

Immune Responses in the Oral Cavity



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The oral cavity is a unique anatomical structure, characterised by the juxtaposition of soft and hard tissues and which is continuously subject to challenge by the external environment and foreign material. Diseases and disorders caused by oral microorganisms are very common and economically important, in particular **dental caries** (loss of tooth integrity caused by bacteria-derived organic acids) and **periodontitis** ('gum disease'; chronic destructive inflammation of the supporting tissues of the teeth caused by anaerobic bacteria). Also, **halitosis** (oral malodour) is caused by sulphide-producing oral bacteria. Oral diseases secondary to systemic disease, e.g. **oral candidiasis**, due to acquired immunodeficiency are of increasing clinical importance. Also, several **autoimmune diseases** such as **Sjögren's syndrome** and **pemphigus vulgaris** have oral manifestations.

Saliva

Saliva is a key component of the host defence against infection in the mouth and patients with **xerostomia** ('dry mouth') have higher levels of dental plaque and an increased risk of periodontitis and candidiasis than otherwise healthy individuals. The saliva contains many molecular elements which restrict microbial growth: for example, **lysozyme** cleaves bacterial cell walls, **lactoferrin** complexes iron ions which are an essential microbial nutrient, and **antimicrobial peptides** such as **histatins** inhibit the growth of *Candida albicans* and *Streptococcus mutans* (the latter being an aetiological agent of dental caries). **Salivary IgA** serves to aggregate oral bacteria such as *S. mutans* and prevent the formation of dental plaque, a biofilm on the exposed surface of teeth which comprises a thriving ecosystem for oral pathogens.

Tonsils

The **tonsils** are immune tissues located towards the back of the mouth; they comprise the **palatine-, lingual- and tubal tonsils** as well as the **adenoids** (pharyngeal tonsils) and are collections of **lymphoid tissue** immediately beneath the epithelium. Together the different tonsillar tissues form a ring of lymphoid tissue known as **Waldeyer's ring** which serves to protect the opening to the pharynx. The tonsils are often a site of bacterial infection, likely because the clefts in which they appear are a site of collection of debris; this can lead to recurring chronic inflammation and tonsillar enlargement (**tonsillitis**).

The periodontium

The tissues which surround and support the teeth (the **periodontium**) are complex and susceptible to acute and chronic inflammation caused by plaque bacteria which accumulate in the space between the tooth and the gum (the **gingival sulcus**). Fortunately, the periodontium has many host defence elements including the **gingival epithelium** which prevents bacterial adhesion by constantly shedding keratinocytes into the oral cavity ('cell turnover') and protecting against invasion by having a substantial keratin component (unlike other tissues of the oral and gastrointestinal mucosa). The connective tissues of the periodontium are highly vascular, facilitating vascular leukocyte emigration in response to infection and the gingival sulcus is bathed with a serum exudate (**gingival crevicular fluid, GCF**) which carries **complement** components as well as **antibodies, neutrophils** and **plasma cells** necessary to prevent tissue invasion by the sub-gingival plaque bacteria. Whereas it is clear the destructive, chronic inflammation that manifests clinically as periodontitis is caused by an excessive and inappropriate immune response to certain pathogenic plaque bacteria, coupled with a failure of the normal processes that limit inflammation and drive tissue repair, we don't yet have a holistic understanding of how the dynamic oral microbiome with its complex cellular and molecular structures interface with the host immune response and modify disease susceptibility. Studies of the oral microbiome will serve as another paradigm for host-microbiome interactions as determinants of health as has been revealed by studies of the gut microbiome.

Medical relevance

Interest in oral immunology has heightened in recent years with the recognition that there are clinical associations between periodontitis and **systemic diseases** other chronic inflammatory diseases of the ageing population (e.g. **rheumatoid arthritis, diabetes and cardiovascular disease**). We are beginning to reveal pathogenic links between these diseases that may inform improved patient management e.g. activation of immune cells such as monocytes by plaque bacteria may contribute to the development of atherosclerosis. Saliva which mixes with GCF in the oral cavity, is a rich and non-invasive source of **disease biomarkers** such as cytokines, tissue destructive enzymes and pathogenic microorganisms, as well as DNA for studies of genetic associations and pharmacogenomics.