

# Oral Anaerobic Bacteria in the Etiology of Ankylosing Spondylitis

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**ABSTRACT:** Ankylosing spondylitis (AS) is associated with periodontitis. Anti-*Porphyromonas gingivalis* and anti-*Prevotella intermedia* antibody titers were higher in patients with spondyloarthritis than in healthy people. Sulfasalazine is an effective antibiotic treatment for AS. Moxifloxacin and rifamycin were also found to be significantly effective. The etiology hypothesis suggests that oral anaerobic bacteria such as *Porphyromonas* spp and *Prevotella* spp contribute to the disease. These bacteria have been identified in AS, and we will discuss their pathogenic properties with respect to our knowledge of the disease. Periodontal pathogens are likely to be responsible for the development of AS in genetically susceptible individuals. This finding should guide the development of more comprehensive and efficacious treatment strategies for AS.

**KEYWORDS:** Ankylosing spondylitis, oral bacteria, etiology

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## Introduction

The term *periodontal disease* (PD) embraces a number of conditions in which the supporting tissues of the teeth are attached.<sup>1</sup> Chronic adult periodontitis is the most common form of advanced PD affecting the general population, and it is a major cause of tooth loss after the age of 25 years.<sup>1</sup>

Ankylosing spondylitis (AS) and other HLA-B27-associated forms of arthritis (eg, reactive arthritis) constitute a relatively common group of arthritides (spondyloarthropathies), affecting up to 2% of White individuals.<sup>2</sup> Epidemiologic and familial data have established a strong disease association with the HLA class I antigen B27, but they also suggest that additional genes modify both susceptibility to AS and the phenotypic expression of this disease.<sup>2</sup> Because AS is associated with periodontitis,<sup>3</sup> those with AS have significantly higher risks of PD.<sup>4</sup> Ankylosing spondylitis and PD are 2 similar diseases from many aspects. The cytokine profiles are almost the same,<sup>5</sup> and both diseases are observed in soft and hard connective tissue.<sup>4</sup>

In 2009, the Assessment of SpondyloArthritis International Society (ASAS) proposed a new terminology for spondyloarthritis (SpA) which is based on the classification criteria that changed the perspective of AS.<sup>6,7</sup> From now on, the axial form of SpA (AxSpA) is equal to the (early) nonradiographic-type (nr-axial SpA) and radiographic-type AS (according to the older modified New York criteria).<sup>8</sup> The advantage of the new terminology is that it includes patients with earlier and less frequent disease and reflects the severity of the spectrum that is seen in the clinical practice.

## Periodontal Disease and Oral Bacteria

The causes of PD are multifactorial in that several bacterial species are involved, interacting with host tissues and cells and

leading to the release of many inflammatory mediators.<sup>1</sup> This in turn leads to the destruction of tooth-supporting structures.<sup>1</sup> These diseases are classified into several groups. Among them, gingival diseases affect gingival tissues with no loss of attachment, whereas periodontitis is accompanied by inflammation within the supporting tissues of the teeth, attachment loss, and bone loss. It is clinically characterized by symptoms such as bleeding gums, bad breath, gingival recession, tooth mobility, and migration. *Porphyromonas gingivalis* is a Gram-negative, obligate anaerobic, nonmotile bacterium.<sup>1</sup>

*Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia* are associated with the pathogenesis of chronic periodontitis.<sup>1</sup> The “red complex” comprises bacteria that are considered to be periodontal pathogens<sup>1</sup> and include these 3. The red complex secretes peptidylarginine deiminases.<sup>1</sup> This review examines the association between oral bacteria and the etiology of AS.

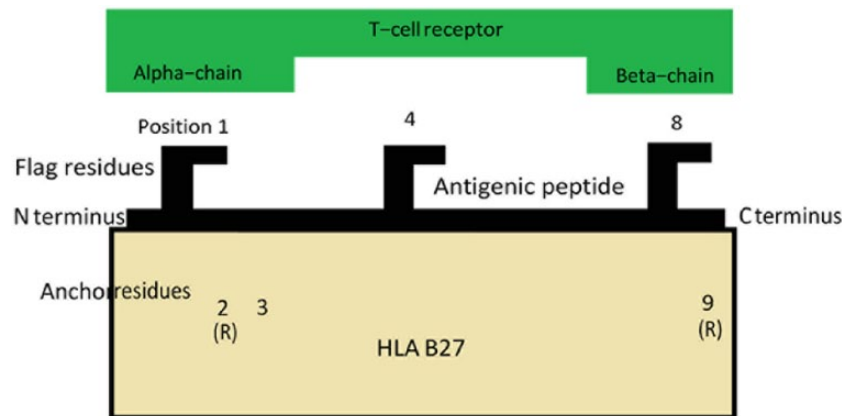
## Periodontal Pathogens and AS

Anti-*P gingivalis* and anti-*Prevotella intermedia* antibody titers were higher in patients with SpA than in healthy people.<sup>9</sup> Sulfasalazine is an effective antibiotic treatment for AS.<sup>10</sup> When reviewing the literature, 8 randomized controlled studies that focused on sulfasalazine use were found<sup>10–17</sup>; however, long-term use results in drug resistance. It is more effective for the peripheral signs than the spinal symptoms of AS.<sup>17</sup>

In yet another study of 22 patients with active AS, a new treatment modality was evaluated and compared with an oral treatment.<sup>18</sup> Rifamycin was found to be significantly effective in the treatment of AS.

In yet another study, researchers used moxifloxacin—a quinolone group antibiotic used to treat anaerobic bacteria—for





**Figure 1.** Antigen presentation in ankylosing spondylitis.

AS treatment in 2007.<sup>19</sup> In this open-label study, moxifloxacin was continuously effective in treating the symptoms and clinical parameters of AS.

The risk of AS in HLA-B27-positive individuals is 2% to 5%, and 90% to 95% of affected White individuals are HLA-B27 positive.<sup>2</sup> Twenty-five subtypes of HLA-B27 have been assigned on the basis of nucleotide sequence homology; they encode 23 different products.<sup>2</sup> The prevalence of these subtypes varies depending on ethnicity, and B\*2705, followed by B\*2702, is the most common subtype in Whites.<sup>2</sup>

Determination of the crystal structure of HLA\*2705 and characterization of the peptide binding properties of it and other subtypes suggest a mechanism for the B27 disease association. Most naturally bound peptides eluted from B27 share arginine at position 2 that interacts with the glutamine at position 45 in the B pocket.<sup>2</sup> These observations suggest that the B pocket may convey specificity for the binding of putative arthritogenic peptide(s).

The polymorphic region of B27, spanning residues 169 to 179, demonstrates homology between bacterial proteins and one of the endogenous peptides presented in vivo by B27 in B27-transfected lymphoblastoid cell lines.<sup>2</sup> Neither B27 transgenic rats nor B27 transgenic mice develop either intestinal inflammation or peripheral arthritis when maintained in germ-free environments. Furthermore, only transgenic rats colonized with defined bacterial cocktails that contain *Bacteroides* spp develop intestinal inflammation.<sup>2</sup> HLA-B27 endogenous peptides include an arginine at the second residue (Figure 1). Peptidylarginine deiminases of oral bacteria might lead to arginine degradation in HLA-B27.<sup>2</sup>

## Conclusions

Periodontal pathogens are responsible for the development of AS in genetically susceptible individuals. This finding should guide the development of more comprehensive and efficacious treatment strategies for AS.

## Author Contributions

MÖ wrote the manuscript. The author read and approved the final manuscript.

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