Rheumatoid arthritis and periodontal disease: biological, clinical, and therapeutic relations

Abstract

A number of clinical and epidemiological studies have been conducted in the past decade to investigate a possible association between periodontal disease and rheumatoid arthritis (RA). The majority of such studies indicate that patients with RA have an increased prevalence of periodontitis and tooth loss. However, because of the great variability in study designs, the strength of the association remains unclear. Furthermore, most available studies are cross-sectional, and therefore, the temporality of the association between periodontitis and RA cannot be evaluated. Emerging evidence indicates that infection with Porphyromonas gingivalis, a bacterium highly implicated in chronic periodontal disease, might have a direct role in the etiology and pathogenesis of the chronic inflammatory response in RA. Additional noncausal pathways include genetic, environmental, and behavioral factors that are common to both conditions. Linking both disorders are the pathways involved in inflammatory bone destruction, suggesting possible shared therapeutic targets and research aims.

Key words: Periodontal disease, rheumatoid arthritis, Porphyromonas gingivalis, cytokines, chronic inflammation, biological therapies
Introduction to rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, immunemediated inflammatory disease that is characterized by synovial inflammation. Left untreated, it can lead to progressive destruction of cartilage and bone that may result in structural damage and functional disability (Gabriel 2001). RA affects women more than men at a ratio of 3:4:1, at virtually any age, but most commonly in middle adult life (Lipsky 2008). Although clinical presentation can vary, the typical picture of established RA is bilateral symmetric inflammatory polyarthritis involving small and large joints in both the upper and lower extremities (Figure 1), with sparing of the axial skeleton except the cervical spine. The predominant symptoms of RA are pain, morning stiffness, and swelling of peripheral joints. Although quite uncommon, systemic (extra-articular) features such as subcutaneous nodules, Sjogren syndrome, lung involvement, or vasculitis can occur. Laboratory findings include anemia of chronic type and increased inflammatory markers in active disease; autoantibodies against the Fc portion of IgG—the so-called rheumatoid factor—and against citrullinated peptides that incorporate the amino acid citrulline (McInnes and Schett 2007) are detected with varying sensitivity and specificity (Gabriel 2001, Lipsky 2008). Diverse genetic, hormonal, immunologic, and environmental factors have been identified as potential players in RA development, leading to heterogeneity of disease presentation and severity. A distinct environmental and genetic background could account for the milder nature of the disease in Greek compared with North European populations. RA in Greek populations is characterized by less inflammatory articular disease, fewer extra-articular manifestations, less severe joint damage, and a high frequency of Ro(SSA) antibodies linked to a higher prevalence of secondary Sjögren syndrome (Drosos et al. 1992, Drosos and Moutsopoulos 1995). Furthermore, Greek RA patients are characterized by a lack of association with human leukocyte antigens (HLA), the absence of amyloidosis alleles, and a weak association with HLA-DR1 and -DR4 antigens (Boki et al. 1992, 1993, Mavragani et al. 2007). In patients with aggressive joint disease, the long-term prognosis of RA is poor. In such patients, studies have shown that the risk of mortality for men with RA is 38% greater (55% for women) than the general population and that life expectancy is reduced by an average of 3-18 years (Yelin and Wanke 1999).

Is there a link between periodontitis and RA?

This is typically assessed clinically. (CI) 2.35-13.84. The definition of RA has been more consistent throughout the studies because the majority of studies employed the American College of Rheumatology (ACR) criteria for defining RA; however, some did use subjective and inaccurate criteria such as self-reported disease and tooth loss as measures of periodontal disease to varying levels of attachment loss in one or more sites of the mouth being considered as presence of disease (de Pablo et al. 2009). Different studies have also investigated the association of RA with varying types of periodontitis (chronic and aggressive, localized and generalized). The definition of RA has been more consistent throughout the studies because the majority of studies employed the American College of Rheumatology (ACR) criteria for defining RA; however, some did use subjective and inaccurate criteria such as self-reported RA (de Pablo et al. 2009).

Some of the larger studies conducted to date are briefly described below (Table 1) as a sample of the type of studies investigating the degree of association between periodontal disease and RA. Pischon et al. (2008) examined 57 patients with RA and 52 healthy controls matched by age, gender, and sociodemographic characteristics. The researchers reported a significant 5.7-fold increase in odds of periodontal disease (mean CAL >4 mm) in RA patients compared with healthy controls with a 95% confidence interval (CI) 2.35-13.84. CAL and PD were significantly higher in subjects with RA compared with control subjects (4.37 ± 1.30 mm vs 3.40 ± 0.89 mm, p <0.001 and 3.71 ± 0.73 mm vs 3.16 ± 0.58 mm, p <0.001, respectively). Significant differences were also found in plaque accumulation assessed by the plaque index (PI) (0.71 ± 0.46 vs 0.44 ± 0.28, p <0.001) and inflammatory gingival status evaluated by the gingival index (GI) (0.83 ± 0.48 vs 0.57 ± 0.39, p <0.003). Pischon et al. (2008) also examined the association of RA with periodontal disease after adjusting for potential confounders. PI studies with relatively small cohorts of fewer than 100 participants. Great variability occurs in study design and particularly in the definitions of periodontitis and RA. Periodontitis is typically assessed clinically by measuring probing pocket depth (PD) and clinical attachment level (CAL) at various sites of dentition. Definitions of periodontitis in the clinical studies of RA vary widely from self-reported disease and tooth loss as measures of periodontal disease to varying levels of attachment loss in one or more sites of the mouth being considered as presence of disease (de Pablo et al. 2009). Different studies have also investigated the association of RA with varying types of periodontitis (chronic and aggressive, localized and generalized). The definition of RA has been more consistent throughout the studies because the majority of studies employed the American College of Rheumatology (ACR) criteria for defining RA; however, some did use subjective and inaccurate criteria such as self-reported RA (de Pablo et al. 2009).

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Οι δείκτες PI και GI συσχετίστηκαν σημαντικά με τα ΕΚΠ (συντελεστής συσχέτισης Spearman $r = 0.59$ με $p < 0.001$ και $r = 0.70$, $p < 0.001$, αντίστοιχα). Η ισχύς της συσχέτισης της RA με την περιοδοντική νόσο μειώθηκε μεν, αλλά παρέμεινε στατιστικά σημαντική μετά από περαιτέρω προσαρμογή για το δείκτη PI, το δείκτη GI, ή και τους δύο δείκτες μαζί.

Οι Abou-Rayya και συν. (2005) συμπεριέλαβαν στη μελέτη τους 50 ασθενείς με ΡΑ που διαγνώστηκαν σύμφωνα με τα αναθεωρημένα κριτήρια (1987) της Αμερικανικής Ομοσπονδίας Ρευματισμού (ARA) και 50 μάρτυρες, όμως ως προς την ηλικία, το φύλο, την κοινωνική κατάσταση και τη στοματική υγεία. Οι συγγραφείς εκτίμησαν παραμέτρους φλεγμονής και στοματικής υγείας που περιλάμβαναν την ουλική αιμορραγία και την τρυγιά. Επιπλέον, συνεκτίμησαν δείκτες της περιοδοντικής νόσου όπως το ΒΘ $>4$ mm, απόφλεξη πρόσφυσης $>4$ mm και τα απολεσθέντα δόντια (μία παράμετρος η οποία δε σχετίζεται πάντα με την περιοδοντική νόσο). Αναφέρθηκαν σημαντικές συσχέτισες της RA με την ουλική φλεγμονή, την τρυγιά, τις περιοδοντικές μετρήσεις και την απόφλεξη δοντιών. Ωστόσο, δεν έγινε σαφής περιγραφή της βαρύτητας της νόσου τόσο στους ασθενείς όσο και στους μάρτυρες. Επίσης, αναφέρθηκε ο αριθμός των ασθενών με ΒΘ $>4$ mm, χωρίς να προσδιοριστεί το ποσοστό των αντίστοιχων θέσεων. Τέλος, η παρουσία αυξημένης τρυγίας και φλεγμονής που δεν ελέγχτηκε, θα μπορούσε να αιτιολογήσει την αυξημένη παρουσία ή βαρύτητα της περιοδοντικής νόσου. Οι συγγραφείς βρήκαν επίσης θετικές συσχέτισες μεταξύ παραμέτρων της RA και της παρουσίας της περιοδοντικής νόσου, υποδηλώνοντας πιθανή συμβολή της μίας κατάστασης στην βαρύτητα της άλλης. Η βαρύτητα του ΒΘ συσχετίστηκε θετικά με τη διάρκεια της RA ($r = 0.62$, $p < 0.001$), τον αριθμό των επώδυνων και διογκωμένων βαρύτητα του ΒΘ ($r = 0.62$, $p < 0.001$), την ταχύτητα καθέξος ερυθρού (TKE) ($r = 0.44$, $p < 0.005$), την οπτική αναλογική κλίμακα ($r = 0.34$, $p < 0.001$), και τη C-αντιδρώσα πρωτεΐνη ($r = 0.41$ με $p < 0.003$). Οι συγγραφείς συσχετίστηκαν επίσης παραμέτρους της RA με το δείκτη παντομογραφίας που δεν αποτελεί μέτρο της περιοδοντικής νόσου, αλλά της γενικής στοματικής υγείας.

Οι De Pablo και συν. (2008) ανέλυσαν στοιχεία από την εθνική μελέτη υγείας και διατροφής των ΗΠΑ (NHANES III, 1988-1994) και συμπεριέλαβαν άτομα άνω των 60 ετών που είχαν υποβληθεί σε οδοντιατρικές και μυοσκελετικές εξετάσεις. Σε αυτή τη μελέτη η διάγνωση της RA βασίστηκε στα κριτήρια του ACR και η διάγνωση της περιοδοντιτίδας καθορίστηκε με την παρουσία μιας τουλάχιστον θέσης με απώλεια πρόσφυσης με απώλεια δοντιών. Οι συγγραφείς αναφέρθηκαν α κριτήρια της RA με το δείκτη παντομογραφίας που δεν αποτελεί μέτρο της περιοδοντικής νόσου, αλλά της γενικής στοματικής υγείας.

De Pablo et al. (2008) analyzed data from the US National Health and Nutrition Examination Survey (NHANES III, 1988-1994) and included participants older than 60 years who had undergone dental and musculoskeletal examinations. In this study, RA diagnosis was based on ACR criteria, and periodontitis was defined as at least one site exhibiting both attachment loss and PD $>4$ mm. Dental status was classified as (1) no periodontitis, (2) periodontitis, and (3) edentulism. Findings indicate that of 4,461 participants, 103 were diagnosed with RA. Diagnosis of RA and edentulism were strongly associated with an odds ratio (OR) of 2.3 (95% CI 1.5-3.3) after adjusting for age, sex, ethnicity, and smoking. The association with edentulism was particularly strong for those with seropositive RA (OR 4.5, 95% CI 1.2-17). Diagnosis of RA was also associated with a greater number of missing teeth (20 vs 16, $p <0.001$), although it was not documented whether these teeth were lost as a result of periodontal disease. The association of RA with the presence of periodontitis was less profound, though present (OR 1.82, 95% CI 1.0-3.2). However, the patient popul-
αυτή τη μελέτη ήταν σημαντική γηραιότερος σε σχέση με τις περισσότερες μελέτες. Συνεπώς, οι ασθενείς με περιοδοντική νόσο ίσας είχαν ήδη χάσει μερικά δόντια λόγω της προσχορμημένης περιοδοντίτιδας, συμβάλλοντας πιθανά στην μεγαλύτερη απώλεια δοντιών στον πληθυσμό με RA.

Οι Κάσερ και συν. (1997) αξιολόγησαν 50 ασθενείς με RA και 101 μάρτυρες όμοιας ηλικίας, φύλου, τόπου και κατανόησης, και τη στοματική υγεία. Οι συγγραφείς ανέφεραν ότι οι ασθενείς με μακροχρόνια ενέργη ΡΑ (μέση τιμή ± SD: 13 ± 8 χρόνια) που λάμβαναν τροποποιημένα αντιαρθροποιητικά (N = 46), κορτικοστεροειδή (N = 38), ή μη κορτικοστεροειδή αντιαρθροποιητικά (N = 43), εμφανίζουν υψηλότερη κατά ουλικές αιμορραγίες (αυξήσεως κατά 50%), μεγαλύτερη ΒΘ (αυξήσεως κατά 26%, 2,9 ± 0,8 mm, p <0,001), μεγαλύτερη απώλεια πρόσφυσης (αυξήσεως κατά 173%, 2,6 ± 1,7 mm, p <0,001), και περισσότεροι από τους λευκούς δόντες (αυξήσεως κατά 29%, 7,2 ± 4,4 mm, p <0,01) σε σχέση με τους μάρτυρες.


Table 1. Studies showing an association between periodontal disease and rheumatoid arthritis

<table>
<thead>
<tr>
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AL: attachment loss, N: number, PD: pocket depth, RA: rheumatoid arthritis

The most severe bone loss was used to classify each patient in this study was substantially older than the populations of most other studies. Therefore, patients with periodontal disease may have already lost some teeth with advanced disease, potentially contributing to the increased tooth loss in the RA population.

Kässer et al. (1997) evaluated 50 RA patients and 101 controls matched for age, sex, smoking status, and oral hygiene. The authors reported that patients with long-standing active RA (mean ± SD: 13 ± 8 years) who were receiving treatment with disease-modifying antirheumatic drugs (N = 46), corticosteroids (N = 38), or nonsteroidal anti-inflammatory drugs (N = 43) had a higher rate of gingival bleeding (increased by 50%), greater PD (increased by 26%, 2.9 ± 0.8 vs 2.3 ± 0.4 mm, p <0.001), greater attachment loss (increased by 173%, 2.6 ± 1.7 vs 0.95 ± 0.7 mm, p <0.001), and more missing teeth (increased by 29%, 7.2 ± 4.4 vs 5.6 ± 4.4 mm, p <0.01) compared with controls.

Finally, Mercado et al. (2001) examined 65 consecutive patients attending a rheumatology clinic for their levels of periodontitis and RA. No differences were noted in plaque accumulation or bleeding on probing between the control and RA groups. Periodontal evaluation included PD and CAL measurements, missing teeth, and radiographic bone loss. The most severe bone loss was used to classify each patient as follows: P0 (no bone loss), P1 (mild bone loss), P2 (moderate bone loss corresponding up to 1/2 of the root length), and P3 (severe bone loss). The percentage of RA patients in the P0 to P1 category was 30.82% vs 66.18% (p <0.05) in the control population.
More patients were in the P2/P3 bone loss category in the RA population, 69.2 vs 33.8% (p < 0.05). When analyzed with logistic regression, RA patients were twice as likely to have moderate to severe bone loss (OR 2.27, 95% CI 1.1-4.6).

A number of studies have also indicated that periodontitis may contribute to the severity of RA. Periodontal treatment with scaling and root planing has been shown to reduce signs and symptoms of RA, including disease activity scores (DAS) and ESR in multiple studies (Ribeiro et al. 2005, Al-Katma et al. 2007).

As illustrated by these studies, there has been great variability in the selection criteria, definition of periodontitis and RA, and selection of controls throughout the study populations; thus, it is difficult to draw conclusions about the level of association between the two conditions. However, the majority of studies conducted to date report a level of association between periodontitis and RA with an OR range of 1.8-6.0 (de Pablo et al. 2009). Future larger scale studies are needed to further characterize this association. Such studies should also document additional parameters, such as years since diagnosis of RA, inflammatory indices of disease activity, severity of disease for both conditions, and serological markers, all of which may influence the level of association. Future studies should also investigate possible common genetic and environmental parameters (such as smoking and HLA-DR loci), which may contribute to the development of both conditions.

This association or coexistence between the conditions could arise either because one is contributing to the etiology and pathogenesis of the other or because similar environmental or genetic parameters govern the manifestation and progression of both. Although many common factors may influence both conditions, interestingly, unlike RA, periodontal disease is not seen primarily in the female population. On the contrary, epidemiological studies indicate a greater prevalence and severity of periodontal disease in men (Albandar 1990, Hyman and Reid 2003). The academic community is currently investigating possible contributions of periodontal disease to the pathogenesis of RA while keeping in mind that similar patterns of genetic susceptibility and common environmental factors such as tobacco use could contribute to both conditions. In addition, symptoms of advanced RA, such as lack of manual dexterity, malaise, and hospitalizations, may influence oral hygiene and level of dental care, rendering patients susceptible to oral diseases.
The peptidyl arginine deiminase (PAD) is a recognized major pathogen of the periodontal lesion (Travis et al. 1997). This feature is the capacity of deiminating arginine in fibrin found in the inflammatory exudate to neutralize the fibrinopeptides A and B (Travis and Mavragani 2007). The PAD suggests that infection with this microorganism is a possible etiologic/pathogenic link between periodontal disease and rheumatoid arthritis. Porphyromonas gingivalis is a well-identified periodontal pathogen and PAD is a recognized major periodontal pathogen (Travis and Mavragani 1997).}

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**Primary Language:** Greek

**Translated to English:**

The peptidyl arginine deiminase (PAD) is a recognized major pathogen of the periodontal lesion (Travis et al. 1997). This feature is the capacity of deiminating arginine in fibrin found in the inflammatory exudate to neutralize the fibrinopeptides A and B (Travis and Mavragani 2007). The PAD suggests that infection with this microorganism is a possible etiologic/pathogenic link between periodontal disease and rheumatoid arthritis. Porphyromonas gingivalis is a well-identified periodontal pathogen and PAD is a recognized major periodontal pathogen (Travis and Mavragani 1997).
κτηριστικό αυτό είναι ιδιαίτερα αξιοσημείωτο αφού οι κτιριολιμωμένες παραλλαγές των α- και β-αλυσίδων της υικες έχουν προταθεί ως «αυτοαντιγονικό» στάχος στη ρεμεταοιδική άρθρωση (Liao και συν. 2009).

Ο πιθανός ρόλος του P. gingivalis στη ΡΑ επιβεβαιώνεται επίσης από μελέτες που υποδεικνύουν ότι οι τίτλοι αντισωμάτων κατά του P. gingivalis είναι σημαντικά αυξημένοι σε ασθενείς με ΡΑ και συσχετίζονται σημαντικά με τους ισότυπους των αντι-CCP αντισωμάτων (κυρίως αντι-CCP-IgM και -IgG2 υποκατηγορίες) που είναι ειδικοί στη ΡΑ (Μοιν και συν. 2006). Η συσχέτιση της ανοσολογικής απάντησης με το P. gingivalis και της συγκέντρωσης των αντισωμάτων της υποκατηγορίας αντι-CCP-IgG2 ίσου είναι ιδιαίτερα αξιοσημείωτο αφού η υποκατηγορία IgG2 αντιρεοπετυσεί την επικρατούσα IgG orο στην απάντηση έναντι της λοίμωξης από P. gingivalis (Whitney και συν. 1992).


Με βάση τα μέχρι τώρα διαθέσιμα δεδομένα, φαίνεται πιθανό ότι το P. gingivalis επηρεάζει την πρώιμη προ-αρθρική φάση της ΡΑ και ίσως βοηθεί στην εγκατάσταση ενός αυτοαισθήματος υποβάθρου όπου διαταράσσεται η ανοχή των T- και B-κυττάρων, επιτρέποντας σε ένα μεταγενέστερο συμβάν αυτοάνοσου υπόβαθρου όπου διαταράσσεται η ανοχή των ασθενών.

Η φλεγμονώδης οστική απώλεια στη ΡΑ και στις περιοδοντικές νόσους, Υπάρχουν κοινές θεραπευτικές προσεγγίσεις; αν και μπορούν να υπάρχει ουσιαστική σχέση μεταξύ της περιοδοντικής νόσου και της ΡΑ, οι δύο αυτές καταστάσεις συνδέονται επίσης με ομοιότητες ως προς την παθογέμνηση και την εκδήλωση.

Inflammatory bone loss in RA and periodontal disease: Are there common treatment modalities?

Although there could be a causal or noncausal association between periodontal disease and RA, the two conditions are also linked by similarities in their pathogenesis and presentation (Mercado et al. 2003, Herman et al. 2008, Smolik et al. 2009). Key features shared between the two conditions are the mechanisms involved in inflammatory-induced tissue and, in particular, bone degradation. During the course of different inflammatory diseases such as RA, psoriatic arthritis, and periodontal disease (Moutsopoulos and Madianos 2006), a confined set of common inflammatory pathways triggers the process of local bone destruction (Herman et al. 2008). Since the early 1970s, accumulating evidence has indicated that the immune and skeletal system share several factors, such as cytokines, transcription factors, and receptors. Furthermore, immune cells and osteoclasts are derived from the same hematopoietic precursor cells. Therefore, there is compelling evidence that these two systems influence each another under both physiological and pathological circumstances.

A clear example of the interrelated nature between the two systems comes from autoimmune and chronic inflammatory diseases such as RA and periodontal disease, in which prolonged and enhanced activation of the immune system leads to massive bone destruction. During inflammation, the balance between bone formation and bone resorption is disturbed in favor of especially noteworthy because citrullinated variants of the α- and β-fibrin chains have been proposed as target “autoantigens” in the rheumatoid joint (Liao et al. 2009).
η μεσολαβητικοί προαγούν την οστική απώλεια μέσω του RANKL (McInnes and Schett 2007, Cochran 2008).

Αντιφλεγμονώδεις θεραπείες έχουν εφαρμοστεί εκτεταμένα στη ΡΑ, σε μια προσπάθεια ελέγχου της χρόνιας καταστροφικής φλεγμονής. Η ευρεία χρήση των μη στεροειδών αντιφλεγμονωδών στην ΡΑ, σε μια προσπάθεια ελέγχου της χρόνιας καταστροφικής φλεγμονής, όπως είναι οι NSAIDs, είναι δυνατή μετά τα δεκαετίες (Kohler και Milstein 1975) και σύντομα έφερε επανάμονοκλωνικά αντισώματα και οι πρωτεΐνες σύντηξης. Η τεχνολογία στην ανάπτυξη στοχευμένων βιολογικών θεραπειών, όπως τα monoclonal antibodies and fusion proteins. Monoclonal antibody technology was first invented more than three decades ago (Kohler and Milstein 1975) and quickly revolutionized the management of malignancies in the context of stem cell and solid organ transplantation, rheumatologic disorders, autoimmune disease, inflammatory bowel disease, infections, and atopic disorders (Shirota et al. 2008).
The most commonly used “biologics” interfere with the action of cytokines, which are soluble mediators of inflammation. Cytokines exert their action by binding to cell surface receptors. The action of cytokines can be blocked by binding the soluble cytokine or preventing its binding to its cognate receptor. The former can be achieved by using monoclonal antibodies against the cytokine or by using a decoy soluble receptor, which will bind to the cytokines in a manner similar to that of cell surface receptors, thereby reducing the levels of free, biologically active cytokines. All of these options have already been successfully used in the treatment of RA. Of three anti-TNF agents approved in the United States, two (infliximab and adalimumab) are monoclonal antibodies, whereas the third, etanercept, is a soluble receptor fusion protein (Keystone 2006, Scott and Kingsley 2006). TNF blockade has been shown not only to reduce clinical symptoms of inflammation, but also to suppress progression of inflammatory bone destruction. Research has identified numerous pathogenetic pathways in RA that represent potential targets for biological therapy beyond the already successful anti-TNF inhibitors (Keystone 2006, Scott and Kingsley 2006). Additional members of the proinflammatory cytokine network,
Εικόνα 2: Γενετικοί και περιβαλλοντικοί παράγοντες επηρέαζουν την ανάπτυξη τόσο της ρευματοειδούς αρθρίτιδας, όσο και της περιοδοντικής νόσου, οδηγώντας στη σύζευξη των κοινών χρόνιων φλεγμονώδων μηχανισμών και τελικά στην οστική καταστροφή. IL: ιντερλευκίνη, RANK: ενεργοποιητής του υποδοχέα του πυρηνικού παράγοντα-κ, RANKL: συνδέτης του RANK, TNF: οστοκαρστικός παράγοντας.

Figure 2: Genetic and environmental factors influence the development of both rheumatoid arthritis and periodontal disease, leading to the engagement of common chronic inflammatory pathways and ultimately to bone destruction. IL: interleukin, RANK: receptor activator of nuclear factor-kappa, RANKL: RANK ligand, TNF: tumor necrosis factor.
IL-17 or anti-IL-23, isos, can be important players in the pathogenesis of disease, but may also lead to the development of therapeutic interventions in this locally destructive disease (Giannobile 2008, Shirota et al. 2008).

**Conclusions**

Although the extent and etiology of the association between periodontal disease and RA continue to be investigated, it has become clear that similar biological mechanisms govern the immune-mediated tissue destruction in both conditions. This realization brings periodontal diseases to the forefront of biomedical research as a model disease for the understanding of the communication between the immune and skeletal systems and for the study of pathways that lead to chronic inflammation, impaired immune regulation, and defective tissue remodeling. The accessibility of the oral tissues and the high prevalence of this chronic inflammatory condition, which affects more than 10% of the general population, renders it an ideal study model. Conversely, the advances already made in the field of research and therapeutics in RA may likely be applicable to periodontal disease and should be seriously evaluated.

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