



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

## INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

<http://doi.org/10.5281/zenodo.2577331>

Available online at: <http://www.iajps.com>

Review Article

### THE MODERN CONCEPT OF THE RELATIONSHIP OF ETIOLOGY AND PATHOGENESIS ON THE COURSE OF PERIODONTAL DISEASES IN PATIENTS WITH RHEUMATOID ARTHRITIS - A REVIEW OF THE LITERATURE

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**Abstract:**

*Analysis of the literature showed significant similarities in the etiology and pathogenesis of periodontitis and RA, in clinical and laboratory characteristics, as well as the significance of the relationship of these pathologies in the economic well-being of the country. The economic consequences of RA, leading to a permanent lesion of the musculoskeletal system, are very significant. RAs are one of the main reasons for the temporary disability of the working population in Russia. Its medical and social significance is due, firstly, to progressive dysfunction of the joints, which leads to a significant reduction in the quality of life of patients; secondly, the defeat of people of working and professional age. Natural is the fact of the deterioration of all vital characteristics of RA patients in combination with periodontal pathology. In this regard, it is relevant to study the dental status, identify its features in RA patients to improve the algorithm for diagnosing and treating periodontal diseases, as well as the rationale for making clinical recommendations for the diagnosis and treatment of rheumatoid arthritis medical measures for diagnosing the disease, the state of medical services: taking primary, dispensary (examination, consultation) and preventive (examination, consultation) of a dentist and updating the order of the Ministry of Health Of the Russian Federation "On approval of the standard of primary health care in rheumatoid arthritis" dated 12.24.2012, №1470n.*

**Key words:** *periodontitis, rheumatoid arthritis, bone mineral density of the jaws*

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*Please cite this article in press S. Tarasenko et al., The Modern Concept Of The Relationship Of Etiology And Pathogenesis On The Course Of Periodontal Diseases In Patients With Rheumatoid Arthritis - A Review Of The Literature., Indo Am. J. P. Sci, 2019; 06(02).*

## INTRODUCTION:

Inflammatory and destructive periodontal diseases are a serious public health problem. They reduce the quality of life, adversely affect aesthetics, lead to disability and loss of teeth, have financial consequences and are chronic diseases with potential negative health effects [1].

Most scientists believe that the leading role in the development of periodontal pathology belongs to the microbial factor. Inflammatory diseases of periodontal tissues, as a rule, are accompanied by oral dysbiosis, the severity of which corresponds to the degree of periodontal damage. Moreover, against the background of pronounced growth of pathogenic and conditionally pathogenic microorganisms, the concentration of representatives of normal microflora decreases. Various microorganisms colonize the glycoprotein-containing layer (dental plaque) above and below the gum edge to form over and subgingival layers of plaque. Supragingival plaque is primarily populated by *Streptococcus Sanguis*, *Streptococcus oralis*, *Streptococcus mutans*, *Actinomyces naeslundii* and *Actinomyces odontolyticus*. Then secondary colonizers join, for example, *Fusobacterium nucleatum*, and soon a conglomerate consisting of millions of gram-positive, gram-negative bacteria and cocci forms, forming a biofilm.

Over time, the microflora of the region of the attached gum moves from predominantly gram-positive to primarily gram-negative aggregates, including a larger number of obligate, anaerobic, gram-negative microbes. Currently, about 500 species of bacteria are isolated from the periodontal pocket, but only 12 of them are associated with the etiology of periodontitis. These pathogens (genotypes of bacteria) of periodontitis are called marker microorganisms. Their detection and analysis is difficult, but important in assessing the clinical status of periodontal disease and further prognosis [2].

Gex. evaluated the subgingival microbiome with healthy periodontal disease and pathology using pyrosequencing of the 16S gene of ribosomal RNA in patients with periodontitis and in the control group. *P. gingivalis*, *Porphyromonas endodontalis*, *Fusobacterium nucleatum*, *Prevotella nigrescens*, *Treponemadenticola*, *Treponema medium* and *Tannerella forsythia* were found in periodontal pockets [3].

Professor A. Grudyanov co-authors found that among the studied microorganisms, growth leaders with the development of periodontitis are *P. gingivalis*, *P. intermedia* and *T. forsythensis*, demonstrating a steady increase in the relative content in the total bacterial

mass by more than 100 times. At the same time there is a gradual decrease in the relative content of *T. denticola*. The number of *A. Actinomycetem comitans* does not have significant differences in healthy individuals and in patients with varying severity of periodontitis. They found that the profile of periodontopathogens of the microbial biocenosis of the periodontal pocket changes significantly during the development of periodontitis: in practically healthy individuals, the total bacterial mass index is about 10<sup>6</sup> equivalent genes per reaction tube, while for patients with mild CGP, this figure is approximately the order of magnitude, reaching 10<sup>7</sup>, and in patients with moderate CGP and severe CGP - is already about 10<sup>8</sup> [4].

The outcome and course of the infection process in the periodontal disease can be predetermined not only by the virulence of the microbes, but also by the genetic polymorphism of the human body. The study of HLA and IL - 1 gene polymorphism may play an important role in identifying susceptibility and predicting the course of inflammatory periodontal diseases. The IL1 gene became one of the first genes for which they showed an association of single nucleotide polymorphisms with inflammatory periodontal diseases. HLA genes are characterized by high polymorphism, which ensures human survival in an infectious environment. It has been established that they are markers of diseases in which the immune system plays a key role in the pathogenesis, and the development of such diseases is 70% determined [5]. A special role in the development and maintenance of chronic inflammation is played by matrix metalloproteinases (MMPs) - Zn<sup>2+</sup> + and Ca<sup>2+</sup> - dependent endopeptidases - enzymes of the catabolism of most extracellular matrix proteins at various stages of the inflammatory process. MMP along with other extracellular proteinases are able to carry out such processes as coagulation, the implementation of the immune response, physiological tissue restructuring. They are secreted by different cells: neutrophils, fibroblasts, epithelial cells, macrophages, vascular endothelial smooth muscle cells, osteoblasts, etc. The same cell can synthesize different MMPs. MMPs act as a key mediator of tissue damage in periodontitis, in dentin erosion. The reason for the increase in the activity of MMPs in this pathology is the imbalance between MMPs and their inhibitors, TIMP. Gelatinases are believed to destroy periodontal tissues during periodontitis, which is confirmed by the discovery of their increased amount in the gingival fluid, which decreases during treatment [6]. In clinical studies it has been proven that MMP 8 is a marker of chronic periodontitis, which causes the destruction of alveolar bone, a violation of neutrophil secretion. An

increase in the number of MMPs 25 is observed in the gingival fluid in gingivitis, chronic and aggressive periodontitis, in contrast to healthy individuals [7].

Tobacco smoking is one of the risk factors for periodontitis, it suppresses the vascular response, usually concomitant to gingivitis and periodontitis, and reduces the body's immune response. Nicotine causes the destruction of periodontal tissues, regulating the release of cytokinin, which probably explains the less pronounced inflammation and bleeding of the gums in smokers [8].

Thus, the development of periodontal disease is influenced by numerous factors: impaired microbiocenosis in the mouth, neuroregulatory disorders, changes in hemodynamics, connective tissue metabolism, mineral metabolism, vitamin deficiency, poor nutrition, traumatic occlusion anomalies, and bad habits [9].

Rheumatoid arthritis is an autoimmune rheumatic disease of unknown etiology, characterized by chronic erosive arthritis, as well as damage to internal organs. RA occurs in 0.5–2% of the adult population and is heterogeneous in disease activity, the degree of bone destruction and the development of extra-articular (systemic) manifestations of the disease. The pathogenesis of RA is based on two closely interrelated processes: antigen-specific activation of CD1 + T-lymphocytes by the Th1 type, characterized by the synthesis of interleukin (IL) 2, interferon  $\gamma$  (IF $\gamma$ ) and IL17, as well as the emergence of an imbalance between the hyperproduction of proinflammatory and anti-inflammatory cytokines with the predominance of the synthesis of the former over the latter. When RA in the synovial membrane, the number of activated B and T lymphocytes, mast cells, macrophages, providing a persistent course of chronic inflammation, significantly increases. Novikov A.A. with co-authors found that the functioning of the "cytokine network" in RA is determined by the complex interactions between its two links: pro-inflammatory and anti-inflammatory. As the main proinflammatory cytokines involved in the pathogenesis of the disease, TNF  $\alpha$ , IL 6 and 1 should be distinguished, which are responsible for the progression of tissue damage, as well as playing a key role in the development of systemic manifestations in RA [10].

The phenomenon of apoptosis is also considered by many authors as one of the leading links in the pathogenesis of RA. This is a disease in which the interaction of the genetic component and environmental factors determines not only the development of the disease, but also its pronounced clinical polymorphism. Studies have shown that

laboratory markers such as antibodies to cyclic citrullinated peptides (ACCP), antibodies to modified citrullinated vimentin, rheumatoid factor — antibodies of the IgM class (RF IgM) — more and C-reactive protein and HLA-DRB1 alleles (SE +) - to a lesser extent, are not only predictors of RA development, but also prognostic markers of destructive joint damage [11].

Undoubtedly, both scientific and practical interest is the fact of the interaction between the ASTsP and SE, originally discovered by Swedish and Dutch scientists, and then confirmed in a number of other foreign studies. It should be noted that a number of studies have established an interrelation between the carrier of SE, the production of ASTsP and smoking [12]. Scientists from many countries of the world in the formation of somatic pathology play an important role odontogenic infection. Periodontal pathogens and their products, as well as inflammatory mediators produced in the periodontal tissue, can enter the bloodstream, causing systemic effects and contribute to the development of systemic diseases. Based on this mechanism, chronic periodontitis has been proposed as a risk factor for not only cardiovascular diseases associated with atherosclerosis, but also bacterial endocarditis, RA, etc. [13].

In the presence of RA, periodontal disease occurs with significant impairment of microcirculation in periodontal tissues. In turn, foci of chronic infection in the mouth can become a triggering and supporting factor in the development of systemic disease. Patients with severe periodontal disease have a higher risk of developing RA. The progression of the underlying disease leads to the rapid development of the inflammatory process in the periodontal tissues, oral mucosa, salivary glands. Clinical supervision by a dentist in patients with RA is both an important preventive factor and a social rehabilitation measure that contributes to the improvement of the quality of life of these patients [14].

Mitronin A.V. with Avakova D.R. It is believed that the manifestations of RA and osteoporosis in the maxillofacial region should be considered as part of a general pathological process with a particular clinical picture, which is currently poorly understood. In their study, they found that in patients with RA, the level of hygiene decreases as the underlying disease progresses [15].

Conducted in various countries of the world - Finland, Norway, Germany, Australia - studies that determined the relationship between periodontitis and RA showed that patients with RA had a significantly higher

prevalence of periodontal diseases, a greater degree of attachment loss, and frequency of tooth loss compared with patients without arthritis [16]. When studying this problem among the population of Belarus, periodontal lesions were found in 93.2% of patients with RA.

The relationship between RA and symptomatic periodontitis is explained by the fact that they are chronic inflammatory diseases of the connective tissue, and the mechanisms of its destruction are the same. Most studies of rheumatoid arthritis focus on the role of *P. gingivalis*. For the first time, a complex hypothesis of the pathogenesis of rheumatoid arthritis with the participation of this bacterium was already formulated in the 21st century and suggested that the humoral immune response to *P. gingivalis* provides an incentive for the development of synovial inflammation. Studies conducted in various areas have confirmed the association of periodontal diseases, *P. gingivalis*, ACCP, and rheumatoid arthritis [17].

Bulgarian scientists M. Pannovek and E. Firkova, based on the fact that the pathogenesis of RA and CP is a series of similar interconnected immune disorders, conclude that the creation of new therapeutic drugs for RA and CP will have a direction on restoring the imbalance between pro-inflammatory and anti-inflammatory cytokines. The therapeutic effect is to suppress pro-inflammatory cytokines and destructive proteases. With the help of bioactive molecules, gene therapy and metalloproteinase inhibitors, it is possible to control both chronic inflammatory diseases [18]. Foreign scientists have shown that the treatment of periodontitis improves the patient's condition in severe rheumatoid arthritis and reduces the pro-inflammatory laboratory parameters of arthritis activity. Patients with rheumatoid arthritis and active periodontitis were also less susceptible to treatment with TNF- $\alpha$  inhibitors, highlighting the potential benefits of treating periodontal disease in TNF-refractory patients [19].

Taranova L.G. with co-authors found that the dynamics of the pathological process in chronic periodontitis in combination with rheumatoid arthritis is closely related to the state of the immune system, as evidenced by a decrease in CD3, CD4, indicators of phagocytic activity of neutrophils, an increase in CD8, immunoglobulins A, M, G and circulating immune complexes. The involvement of immune mechanisms has been established in the formation of chronic periodontitis in patients with rheumatoid arthritis. The differences in immunological parameters depend on the age of the patients, the duration of the disease and the activity of the inflammatory process [20].

Grinin V.M. with co-authors, studying the clinical features, the prevalence and intensity of dental caries, periodontal pathology in RA patients, that at 100% prevalence in RA patients with generalized forms of periodontal disease, moderate or severe periodontal disease predominated (49.4% and 45.5%) [14]. The hygienic and clinical state of periodontal tissues in these patients was worse than that of somatically healthy individuals. Studies conducted in various areas confirm the association of periodontal disease, *P. gingivalis*, ACCP, and rheumatoid arthritis [17].

Thus, the interaction and interdependence of somatic and dental pathology reflects their comorbidity. In this regard, the development of interdisciplinary interaction between dentists and doctors of other specialties, aimed at developing common approaches to the treatment and management of patients with somatic and dental diseases, becomes an urgent problem of modern medicine [21].

Scientists from the Republic of Belarus conducted research involving 78 dental patients, which were divided into three groups: 1st group - patients with RA - 23 people, 2nd group - patients with preclinical stages of RA - 34 people, 3rd group - patients with hereditary predisposition (relatives of patients with rheumatoid arthritis) - 21 people. In the total sample, patients had an unsatisfactory level of oral hygiene by OHI-S index. In the group of patients with RA, the hygiene index OHI-S was  $2.1 \pm 0.78$ , which corresponds to unsatisfactory hygiene. In the group of patients with preclinical stages of rheumatoid arthritis, the OHI-S hygiene index was  $2.3 \pm 0.87$ . In the hereditary predisposition group, the OHI-S hygiene index was  $1.54 \pm 0.91$ , which corresponds to satisfactory hygiene. In the total sample, patients had a moderate degree of inflammation of the gums using the GI index. In the group of patients with RA, the gingival index GI was  $1.9 \pm 0.81$ . In the group of patients with preclinical stages of rheumatoid arthritis, the gingival index GI was  $2.2 \pm 0.6$ . In the group of patients with hereditary predisposition, the gingival index GI was  $1.45 \pm 0.37$ . *P. gingivalis* DNA in the total sample was found in 24 patients out of 40 examined (60%). In the prevailing number of cases, *P. gingivalis* DNA was detected in persons suffering from chronic periodontitis. When analyzing the detectability of *P. gingivalis* DNA in close relatives, the inheritance of *P. gingivalis* DNA by older children was found in 100% of cases [22].

Numerous studies indicate a correlation between the severity of inflammatory periodontal diseases and the degree of loss of bone mineral density (BMD) [23]. Foreign scientists tried to assess the relationship between bone destruction of the wrist and periodontal



rheumatoid arthritis [24].

Periodontal capillaroscopy in RA patients assessed the visibility, direction and tortuosity of capillaries, the presence of possible hemorrhages, the average size of capillary loops and their apparent number per unit area. In patients with RA, a reduced transverse size of the capillaries could be detected in combination with an increase in the number and length of capillaries [25].

Analysis of the literature showed significant similarities in the etiology and pathogenesis of periodontitis and RA, in clinical and laboratory characteristics, as well as the significance of the relationship of these pathologies in the economic well-being of the country. The economic consequences of RA, leading to a permanent lesion of the musculoskeletal system, are very significant. RAs are one of the main reasons for the temporary disability of the working population in Russia. Its medical and social significance is due, firstly, to progressive dysfunction of the joints, which leads to a significant reduction in the quality of life of patients; secondly, the defeat of people of working and professional age. Natural is the fact of the deterioration of all vital characteristics of RA patients in combination with periodontal pathology. In this regard, it is relevant to study the dental status, identify its features in RA patients to improve the algorithm for diagnosing and treating periodontal diseases, as well as the rationale for making clinical recommendations for the diagnosis and treatment of rheumatoid arthritis medical measures for diagnosing the disease, the state of medical services: taking primary, dispensary (examination, consultation) and preventive (examination, consultation) of a dentist and updating the order of the Ministry of Health Of the Russian Federation "On approval of the standard of primary health care in rheumatoid arthritis" dated 12.24.2012, №1470n.

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