Bacterial Pathogens and the Microbiome

Thad W. Vickery, BA[a], Vijay R. Ramakrishnan, MD[b,*]

KEYWORDS

• Bacteria • Chronic rhinosinusitis • Microbiome • Culture-independent microbiology • Sinusitis

KEY POINTS

- The sinuses are not sterile. A population of bacteria is present in both health and disease, roughly in the same overall abundance, but qualitatively different in its makeup.
- As of yet, no single bacterial species or set of species has been definitively shown to be protective or causative in chronic rhinosinusitis (CRS).
- The overall function of the bacterial community may be most important, rather than the presence or absence of a single pathogen.
- Therapies used to treat CRS may induce microbiome alterations.
- Further research is indicated and required in this exciting field.

INTRODUCTION

Chronic rhinosinusitis (CRS) continues to be one of the most prevalent health care problems in the United States. Despite the significant morbidity, loss of productivity, and health care costs associated with CRS, the underlying processes that lead to disease remain poorly understood. The nonspecific clinical symptoms of nasal obstruction, rhinorrhea, facial pain, and anosmia may represent a common end point for various inflammatory mechanisms occurring in different anatomic areas. CRS is increasingly being appreciated as a clinical syndrome with a wide spectrum of overlapping disease physiology. For instance, CRS with nasal polyps (CRSwNP) often is

Disclosure Statement: The authors have no financial conflicts of interest to disclose. Research reported in this publication was supported by the National Institute On Deafness And Other Communication Disorders of the National Institutes of Health under award numbers K23DC014747 (V.R. Ramakrishnan) and T32DC01228003 (T.W. Vickery). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

[a] University of Colorado School of Medicine, 13001 East 17th Place, Aurora, CO 80045, USA; [b] Department of Otolaryngology, Head and Neck Surgery, University of Colorado, 12631 East 17th Avenue, B205, Aurora, CO 80045, USA
* Corresponding author.
E-mail address: Vijay.Ramakrishnan@UCDenver.edu

Otolaryngol Clin N Am 50 (2017) 29–47
http://dx.doi.org/10.1016/j.otc.2016.08.004
oto.theclinics.com

characterized by eosinophilic inflammation and increased production of histamine, IL-5 and IL-13,[1] whereas CRS without nasal polyps (CRSsNP) is often considered a predominantly neutrophilic disease characterized by high levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF) α.[2] In practice, however, there are patients with CRSsNP with high levels of eosinophils and patients with CRSwNP who exhibit robust neutrophilic infiltration within the sinonasal epithelium. Thus, our classification of CRS in clinical practice is often not as simple as we would prefer.

Chronic Rhinosinusitis Pathophysiology and Immune Homeostasis

CRS is characterized by persistent inflammation, a dysregulated immune response, and host-microbial interactions that together result in disruption of epithelial barrier function, poor wound healing, tissue remodeling, and clinical symptoms. Historically the significance of bacteria in acute and CRS has focused on the interactions between a single bacterial pathogen and its host. However, developing concepts in microbial ecology, laboratory methods in culture-independent microbiology, and bioinformatics are furthering our capacity to study complex microbial communities as an entire functional unit. The nasal cavity and paranasal sinuses are the first tissues exposed to airborne environmental challenges, including pathogenic and nonpathogenic bacteria, viruses, fungi, allergens, and toxins. The mucosal surface uses several immune mechanisms to promote homeostasis, which can be broadly divided into innate and adaptive immunity. Many host factors impact the functionality of the immune response that is thought to predispose individuals to the development of CRS.[3]

Innate versus adaptive immunity

Innate immunity classically refers to the nonspecific defense mechanisms that are rapidly activated following exposure to antigenic material and confer immediate protection. Within the upper respiratory tract, this includes the physical barrier provided by the ciliated pseudostratified columnar respiratory epithelium that lines the sinonasal cavity. This resilient barrier contains interspersed goblet cells that secrete a viscoelastic mucous layer atop the epithelial surface composed of high-molecular-weight glycoprotein mucins and heavily glycosylated molecules. In conjunction with beating cilia, the enriched mucous layer promotes nonspecific mucociliary clearance of microbes and irritant particles.[4] Barrier dysfunction can contribute to CRS; when coupled with defects in mucociliary clearance that promote bacterial colonization, bacterial invasion and further barrier disruption may occur.[3,5] Classic genetic defects in ciliary function, such as cystic fibrosis and primary ciliary dyskinesia, are often used as examples; but acquired ciliary dysfunction occurs in CRS as well.[6] Poor barrier function and dysfunctional mucociliary clearance are host defects that predispose individuals to pathogen colonization and the development of recurrent infection.[7–9]

Sinonasal epithelial cells secrete enzymes, opsonins, defensins, permeabolizing proteins, and other endogenous antimicrobial products into the apical mucous layer. These host defense molecules are important for directly neutralizing microbes and recruiting inflammatory cells that modulate the immune response. Specifically, epithelial cells secrete enzymes, such as lysozyme, peroxidases, and chitinases, and the small cationic permeabolizing proteins, such as the defensins and cathelicidins. Additionally, proteins, such as lactoferrin, mucins, C-reactive protein, and secretory leukocyte proteinase inhibitor, collectively provide protection from bacteria, fungi, and viruses at the apical surface.[9–11]

When pathogens do invade the sinonasal epithelium, circulating professional phagocytes, possessing pattern recognition receptors (PRRs) on their cell surface, recognize pathogen-associated molecular patterns and damage-associated