Advancing the understanding of complex rhinologic problems

Each issue of the American Journal of Rhinology and Allergy presents cutting edge basic and clinical research within the fields of allergy and rhinologic diseases. The current issue is no exception, with a diverse array of innovative studies from a worldwide collection of contributors. Readers will find basic and translational studies that explore the immunologic basis of allergic rhinitis (AR) and chronic rhinosinusitis (CRS), as well as clinical and technical studies that explore issues ranging from rhinoscleroma to cerebrospinal fluid leak repair. The July/August issue certainly highlights the mission of the AJRA, with subject matter for basic scientists and clinicians alike.

Chronic rhinosinusitis and allergic rhinitis are becoming increasingly prevalent, however, our understanding of the pathophysiology and immunologic contributors to disease development and progression remain poorly understood. Leading off the current issue, Shimizu et al. investigate the impact of tissue remodeling and the extrinsic coagulation cascade on the pathogenesis of CRS. They found that the coagulation pathway proteins, tissue factor and tissue factor pathway inhibitor, are expressed in nasal secretions and nasal epithelial cells and hypothesize that upregulation of these factors may play an important role in fibrin deposition, tissue remodeling, and nasal polyp architecture. Studies like this should ultimately lead to new and more effective therapies for CRS, but the mainstay for medical management continues to be glucocorticosteroids. In this issue, Kook et al. assess polyp-derived epithelial cell expression of enzymes involved in glucocorticosteroid metabolism and correlate enzyme expression with cortisol levels. Their results suggest that expression of the enzyme 11β-hydroxysteroid dehydrogenase may mediate the anti-inflammatory effect of glucocorticosteroids by increasing levels of endogenous cortisol.

CRS results in many symptoms that adversely affect quality of life, with olfactory dysfunction representing one of the primary complaints of many patients. As detailed by Joo et al. in this issue, loss of the sense of smell can be associated with both depressed mood and suicidal ideation. Unfortunately, regardless of etiology, there are few proven interventions for the long-term management of olfactory dysfunction. Improvement in olfactory outcomes following endoscopic sinus surgery is reported by Gupta et al., however, aggressive removal of polyps from the olfactory cleft itself remains somewhat controversial. Kuperan et al. evaluated the benefit of endoscopic olfactory cleft polyp surgery on olfaction in a randomized single-blind study. Their results showed a statistically significant improvement in objective olfactory outcomes six months postoperatively for patients receiving surgery of the olfactory cleft. Though long-term data is still lacking, the current report suggests that directly addressing olfactory cleft polyposis during endoscopic surgery may provide some benefits in olfactory function.

Allergic fungal sinusitis (AFS) continues to be a particularly challenging form of chronic sinus disease with a high recurrence rate. In this issue of AJRA, White et al. set out to determine whether bony erosion patterns in AFS correlate with patient characteristics and other clinical parameters. In their cohort, erosion of bone was more common in younger and African-American patients, suggesting that these populations may mount a more severe inflammatory response. With the exception of corticosteroids, few medical interventions are consistently effective for AFS. The use of oral antifungals as an adjuvant therapy has been previously proposed by Gan et al. with conflicting results. Patro and colleagues present their results of a randomized prospective study that evaluated the use of itraconazole preoperatively for management of AFS. Interestingly, patients receiving oral steroids and itraconazole experienced a reduction in disease burden based on clinical, radiologic, and endoscopic parameters, compared to those receiving steroids alone. This article highlights the potential of oral antifungals as an adjunctive management for AFS, while perhaps furthering controversy regarding the putative effectiveness of this intervention.

Numerous pro-inflammatory and anti-inflammatory cytokines contribute to allergic responses and symptom development in patients with AR. In this issue of AJRA, Yokota et al. use an allergic mouse model to explore the role of interleukin 35 (IL-35) on the inflammatory response. They found that IL-35 reduces the production of pro-inflammatory cytokines while simultaneously increasing the expression of anti-inflammatory cytokines. Collectively, their study suggests that IL-35 inhibits allergic T cell responses, potentially distinguishing it as a therapeutic target. An equally impactful study by Mo and colleagues evaluates the use of mesenchymal stem cells (MSCs) for the treatment of AR [Mo et al]. Using the same allergic mouse model, they found that injection of human tonsil-derived MSCs could reduce allergic symptoms, eosinophilic infiltration and production of pro-allergic cytokines. This highlights the potential of regenerative medicine and stem cell therapy as potential treatment modalities for AR and other immunologic diseases. Finally, Liu et al. explore the physiologic role of the cold receptor, TRPM8, in the nasal mucosa. Antagonists of TRPM8, such as menthol-containing medications and natural remedies, are often used to address symptoms in patients with and without AR. The basic science behind nasal mucosal temperature sensation and its effect on patient symptoms remains poorly understood, but the current study highlights a possible role for cold receptors in nasal pathophysiology. Additional articles by Jang and Kim as well as Degirmenci investigate the role of nasal provocation tests in AR diagnosis and explore the relationship between AR and autoimmune thyroiditis.

While continued research into the immunologic basis of AR will likely result in new and more effective therapies, current treatment continues to rely on nasal steroid sprays and other topical medica-tions. An article by Berger et al. in this issue of AJRA seeks to systematically review currently available intranasal sprays used for maintenance therapy. Analyzing 20 studies, the authors found that the use of MP-AzeFlu, a single formulation nasal spray of azelastine hydrochloride and fluticasone propionate, provided greater symptom relief than either azelastine or fluticasone alone, confirming the importance of both topical antihistamines and corticosteroids in the management of AR. Many patients seek alternative treatments or...
homeopathic regimens to address their AR symptoms. In this issue, Peng et al.\(^4\) systematically review the literature to define possible roles for probiotics in AR management. Their meta-analysis of 11 randomized controlled trials showed a significant improvement in quality of life scores and nasal symptom scores with use of probiotics compared to placebo. Another nontraditional treatment for AR, endonasal phototherapy, is assessed by Cho et al.\(^4\). In their systematic review, the results of 13 trials evaluating the use of phototherapy in AR are analyzed, and collectively suggest that phototherapy may reduce nasal symptoms and improve quality of life in some patients. Taken together, these unique systematic reviews highlight the potential for nontraditional therapies in AR management.

Surgery remains a cornerstone of disease management for both CRS and AR. This issue of AJRA presents several exciting research studies that detail novel surgical techniques. Surgery of the inferior turbinate and septum is commonly employed to reduce nasal obstruction, with multiple techniques having been reported in the literature. In a ‘How I Do It’ article, Barham and colleagues\(^4\) detail the medial flap inferior turbiplasty, a mucosal preserving approach that reduces nasal obstruction while hypothetically maintaining physiologic function. This report details yet another turbinate reducing technique for the rhinologic surgeon, with possible benefits compared to commonly used submucosal electrocautery and powered turbinoplasty. Many surgeons now employ endoscopic techniques when performing both septoplasty and rhinoplasty. In an article by Zuo et al.,\(^4\) results are reported for a tension-relaxing endoscopic septorhinoplasty approach for patients with nasal obstruction due to both a deviated septum and crooked nose. This technique was rapidly performed and resulted in a significant improvement in both esthetic appearance and objective measures of nasal obstruction. Rhinoscleroma, though not commonly encountered in the United States, is an endemic granulomatous disease in parts of the Middle East. Surgical management of rhinoscleroma is challenging, with a propensity for scarring and disease recurrence. In this issue, Awad and Hammad\(^4\) detail their results with topically applied mitomycin C as an adjuvant to surgical therapy for rhinoscleroma. Their double-blind, randomized controlled trial found that use of topical mitomycin C reduced both granulation tissue and adhesions after surgery.

When discussing surgical approaches, it is important to recognize that our specialties continue to navigate financial burdens imparted by the health care system. A renewed focus on achieving expected outcomes while simultaneously reducing costs is confronting health care practitioners at a rapid pace. Finally, Hsu et al.\(^4\) present results of endoscopic cerebrospinal fluid leak repair during active infection with either sinusitis or meningitis. Though one might expect higher rates of failure in this setting, they instead report successful repair and no complications in a cohort of nine patients. While additional studies are needed, this study provides early evidence suggesting that endoscopic CSF leak repair can be safely and successfully performed in these patients.

We hope you will enjoy this issue of the American Journal of Rhinology and Allergy. The basic, translational, and clinical research presented in the July/August issue is a signature example of the content readers have come to expect. The AJRA continues to advance our understanding of complex rhinologic problems and highlights the diverse subject matter in our specialties.