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Interrelation of the parodontium diseases with endocrine diseases (according to the literature)

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The study of the mechanisms of the pathogenesis of parodontal disease continues to be an urgent problem of modern dentistry. This is due to the high level of inflammatory and dystrophic-inflammatory forms of the disease among the patients in various populations, the development of a progressive course in those with concomitant systemic pathology [2,5,17,31].

It has been established that the scientific concept of prevention and treatment of periodontal diseases is based on the proven role of correction of risk factors of their occurrence: elimination of local harmful factors, normalization of metabolic, microcirculatory, immunological and endocrine disturbances. [5,15,23,41].

Hormonal imbalance has been shown to play a leading role in the pathophysiology of systemic changes and to cause mutually aggravating pathological conditions [9, 36].

Numerous clinical and experimental studies have established that persons with diabetes mellitus (DM) in most cases have dental pathology [1,30].

According to estimates of the International Diabetes Mellitus Federation, about 380 million people in the adult population are currently suffering from diabetes. In recent years there has been an increase in its prevalence and incidence, especially in developed countries, where this disease accounts for up to 6% of the population. This figure has a steady tendency to increase, which is primarily manifested in the age groups over 40 years old. Every 10-15 years, the number of patients with diabetes doubles [29]. This disease is characterized by all types of metabolic disorders and generalized lesions of small blood vessels, microangiopathy.

Angiopathies have been proven to play a role in the pathogenesis of parodontal disease among those with DM patients. Since parodontosis is characterized by various vascular disorders that in many ways resemble diabetic angiopathy, proving the presence of the latter in periodontitis is not easy. The starting point of diabetic microangiopathies is impaired carbohydrate metabolism disorder, which determines the functional and structural integrity of the vascular basal membrane [38].

Hormone-dependent changes in the immune system are also of particular importance. Thus, immune response abnormalities have been identified in DM, resulting in decreased neutrophil functional activity and a hyperreactive monocytic response, resulting in periodontal damage [14].

Current data indicate that among children with DM parodontal disease occurs 2-3 times more frequently than among adults. Studies conducted by Khomenko L.O. (2008) demonstrated a high prevalence of gingivitis (about 70%) among this contingent of children. Children 3-17 years old with I DM have disorders of bone metabolism, bone tissue mineralization, and pathological processes in the periodontium. The most significant differences in these disorders compared to healthy children were observed in the early preschool age (3-6 years) [30].

Clinical and dental studies [24] have shown that parodontal diseases occur more frequently among DM patients - 94%. In the majority of cases, inflammatory forms of periodontal tissue lesions occur -86%. X-ray examination conducted in people with diabetes revealed low mineral saturation of the lower jaw bone tissue. Particularly pronounced changes were noted in the lower alveolar ridge. The authors also note a reliable correlation between the decrease in bone mineral density of the jaw and the duration of DM.

Conducted basic research shows that metabolic disorders and their degree of activity among patients with 2 DM have a causal relationship with the occurrence and development of dystrophic and inflammatory periodontal diseases [3,8,18]. The development of various forms of periodontal diseases among patients with 2 DM is determined by the complex of pathological conditions, the time of their occurrence and their degree of severity [8]. When examining patients with the subcompensated form of type 2 DM, an inactive course of generalized parodontitis was registered in most cases. A characteristic feature of metabolic metabolism in this group of patients was a combination of both lipid storage and carbohydrate metabolism disease. Among decompensated patients with 2 DM, metabolic disorders caused a progressive inflammatory and destructive process in the parodontium. Most patients showed rapidly progressing periodontitis with a more aggressive pathological process in the periodontium. As noted by Bobyrev and others (2008), periodontitis occurs with the same frequency in both type 1 and type 2 of diabetes, and its more severe manifestations are characteristic of type 2 diabetes - moderate 31.3%, severe - 50%.. The weight of clinical symptoms of parodontal tissue lesions corresponds to the depth of metabolic disturbances. If in mild and moderate severity periodontitis of type 1 DM the activation of free radical oxidation (FRO)-lipids on the background of moderate disturbance of lipid metabolism is in the foreground, then in type 2 DM the disturbance of lipid metabolism over activation of FRO-lipids processes. These differences are smoothed out among severe periodontal symptoms in type 1 DM and type 2 DM patients.

When studying cytokine profile parameters in the oral epithelium of children with 1 DM taking into account the existing metabolic disorders, an imbalance in the system of cytokine regulation in children was found [18]. Molecular genetic study of relative mRNA levels of proinflammatory cytokines IL-1 β and -17A and anti-inflammatory IL-10 in the oral epithelium of children revealed that against the background of DM the relative mRNA levels of IL-1 β and IL -17A were significantly increased and the mRNA expression level of IL-10 was low. Studies in the IL1B, IL4 and IL6 genes demonstrated a relationship with concomitant periodontitis and type 2 diabetes, increasing evidence of a common genetic component between these diseases and contributing to the understanding of their common pathogenic mechanisms. [39].

It has been proved that among patients with 2 DM there is a reliable relationship between the indicators of immune activation by cytokines and clinical manifestations of the disease. During the latent course of the disease there were immune dysfunctions characterized by moderate levels of hyperproduction and serum concentrations of IL-1β, IL-2, IL-4, IL-6, IL-10. Against the background of the progressive course, a significant increase in the production level of IL-1β, IL-8, TNF-α and a decrease in the serum concentration of IL-2, IL-4, IL-10 were found. [8].

Also, some authors believe that the susceptibility and severity of periodontal disease is exacerbated in DM, with the effect on the disease process being inversely proportional to the level of glycemia. Experimental studies suggest that type 1 DM and type 2 DM increase inflammation in periodontal tissues, impair new bone formation and increase RANKL (ligand-receptor system RANKL/RANKL/OPG - a key link in bone tissue homeostasis, directly regulating osteoclast differentiation and osteolysis) expression in response to a bacterial response. High levels of glucose, reactive oxygen species and glycation end products end up in the periodontium of diabetic patients and lead to increased expression of inflammatory cytokines such as tumor necrosis factor and interleukin-1. In addition, animal studies suggest that there are several types of cells affected by diabetes in periodontal tissues, including leukocytes, vascular cells, mesenchymal stem cells, fibroblasts of the periodontal connection, osteoblasts and osteocytes [40]. Patients with type 2 DM have a high risk of rapid development of chronic periodontitis (CP). The actual presence, large number and bactericidal action of immune cells causes increased inflammation caused by the antigen, which contributes to the development of both diseases. [42].

Steroidal sex hormones such as estrogen and estradiol are known to affect bone mineral metabolism. Other hormones responsible for bone metabolism include progesterone, testosterone, androstenedione [44]. Among the listed hormones, estrogens, progesterone and testosterone are more related to the mechanism of periodontal disease pathogenesis. [37,49].

The endocrine dependence of productive forms of inflammation in the parodontium during pregnancy is evidenced by the research of A.V. Borisenko, A.A. Sheker (2008). Thus, the examined pregnant women with obstetric pathology, overgrown against the background of hormonal imbalance, namely, when the level of estrogen in pregnant women increased against the background of progesterone deficiency, the cytological study of the gingival and periodontal pockets contents showed inflammatory smears with proliferation signs.

At present, a direct connection between the natural decline in ovarian function and changes in a woman's body has been established. When the endocrine function of the ovaries decreases, the process of osteogenesis in the body, including the periodontium, slows down [25], and the decrease in estrogen levels contributes to the active progression of bone tissue destruction. [10].

Significant changes in periodontal tissues are noted among menopausal women. A decrease in estrogen levels leads to inhibition of osteoblast function, increased sensitivity of bone tissue receptors in osteoresorptive action of parathyroid hormone.

Estrogen deficiency, typical for the menopausal period, leads to accelerated bone remodeling, an imbalance between bone resorption and formation, accelerated loss of bone mass, osteoporosis and its complications, increases the risk of parodontal disease [26].

Bogdan A.S. (1999) proved that among premenopausal women, generalized periodontitis had a chronic course with marked atrophic changes and deterioration of the structural and functional state of the periodontium. The initial phase of menopause was characterized by estrogen deficiency and increased bone resorption. One of the characteristics of these disorders in early menopause in women is changes in biomarkers of hormonal disorders and endothelial dysfunction in the systemic

blood flow and disturbed balance of o and anti-inflammatory cytokines in Jasenewo fluid. It has been established that high concentration of intercellular mediators of inflammation in Jasenewo fluid in patients with inflammatory periodontal diseases is the cause of periodontal pocket, alveolar bone dystrophy, changes in the composition and properties of oral fluid. Changes in hormonal regulation among menopausal women affect the decrease in estradiol levels, increase in endothelial vascular growth factor and endothelin-1 indicators, which complicates the course of periodontal disease. In addition to participation in the regulation of vascular tone, ENDOTELIN participate in bone remodeling. According to the authors, the increased density of gingival epitheliocytes immunopositive to endothelin-1 can be a diagnostic criterion of the severity of periodontal pathology. As noted by the author, the increased concentration of proinflammatory cytokines (MCP-1 and IL-8) in the Jasenie fluid among menopausal women is the result of microcirculatory disorders and inadequate immune response to microflora. [25].

Studies conducted by Beloklitskaya G.F. and Pogrebniak V. (2004) to study the structure of periodontal diseases in women with estrogen deficiency that accompanies physiological and surgical menopause, complicated by post-castration syndrome found a direct link between the estrogenic saturation of oral fluid and the state of periodontal tissues. Thus, no radiological changes in the bone structure of the jaw were found among women of reproductive age. The examined women in the period of surgical menopause complicated by post-castration syndrome had the saturation of oral liquid with estrogens and in the majority of cases the genralized periodontitis of different severity was diagnosed.

Estrogen deficiency in postmenopause is well-known risk factor for various diseases, including bone tissues [50]. Assessment of the state of bone tissue of the alveolar processes of the jaws in postmenopausal women against the background of anticoagulants and β-adrenoblockers revealed venous stasis and proliferation in the periodontal tissues, according to the authors [10], leads to the decrease in the density of the entire skeleton and jaws in particular, as it indirectly causes disruption of osteocalcin synthesis - the protein around which calcium crystallizes. A study of changes in circulating levels of two matrix metalloproteinases, MMP-2 and MMP-9 in the postmenopausal period, has been associated with local and systemic loss of bone mass, and progression of periodontitis with loss of alveolar bone density and bone height. [48].

According to studies conducted in women taking hormonal contraceptives for the purpose of pregnancy planning, a significant level of inflammatory and dystrophic-inflammatory periodontal disease was noted. The authors found an increase in periodontal pocket depth, compromised epithelial attachment integrity, and increased gingival index (GI) levels as early as six months after taking oral contraceptives. [5,47].

Orishchenko V.Yu. (2004). studying the influence of neuroendocrine regulation on the development of pathological conditions in periodontal tissues he found out that the increased somatotropic activity of pituitary gland and glucocorticoid function of adrenal glands with simultaneous suppression of glandular function contribute to peripheral beta-adrenergic blockade with microcirculation disorder. Analysis of glucocorticoid function of the adrenal glands revealed increased

secretion of adrenocorticotropic hormone and cortisol among young patients with periodontal disease regardless of the disease severity.

According to the World Health Organization, thyroid disease ranks second after diabetes mellitus. Numerous studies have established the onerous influence of thyroid diseases on the incidence and course of periodontal diseases. The relevance of these pathological conditions determines the interest in the study of their combined course in order to identify the peculiarities as well as the need to develop new modern strategies of medicinal care. [24,9,34].

Assessment of the periodontal complex among children who suffer from diffuse nontoxic goiter found significantly worse indicators of periodontal tissues, which tend to progress with age. [6].

Korsak Yu.V. (1999) studying clinical features of the course of generalized periodontitis in patients with thyroid gland dysfunction of radiation genesis to corrective therapy and after it found that the difference of thyroid gland dysfunction in patients with generalized periodontitis changes clinical picture of the disease, complicates its course with development of more pronounced deviations in immune system. Thus, the examined patients with hypothyroidism who were not exposed to radiation were found to have periodontal inflammation of a sluggish course, a tendency for chronicity of the pathological process. In patients with hyperthyroidism of radiation genesis a rapid progression of resorption of interdental alveolar septa and more pronounced clinical manifestations in the periodontium were noted.

Repetskaya A.N., Rozhko M.M. and others (2020) found a significantly higher prevalence and intensity of periodontal tissue diseases among young patients with hypothyroidism compared to those without endocrinological pathology in all age groups. Periodontal diseases in patients with primary hypothyroidism lasting from 1 to 5 years were registered in about 80% of cases; when the concomitant pathology lasted more than 5 years, the number of patients with dystrophic-inflammatory forms of periodontal diseases reached about 90%. Rapid progression of the pathological process in the periodontium was observed with age.

According to Schneider O.L. (2008) periodontitis on the background of primary hypothyroidism is characterized by a long latent course with pronounced clinical manifestations in the form of gingival recession and pronounced loss of clinical attachment. The author notes that Porphyromonas gingivalis; Actinobacillus actinomycetemcomitans; Treponema denticola; Bacteroides forsythus; Prevotella intermedia are detected in periodontal pockets in this contingent of patients. Cytological examination shows a moderate leukocytic infiltration, without detection of immunocompetent cells.

Yakubova I.I. and others (2008) point out that parathyroid gland dysfunction, which causes changes in the tone of the autonomic nervous system and vascular system, in the gums, form disorders of calcium metabolism, hypovitaminosis C, A, E and play a definite role in the development of periodontal disease in pregnancy.

Zubachik V.M. et al. (2011) in an experimental study on the emergence, course, treatment and prevention of periodontitis against the background of primary hyperparathyroidism (PHPT), indicate hyperactivation of thyroid hormones, which contributes to the release of osteoclasts bi-destructive proteases, in particular bone elastase, that causes destruction of the organic matrix of bone tissue. Disturbance of mineral metabolism in the bone tissue of the jaw finds its manifestation in the loss of

its main mineral components - calcium and phosphorus, and imbalance of the physiological antioxidant system is manifested in the increase of peroxidation products - malondialdehyde and reduced activity of catalase.

Conclusions. The review of domestic and foreign scientific publications gives grounds to state the negative effect of endocrine gland function disorders on the course of the pathological process in periodontium. In spite of the great number of studies the mechanisms of hormones' influence on the bone metabolism of periodontal tissues haven't been studied completely. Researches in this direction allow to establish diagnostic and prognostic criteria of periodontal lesion severity in case of functional changes of endocrine system in order to develop complex interdisciplinary approach of individual treatment tactics for each group of patients**.**

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