Recent expert panels have defined chronic rhinosinusitis (CRS) as a clinical syndrome rather than a discrete disease entity, with emphasis on chronic inflammation rather than infection [1]. In the past CRS was believed to be secondary to anatomic abnormalities leading to ostial obstruction and/or persistent bacterial infection. Symptomatic recurrence of CRS despite adequate surgery, however, resulted in general acceptance of the concept that no one causative factor can fully explain the clinical heterogeneity and pathologic manifestations of the condition. There is growing consensus toward the concept that CRS results from multiple factors that may be working simultaneously or independently in an individual patient. Potential contributing sources can be categorized into: host factors, including anatomic abnormalities, allergy, immune dysfunction, mucociliary defects, metabolic perturbations, such as aspirin intolerance; and environmental factors including micro-organisms, biofilm formation, osteitis, fungal colonization associated with eosinophilia, and bacterial superantigens. The focus of this chapter will be on the hypothesized role of bacterial superantigens (SAg) in CRS with nasal polyps.

Chronic rhinosinusitis is commonly classified into CRS without polyps (CRSsNP) and CRS with polyps (CRSwNP) with SAg playing a proposed role thus far only in the latter. Overall, CRS affects approximately 15% of the American population [1], while CRSwNP occurs in about 20% of those patients with CRS [2]. Patients with polyps represent a distinct group that is clinically more symptomatic and particularly refractory to both medical and surgical therapy. CRSwNP is frequently linked to steroid-dependent asthma and aspirin intolerance. The most common pathology of the sinus mucosa in CRSwNP is similar to that seen in the bronchial mucosa of asthmatics, infiltrates consisting mainly of lymphocytes, plasma cells, and eosinophils. Histologically, nasal polyposis is characterized by a chronic eosinophilic inflammatory pattern in 70–90% of cases [3], tissue edema, and local IgE production. Histologic findings in CRSsNP in general reveal much less tissue eosinophilia and edema with more prominent glandular hyperplasia [4]. The above division of CRS into eosinophilic CRSwNP and relatively non-eosinophilic CRSsNP is somewhat artificial, since polyps with minimal tissue eosinophilia exist in both cystic fibrosis and...
Superantigens are proteins of microbial or viral origin known for their potent lymphocyte-transforming (mitogenic) activity toward human T lymphocytes. Microbial SAgs are powerful modifiers of the immune system, which may result in massive T-cell activation, cytokine release, and in some cases systemic shock. SAgs are able to trigger excessive and aberrant activation of T cells by bypassing the normal antigen processing step. As depicted in Fig. 1.9,1, during a conventional response, an antigen is recognized and processed within an antigen processing cell (APC). Peptide fragments of the processed antigen are displayed in the peptide binding groove of the major histocompatibility complex (MHC) class II molecule on the surface of the APC. These fragments are presented to surrounding T lymphocytes. Only those CD4+ T cells that recognize the MHC class II molecule with the bound peptide fragment will be stimulated. This is an extremely specific response that activates only a tiny fragment of the host T-cell population (less than 0.01%) [9,10]. In contrast, SAgs bind as intact molecules to a region outside the peptide binding groove of the MHC class II molecule (Fig. 19.1). SAgs stimulate both CD4+ and CD8+ T cells in an MHC II-dependent manner; however, T-cell receptor (TCR) recognition is not MHC-restricted [11]. Binding to the MHC class II molecule outside the antigen-binding groove prevents the TCR from having cognate recognition of the surface of the MHC molecule, which would be required for usual antigen presentation. SAgs bind to the V-beta domain of the TCR and any T cell bearing the appropriate V-beta type will be stimulated by the SAg regardless of the MHC allotype. It is the bridging of the TCR and the MHC class II molecule that leads to massive proliferation and release of cytokines, chemokines, and adhesion molecules, T cell activation, activation-induced apoptosis and anergy [12]. In contrast to the conventional antigen response, which activates less than 0.01% of the host T-cell population, SAgs may activate up to 25% [13]. Concentrations of less than 0.1 mg/mL of the bacterial SAg may be enough to stimulate an uncontrolled T-cell response, leading to systemic collapse, shock, and death [14].

### What Are Superantigens?

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