Local Drug Delivery

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KEYWORDS

• Sinus surgery • Topical • Irrigation • Spray • Steroid
• Surfactant • Mucoadhesion

Respiratory epithelial damage, mucus hypersecretion, mucociliary dysfunction, and the release of proinflammatory products at the sinus mucosa all mediate the prolonged inflammation of chronic rhinosinusitis (CRS).[1] The perceived role of local microbial flora in CRS has evolved from one of causation to disease modifer.[2] Although there has been a shift to anti-inflammatory therapies in CRS,[3,4] bacteria and fungi are still likely to be powerful mediators of inflammation. The current model of CRS pathophysiology focuses on the interaction of the inflammatory mucosal disease with microbial flora and the failure of the mechanical and innate immunity (**Fig. 1**). Current systemic agents, such as oral or intravenous antimicrobials or anti-inflammatories, have significant side effects and are not successful in many patients. This problem has led rhinologists to examine local delivery of topical therapies. These treatment strategies are important in the management of the disordered inflammation of CRS, and are likely to be pivotal to modifying the expanding pathologic mechanisms that mediate this disease.

The general therapeutic goal of topical management may also lie between potentially competing actions of mechanical lavage and pharmaceutical intervention. The mechanical removal of mucus, antigen, pollutants, inflammatory products, and bacteria/biofilms is often targeted with topical approaches. These interventions rely on high-volume positive pressure solutions to provide shearing forces with additives to alter air-surface-liquid (ASL) tension. However, the same approach may not be appropriate for delivery of pharmaceutical preparations. Complete sinus distribution, prolonged mucosal contact time with local absorption, and minimal wastage are often the desired properties. There is currently a wide array of antimicrobial, anti-inflammatory and immunomodulatory agents being investigated for CRS, which are beyond the scope of this article. The discussion here focuses on modern concepts in local drug therapy, for the macroscopic factors that affect distribution within the sinonasal system and those factors within the microenvironment that influence absorption (**Table 1**).

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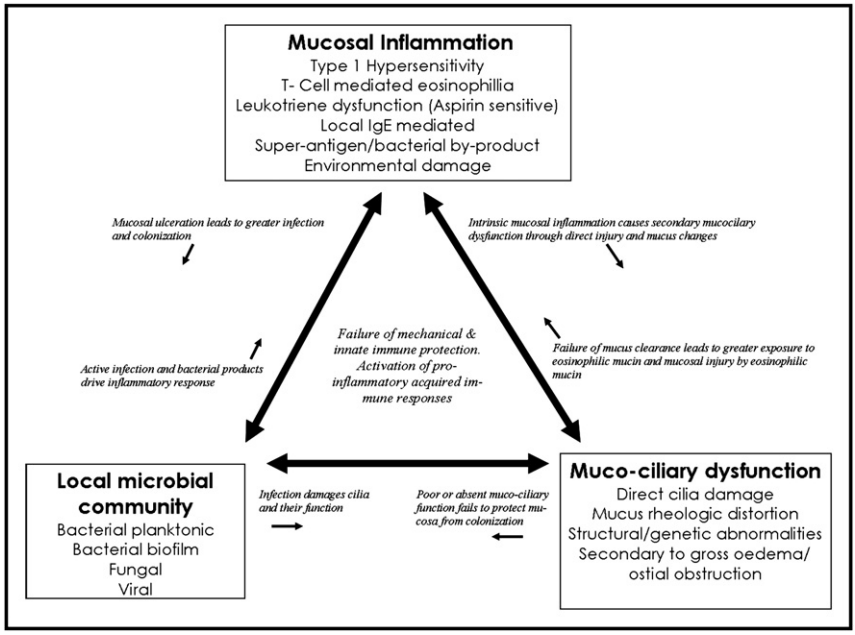

Fig. 1. Pathophysiologic interaction of intrinsic mucosal inflammation, microbial flora, and mucociliary dysfunction. Current topical therapies can affect all 3 interacting processes: the ability to substitute for loss of mucociliary clearance and alter mucus rheology, delivery of steroids to intrinsic mucosal inflammation, and antimicrobial therapies. (*Courtesy of* Division of Rhinology, St Vincent's Hospital; with permission.)

MACRODELIVERY

The ability of the drug to reach the appropriate anatomic region in the paranasal system will always be important, and has been the subject of much research in the past 5 years. Delivery techniques, surgical state of the sinus cavity, delivery device, and fluid dynamics (volume, pressure, position) have a significant impact on the delivery of topical therapies to the sinus mucosa.

Sinus Surgery

Distribution of topical solution to the unoperated sinuses is limited,[5] and in the setting of CRS with mucosal edema it is probably only on the order of less than 2% of total

Table 1
Factors influencing mucosal drug delivery

Local Absorption (Micro)	Sinonasal Distribution (Macro)
Mucus blanket	Surgical state
Mechanical obstruction to diffusion	Device
Cell surface charge	Position
Mucin and protein binding	Volume
Mucociliary clearance	Pressure
Mucosal residence time	Anatomic dimensions of surgical cavity