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Periodontal disease and periodontal bacteria as triggers for rheumatoid arthritis

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A B S T R A C T

There is an epidemiological association between periodontitis and rheumatoid arthritis (RA), which is hypothesised to lead to enhanced generation of RA-related autoantibodies that can be detected years before the onset of RA symptoms. Periodontitis is a common dysbiotic disease; tissue damage occurs because the immune system fails to limit both the resident microbial community and the associated local immune response. Certain periodontal bacteria, including *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, may contribute to RA autoantibody production through direct post-translational modification of proteins or, indirectly, by influencing neutrophil-mediated neo-epitope generation. Oral bacteria that invade the blood may also contribute to chronic inflammatory responses and generation of autoantibodies. The putative association between periodontitis and the development of RA raises the potential of finding novel predictive markers of disease and disease progression and for periodontitis treatment to be included in the future as an adjunct to conventional RA immunotherapy or as part of a preventive strategy.

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Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease that manifests as chronic polyarthritis. There is increasing evidence that the initiating events that result in the generation of RA-related autoantibodies, which can be detected years before the onset of RA symptoms, occur at mucosal sites distant to the joints [1–5]. Inflammatory processes in response to environmental triggers, including infections, in the lungs and the mouth have been strongly implicated and, recently, also in the gastrointestinal and genitourinary tracts [4–7]. This review concentrates on the contribution of oral disease, specifically periodontal disease, and oral bacteria in the development of RA.

Periodontal diseases are common oral inflammatory conditions that occur in response to bacterial plaque biofilms, causing damage to the gingivae (gums), periodontal ligament and alveolar bone, all of which form the supporting tissues of the teeth (Fig. 1). Severe periodontitis occurs in 2–20% of most adult populations, affecting 300 million people worldwide [8]. In the UK, 3–4 million currently suffer from advanced periodontitis at a cost of £2 billion/year to the National Health Service (NHS). Associations have emerged between periodontitis and a growing list of chronic conditions including atherosclerosis, diabetes and RA [9–11].

Association between rheumatoid arthritis and periodontal disease

RA and periodontitis display some pathogenic similarities, such as the host immune response leading to soft tissue inflammation with subsequent hard tissue destruction, and certain risk factors, including smoking and excess weight or obesity, although some studies only show associations at specific stages of disease aetiology [12–17]. The significant RA risk attributed to the shared epitope HLA-DRβ1 (SE) is well established [18], but associations of specific human leukocyte antigen (HLA) molecules with chronic periodontitis are unclear.

Multiple studies have shown an epidemiological association between periodontitis and RA, and these have been reviewed recently [6,19,20]. Inconsistent diagnosis of periodontal disease may have

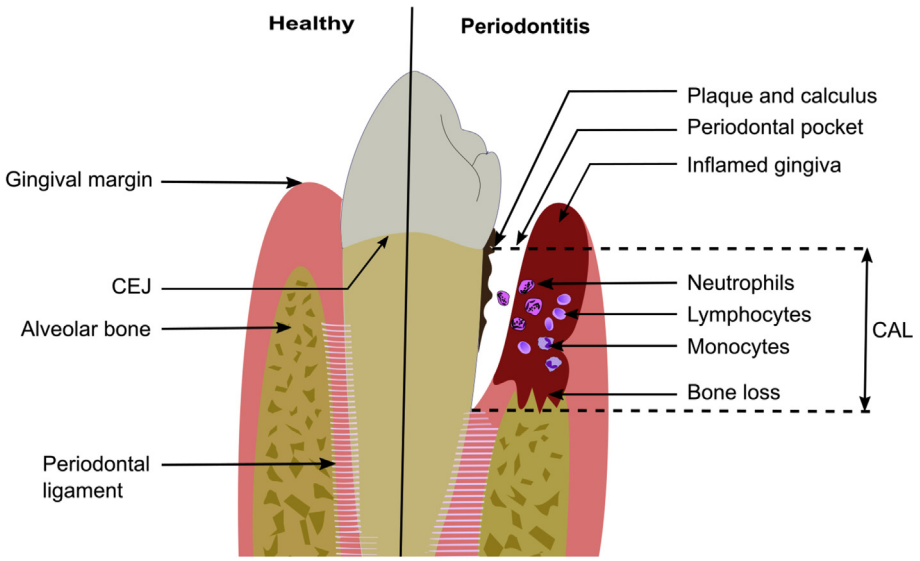

Fig. 1. Diagram comparing a periodontally healthy site (left panel) with a periodontitis site (right panel). Dental plaque and calculus accumulate at the tooth-gingiva margin and extend subgingivally. The activities of subgingival plaque and the host defences lead to inflammation and tissue damage. The gingiva becomes detached from the root surface, forming a periodontal pocket, which is highly anaerobic and allows further expansion and development of subgingival plaque. Increasingly severe destruction of tissues results in the gradual recession of the supporting alveolar bone. Clinical attachment loss (CAL) is the distance from the cemento-enamel junction (CEJ) to the base of the periodontal pocket and is measured using a periodontal probe.

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