different and overlapping conditions, including chronic rhinosinusitis (CRS), allergy, asthma, infection (fungal or bacterial), and aspirin sensitivity.

Epithelial injury or pathogenic challenge in the upper airways can result in the secretion of epithelial-derived cytokines (TSLP, IL-33, and IL-25), termed “alarmins,” that trigger the activation of various immune cells associated with type 2 inflammation.

One of the cell types stimulated by these alarmins is the dendritic cell, which is a key component of the adaptive immune response, facilitating sensitization to allergens or antigens. Sensitization is initiated when new antigens are captured by dendritic cells.

The dendritic cells then migrate to the lymph nodes.

The antigens are presented to naive T cells, leading to their differentiation into type 2 T-helper, or “Th2,” cells. Antigen binding to T cells results in the release of different type 2 cytokines, including IL-4, IL-5, and IL-13. These cytokines play important roles in driving type 2 inflammation via various mechanisms, including stimulation and/or recruitment of different types of immune cells (eg, eosinophils, basophils, T cells). For example, a key role for IL-4 is the stimulation of B-cell activation.

B-cell activation triggers the creation and release of polyclonal IgE antibodies.

The secreted IgE binds to the IgE receptor on the surface of mast cells as well as basophils, eosinophils, and dendritic cells, priming their response for future exposure to the same antigen.

On the next encounter with the antigen particle, receptor-bound IgE on the surface of mast cells bind the antigen and cross-link.

This results in the release of various immune mediators that continue to drive the inflammatory response.

Elevated local IgE is often seen in the nasal polyp mucosa, independent of serum IgE. In the serum, total IgE consists of both free and immune cell–bound IgE antibodies.

Free IgE antibody circulates prior to binding to IgE receptors on immune cells. This form of IgE may not be specific to a particular antigen.

IgE antibody that is bound to an immune cell, such as a mast cell, can be specific to a particular antigen.

For example, patients with nasal polyps can exhibit colonization of *Staphylococcus aureus*, which produces enterotoxins that act as antigens, resulting in the production of specific IgE antibodies.

In addition to the role of IL-4 in stimulating antibody production by B cells, other type 2 cytokines play important roles in stimulating and recruiting various immune cells involved in the inflammatory response…

IL-5 stimulates the proliferation, differentiation, and maturation of eosinophils in the marrow, and contributes to the prolongation of eosinophil survival.

IL-13, along with IL-4, drives cellular recruitment of various types of immune cells, including macrophages, Th-2 cells, basophils, and eosinophils, to the site of the inflammatory response.

In the context of the nasal cavity, IL-13 also stimulates production of mucus and the cross-linking and deposition of fibrin, which leads to tissue remodeling, a key factor in nasal polyp formation.

What does this inflammatory process look like in a developing polyp? Here, we have a simple example of healthy nasal mucosa that is colonized with microbes, such as *S aureus*.

Colonization with microbes triggers the activation of immune cells, the production of IgE, and the release of various immune mediators. The increased abundance of microbes results in injury to the mucosal barrier, further triggering an inflammatory response.

The recruitment and expansion of inflammatory cells, such as eosinophils, leads to tissue inflammation and swelling, as well as deposition of cross-linked fibrin.

Chronic inflammation with tissue remodeling due to profound inflammatory cell expansion and loss of submucosal glands can ultimately result in the formation of protrusions in the lining of the nasal sinuses or nasal cavity.

Nasal polyps are often characterized by thickening of the respiratory epithelial basement membrane, mucosal alterations in the respiratory epithelium and submucosal edema, and the presence of inflammatory infiltrate.

Patients with nasal polyps may present most commonly with reduction or loss of smell, nasal obstruction or congestion, rhinorrhea, postnasal drip, and headache or facial pain.

In summary, nasal polyposis in association with various comorbid conditions can be driven by a type 2 inflammatory response.

Epithelial tissue injury and/or pathogenic challenge can trigger the activation of different immune cell types and the production of type 2 cytokines, including IL-4, IL-5, and IL-13, which play key roles in further stimulating and recruiting various immune cells and cell mediators.

In addition, IgE antibodies, produced in response to antigen exposure in the upper airways, bind to and activate the various immune cells, further driving the inflammatory response.

Overall, this immune cascade can lead to profound inflammation and swelling in the nasal sinuses and cavity, resulting in the formation of nasal polyps and their associated clinical symptoms.

Chapter 3: Understanding the Patient Journey with Nasal Polyps

Narrator:
This video explores the patient journey with nasal polyps. Our goal is to understand the patient experience from initial symptom onset and diagnosis, through disease management strategies and their relationship with health care professionals.

For many, symptoms feel familiar at first, similar to a cold or allergies.

Patient:
I had horrible congestion that nothing helped. I thought it was just allergies...but to my frustration, nothing helped at all.

Narrator:
They try over-the-counter antihistamines or decongestants.

Some people seek medical help right way. Others wait months, or even years, to see a doctor — they've simply adapted to their symptoms.

Patient:
I had bad allergies as a child. I can remember having sinus headaches. The constant infection, one right after the other all the time, whether in season or out of season.

Narrator:
But symptoms ultimately worsen and expand, impacting daily life and requiring medical attention.

Patient:
I couldn't breathe.... I couldn't taste stuff. You feel like you're missing something.

Narrator:
Initial visits are with primary care physicians, or urgent care staff, who often diagnose patients with sinus infections or allergies.

Patient:
I would get a cold or congestion and it would turn into a sinus infection that would not go away. I just went to urgent care. They'd put me on antibiotics. They said I have a sinus infection.

Narrator:
Treatment consists of antihistamines, steroids, and antibiotics but many experience persistent symptoms and repeat visits.

Patient:
I just went to my general PCP. I talked to him and he thought it was allergies. He prescribed me [a steroid nasal spray] and I took that for probably 4 months or so.

Narrator:
Mounting frustration and financial burden cause many to take a break in medical care or seek another doctor.

Eventual referral to specialists, including ENTs and allergists, facilitates a proper diagnosis.

Patient:
I referred myself. I was actually talking to a coworker about it…they had a lot of the same problems and talked about this wonderful ENT that they were going to. I took it upon myself just to go and see him.

Narrator:

Diagnosis results in a range of emotions, from anxiety and fear to validation and relief.

Patient:
It was like a blessing and a curse to be like, “Okay, I have an answer now,” but at the same time, “I have these polyps. Now what?” It was a two-faced diagnosis.

Narrator:
Patients want to understand their diagnosis, but complete information and support groups are difficult to find.

Patient:
There’s definitely information, but it’s more overall sinus health. I don’t know that it sheds a lot of light on it as much as it should, as much as other things like allergies.

Narrator:
Patients ultimately begin treatment hopeful but anxious.

For some patients, current recommended medical therapies relieve symptoms and decrease nasal polyps, although the duration of clinical benefit is variable.

For others, frustrations with treatment continue even after diagnosis, because some therapies are similar to those received previously.

Patient:
I felt like the treatment was the same...

Narrator:
Symptoms can continue, with disabling flares that significantly impact daily living.

Patient:
I miss work every time I have a flare up. I’m just too uncomfortable. Usually it’s 3 to 4 days.

Narrator:
Additional diagnosis, such as AERD, may also occur. As quality of life worsens and treatments prove ineffective, patients consider surgery.

Patient:
I tried antihistamines, at least 10 different nose sprays, decongestants, antibiotics, [an anti-inflammatory], vitamins, special diets...

Narrator:
The decision to move forward with surgery is associated with feelings of both fear and hope.

Patient:
I didn’t really want to do the surgery. I may have to. It may be my last option.

Narrator:
Initial results from surgery can provide a sense of relief both physically and emotionally.

Patient:
I went home and rested, and after about a week or two, I felt like a brand-new person. I could breathe, I wasn’t snoring, I could taste stuff, which was wonderful. It didn’t last long though.

Narrator:
For some patients, surgery, often combined with medical therapy, can provide long-term symptom relief and improve quality of life.

For others, relief is short-lived as symptoms recur, leaving them devastated and overwhelmed with what the future holds.

Patient:
When you talk about surgery, you always expect it to be something permanent, not something that’s going to recur, especially when it comes to something getting removed. You’ve wasted everything to be back in the same position you were before it all started.

Narrator:
Patients wonder if they will need repeated surgeries…if the cycle of suffering, treatment, and recurrence will continue.

Patient:
You get depressed. Is this going to be the cycle, every 3, 4 years, I’m gonna have to go through surgery again? It’s relentless.

Narrator:
Patients may take a break in medical care or seek another doctor to identify different methods to treat their symptoms and prevent flares.

Patient:
I keep wavering on wanting to go back and see my ENT again. I do, but then it's like you almost know what the process is going to be. I don't know if I want to deal with that again

Narrator:
Overall, patients experience a loss of normalcy, accepting the symptoms and poor quality of life as simply a part of their lives.

Patient:
Just being able to breathe normally, not breathing like there's an obstruction there. That has been my issue. I wish I just had normalcy.

Narrator:
Some consider nasal polyps to be a part of who they are — their struggles are permanent and never-ending.

Patient:
This is me now. I don't smell. My nose is always stuffed. I never get a solid night's sleep. I'm a sickly person in a sense.

Narrator:
In order to better address the needs of patients experiencing nasal polyps, there are key milestones along their journey where optimal care depends on a proactive and integrated approach, including both primary care and specialty physicians, as well as the patients themselves.

At diagnosis, it's important to understand the patient's symptoms, disease severity, and impact on his or her quality of life. Patient history can provide insight into how long symptoms have been occurring.

PCP:
Most patients, if you talked to them, if they're seeing you for the first time for symptoms of nasal obstruction, it's been years and years, all the way to childhood.

Narrator:
Physicians should consider what treatments have been tried, as well as other available options. Presence of comorbidities, such as allergies, should be considered, along with specialist collaboration.

Allergist:
Individuals who have highly expressed atopic disease...such as allergic rhinitis, asthma, eczema…are known to have a higher incidence of nasal polyps.

Narrator:
It's also important to find out what the patient understands about his or her diagnosis, and what educational support may be needed.

ENT Specialist:
This is the beginning of a chronic disease that's not life-threatening, that may require surgery several times and medication.

Narrator:
Upon recurrence of nasal polyps, reevaluation of symptoms and disease severity may be needed, as well as consideration of any new contributing factors, such as infection.

ENT Specialist:
People with repeated infections and sinusitis will have secondary polyps. They're a little bit different than the allergic polyps.

Narrator:
New and existing comorbidities, such as asthma, should also be reevaluated in collaboration with appropriate specialists. Additional management options should also be considered.

ENT Specialist:
By the time they come to ENTs, they've tried everything.

Narrator:
Where medical treatment has proven ineffective, surgery may be considered. It is important to discuss different treatment options, as

well as expectations for outcomes, with a patient and take into account his or her opinions.

ENT Specialist:
It's very much up to the patients. Our patients are a very switched on bunch of people. They totally like to be involved in their decision.

Narrator:
When discussing surgery, it is important that the patient understands the potential outcomes.

Patient:
It's not a 100% that it won't recur after surgery.

Narrator:
At this stage, reevaluate what the patient needs with regard to education and support.

A multidisciplinary approach is also key for determining the need for supportive treatment.

ENT Specialist:
If you just remove the polyps, more likely than not—and we're looking at 70% or 80% probability—they're going to recur.

Narrator:
Finally, discuss a plan for potential recurrence with the patient.

Optimal integrated care for patients with nasal polyps depends on several key principles. Primary care physicians must understand the full scope of a patient's experience, different treatment modalities, and the impact of comorbidities.

Specialist physicians must share this understanding and work to coordinate care with the goal of a holistic treatment approach.

As a member of his or her own care team, the patient should be provided with the education and support needed to understand the disease and feel empowered as an active partner in decision-making at all stages of the journey.