Editorial: The pathophysiology of sinonasal conditions and novel therapeutic options

The May issue of the *American Journal of Rhinology and Allergy* includes a high-quality blend of articles investigating the pathophysiology of sinonasal conditions and novel therapeutic options. Quite a few articles in this issue delve into the pathophysiology of chronic rhinosinusitis (CRS). Decreased apoptosis of cells in nasal polyps (NPs) has been speculated as the cause of persistent inflammation observed in CRS with NPs (CRSwNP); however, there is a paucity of literature in this field. In this issue, Kupper et al. report lower expression of factors involved in apoptosis; caspases 3, 7, and 9; and p53 protein in NP tissue compared with control tissue. They conclude that reduction in these factors involved in apoptosis may be responsible for the higher proliferation of inflammatory cells in CRSwNPs. Another innovative article in this issue addresses the immunomodulatory role of lysosphosphatidic acid (LPA) in CRS. LPA signaling through its receptors has been described in numerous cell types and alterations in LPA signaling may contribute to disease development in many organ systems including cardiovascular and neurological disorders, cancers, and bone disorders. Novel therapeutic targets against LPA signaling are being actively investigated. This area of signaling has not been studied in upper airways previously. Park and colleagues found that LPA, a phospholipid derivative, and autotaxin, the enzyme responsible for the generation of LPA, as well as LPA receptors 1–3, were elevated in CRS with and without polyps. In addition, they showed that sinus mucosa explant stimulated with LPA produces cytokines typically associated with CRS.

MUC5AC gene has been implicated in mucus hypersecretion and airway inflammation in respiratory disease and up-regulated expression of MUC5AC gene has been shown in CRS. Lee and colleagues studied the effect of cholesterol depletion by lovastatin on expression of MUC5AC mRNA expression in NCI-H292 cells. They showed a p38 MAPK–dependent decrease in MUC5AC expression with chronic cholesterol depletion. This could be a possible therapeutic target to decrease mucus secretion associated with sinonasal disease. Lee et al. characterized effects of smoking in a murine model of eosinophilic rhinosinusitis with NPs. The mice with smoke exposure had more severe symptoms and increased number of NPs associated with eosinophilic inflammation and subepithelial fibrosis.

Two articles in the current journal address the frustrating problem of recurrent sinus disease despite surgery in patients with CRS. Van Zele and colleagues addressed this issue by studying the differences in inflammatory mediators in those with recurrent disease after surgery compared with nonrecurrent CRSwNP. Levels of IL-5, specific IgE to *Staphylococcus aureus* enterotoxins, eosinophilic cationic protein, and IgE were elevated in NPs from patients with recurrent disease compared with those without recurrent CRSwNP. Interestingly, they noted that interferon γ protein levels were higher in nonrecurrent CRSwNP. Clinically, asthma and aspirin intolerance were associated with recurrent disease. Vlamink and colleagues followed 221 patients who underwent endoscopic surgery for 3 years. Presence of tissue eosinophilia and eosinophilic mucin was associated with increased likelihood of CRS recurrence after surgery while the presence of fungal hyphae did not predict recurrence of disease.

An investigation pertinent to wound healing by Shin and colleagues establishes that prostaglandin E₂ reduces the migration of nasal fibroblasts via E-prostanoid (EP2 and EP4) receptors and that this inhibition may be mediated by cAMP elevation. Targeting EP receptors may provide opportunities to promote wound healing after surgery. Finally, a cross-sectional study from Iran assessed the prevalence of aspirin sensitivity among patients with CRSwNP. Nabavi et al. studied the epidemiology of aspirin-exacerbrated respiratory disease in Iranian patients with CRSwNP by oral challenge with aspirin. In their study of 80 subjects with CRSwNP, 14 (35.8%) had a history of aspirin sensitivity while 39 (48.8%) subjects had a positive challenge. Self-reported history of aspirin hypersensitivity, concomitant asthma, previous polyp surgery, and high polyp scores were associated with a positive oral aspirin challenge in patients with CRSwNP.

On the topic of nasal surgery, this month’s journal contains an article by Seth and colleagues who addressed the issue of optimal L-strut preservation during endoscopic septoplasty by establishing intranasal landmarks in a cadaveric study. They concluded that the inferior turbinate and vertical middle turbinate attachment can be used to guide the extent of cartilage resection during surgery. Another surgical study evaluated the efficacy of CO₂ laser, radiofrequency and electrocautery for inferior turbinate surgery. All three methods improved symptoms as measured by a visual analog scale at 1 month and 1 year postoperatively and there was no significant difference between the three methods. Su et al. compared the effects of two different surgical approaches for vidian neurectomy on laceration and dry eye syndrome. Their results showed that in the first 7–10 days after the procedure, patients who underwent only proximal nerve stump cautery had less postoperative dry eye problems than patients who had both their proximal and distal nerve stump cauterized.

The current issue of the *American Journal of Rhinology and Allergy* is notable for articles investigating the pathogenesis of allergic rhinitis (AR). A provocative study by Huang and colleagues addressed the issue of prevention of allergen sensitization. They used the knowledge that recombinant DNA plasmids encoding allergens may activate Th1 and dampen Th2 responses by injecting recombinant plasmid Cyn d 1 in neonatal BAL/c mice. They found heightened Th1 response as shown by production of interferon γ and reduction of Th2 response and specifically lowered specific IgE responses and IL-4 in spleen cells. These results, although in animal studies, suggest that allergen-encoded DNA may be a possible intervention to prevent allergic diseases in the future. An epidemiological study of AR in Mexico affirmed the Allergic Rhinitis and Its Impact on Asthma's classification of AR as intermittent or persistent and mild, moderate, or severe. Larenas-Linnemann's study included blinded skin testing and questionnaires of subjects with AR in Mexico. The results suggest that the World Health Organization Allergic Rhinitis and Its Impact on Asthma classification of AR may be more appropriate than the previously used system of classifying AR as seasonal or perennial. The severity classification may be better suited for AR clinical trials as well.

In an interesting study of immunotherapy (IT), Janciauskiene and colleagues studied markers of apoptosis in patients undergoing IT for AR. Gelsolin is a protein that inhibits apoptosis by stabilizing the mitochondria. The authors showed that gelsolin levels were higher in those who received IT compared with those without IT. Thus, markers of apoptosis may possibly predict response to IT in patients with...
AR. A mechanistic study offers new insight into the effects of IT on T regulatory (Treg) cells. The study analyzed histamine receptor (H2R) on Treg cells in the blood of patients with AR compared with controls. H2Rs were up-regulated on Treg cells after pollen exposure and IT decreased the number of H2R+ Treg cells in blood. This may be one of the possible mechanisms for IT’s anti-inflammatory action. It was associated with improvement in symptom scores, decrease in rescue medication use, and decreased nasal eosinophilia. Another translational study in the field of rhinitis explored the possible mechanism by which azelastine, a topical antihistamine, is beneficial in the treatment of nonallergic rhinitis. The study from the University of Cincinnati reported that azelastine, similarly to capsaicin, exhibited rescue medication use, and decreased nasal eosinophilia. Another IT was associated with improvement in symptom scores, decrease in be one of the possible mechanisms for IT’s anti-inflammatory action.

In another pertinent study, Ozkiris Ringer’s performed better than normal saline and hypertonic saline. Test scores, visual analog scores, and endoscopic evaluation. Lactated er’s, and hypertonic solution improved 20-item Sino-Nasal Outcome clinical care of patients. In the field of sinonasal diseases that are important in research and role in measuring outcomes. Once again, the May issue of the journal also has thought-provoking articles on therapeutic options that should be of interest to all those researching and taking care of patients with sinonasal diseases. Although complementary and alternative medicine practices are followed by many patients with respiratory diseases, there are very few studies addressing their immunomodulating effects. Lai et al.17 studied the effect of Myrtol® (G. Pohl_Boskamp, Hohenlockstedt, Germany), a phytopharmaceutical that is a distillate of a mixture of essential oils of eucalyptus, sweet orange, myrtle, and lemon, on mucociliary transport. Myrtol® accelerated mucociliary transport velocity when applied to human sinonasal epithelial cultures and thus could benefit mucociliary clearance in the upper airways. Low et al.18 added to the literature on the use of saline rinses in CRS. They showed that normal saline, lactated Ringer’s, and hypertonic solution improved 20-item Sino-Nasal Outcome Test scores, visual analog scores, and endoscopic evaluation. Lactated Ringer’s performed better than normal saline and hypertonic saline. In another pertinent study, Ozkiris et al.19 evaluated the efficacy of four different local anesthetics that are typically used before fiberoptic rhinoscopy. Lidocaine and prilocaine were most effective in providing local anesthesia during the nasopharyngeal endoscopic examination.

Finally, in an invited article, Benninger and colleagues reviewed different diagnostic criteria used to evaluate rhinosinusitis and their role in measuring outcomes. Once again, the May issue of the American Journal of Rhinology and Allergy contains a diverse array of articles in the field of sinonasal diseases that are important in research and clinical care of patients.

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