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***BIOLOGICAL MARKERS IN  
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Collection of abstracts "**Biological Markers in Fundamental and Clinical Medicine**" (*official specialized scientific journal of The Czech Republic, registration number MK CR E 22955*) by the publishing center of The ESCBM provides its lanes for information materials in the field of scientific research of modern biological markers in clinical and experimental medicine, pharmacy, and fundamental biology. The collection publishes abstracts of scientific and practical conferences, seminars, symposia, dedicated to the study of molecular-biochemical and functional markers, playing a role in pathogenesis, diagnosis, prognosis, as well as assessing the monitoring of the treatment effectiveness for the various systems and organs diseases. **Among the priority topics of the journal there is the research of molecular mechanisms of diseases pathogenesis, the study of the structure and functions of peptides, nucleic acids, nucleotides, lipids and other biologically active components of body cells.**

The collection is intended for fast and systematic publication of abstracts, containing the results of author's research, reviews highlighting major developments in the field of biological markers, short messages, new experimental and clinical studies, which use biological markers, as well as proposing new principles and methods for the study of biological markers.

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/MMP-8/, interleukin (IL)-1 $\beta$ , interleukin IL-6, prostaglandin PG E2 and tumor necrotizing factor (TNF)- $\alpha$  carry the potential for proper diagnosis of diseases of gingivitis and periodontitis [7]. In salivary samples of patients suffering from chronic renal failure have been recorded significantly high levels of nitrogenous oxide. After routine procedures of hemodialysis in the salivary samples of these participants in the investigation have been recorded considerable concentrations of immunoglobulin A and G, and of C-reactive protein (IgA, IgG and CRP). Therefore, the quantity of these indices in saliva can play important role in the process of monitoring of renal disorders [8]. Saliva contains local and systemic biochemical compounds with considerable diagnostic value, applicable for detection of periodontal disorders. The early stage of periodontitis, known as gingivitis, in the predominant portion of cases proceeds asymptotically, which explains the need of application of sensitive, reliable methods. Identification of salivary biomarkers is a non-invasive laboratory approach for early diagnostics of the destructive diseases of periodontal apparatus. Periodontal disorders are varying in a wide range of clinical manifestation from plaque-induced gingivitis to multi-aspect clinical findings of reflective (aggressive) forms of periodontitis, including periodontitis associated to systemic diseases [9, 10].

Conclusion: Definite priorities of saliva as diagnostic medium are influenced by contemporary high technology innovations, namely enzyme-associated fluorescence technique, Western blot assays, polymerase chain reaction (PCR).

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### USE OF INDICATORS OF OXIDATIVE STRESS AND HSP 70 PROTEIN AS MARKERS IN THE DIAGNOSTICS OF DENTAL DISEASES

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The most important triggering factor in the initiation of the pathological process is the formation of the dental plaque as a multilayered microbial biofilm with parodontopathogenic microorganisms. They include the causative agents of the chronic inflammatory process in the periodontal disease, such as *Tanarella forsythensis*, *Porphyromonas gingivalis*, *Treponema denticola*, and the inducer of acute aggressive inflammation of *Actinobacillus actinomycetemcomitans*. In these conditions, the resistance of microflora to various protective factors is determined by heat shock proteins HSP70 [1-3]. Paternal-recognition receptors (PRRs) perceive microbes with these new proteins as «strangers.» All these parodontopathogens are a source of lipopolysaccharides (LPS) capable of interacting with cells of damaged epithelium, neutrophilic granulocytes, monocytes / macrophages, fibroblasts via Toll-like receptors (TLR). The process of parodontopathogens interaction with TLR cells differs significantly from that of normal biofilm microflora [2]. With the predominance of pathogenic microflora through TLR, a continuous flow of signals is provided activating the macrophages and other immunocompetent cells carrying these receptors and induce them to chemotaxis, the secretion of pro-inflammatory cytokines (tumor necrosis factor  $\alpha$  (TNF $\alpha$ ), interleukins (IL) -1,6, -8, the release of matrix metalloproteinases and other enzymes, the production of immunoglobulins specific for microbial antigens

produced with the involvement of chemokines of T- and B- lymphocytes [1, 3-5]. Release enzyme substances take part in the degradation of collagen and other extracellular matrix proteins, causing the lost contact between the periodontium and the bone. Quite large is the role of pro-inflammatory cytokines, which, in addition to induce inflammatory changes in the tissues, are able to activate osteoclasts and thus promote bone resorption of the alveolar processes. A complicated complex of molecules arises, including electrolytes and other small molecules, proteins, cytokines, antibodies, bacterial antibodies, enzymes, degradation products of connective and bone tissue in the gingival-cervical fluid [6, 7]. Due to the clinical and experimental works, and also, on the basis of the data obtained by us, concerning heat shock proteins, the most interesting is HSP70 as a stress protein, which is an important diagnostic and prognostic indicator of the severity of pathological processes. Of particular interest, for today, is the molecular regulation of HSP70 oxidative and nitrosating stresses, which are unchanged companions of inflammatory diseases of the oral cavity. In order to establish the direction and severity of antioxidant prooxidant processes in the oral cavity, in clinical studies, the determination of the concentration of the nitrosating stress marker - nitrotyrosine, is widely introduced. In connection with the above, the purpose of this work is to evaluate the role of the heat shock protein Hsp 70 and nitrotyrosine in the development of chronic parodontal diseases [8-9].

**Materials and methods.** 47 patients (25 men and 22 women) with chronic generalized parodontitis aged from 25 to 50 years were examined. The control group consisted of 15 residents of Zaporozhye city of the corresponding sex and age, who did not have somatic or dental pathology. When assessing dental status, the level of oral hygiene was determined using the simplified index OHI-S (Green, Vermillion, 1969), the state of teeth according to the CFR index. As an integral need measure for the treatment of parodontal diseases, the CPITN index proposed by WHO (1978) was calculated. The severity of gingival inflammation was determined from the reversible PMA index, modified by C. Parma (1960), the severity of the destructive processes in the parodontium was detected according to the parodontal index PI (A. Russel, 1956), the degree of bleeding gums was identified using the PBI bleeding index according to U.P. Saxer and M.R. Muhlemann (1975). In all the investigated patients, the oral liquid was obtained 10 minutes after rinsing the oral cavity with saline by spitting into plastic tubes. After centrifugation at 3000 rpm./min. 1,5 ml supernatant liquid was collected during 5 minutes, the resulting substrates were placed in eppendorfs and stored at - 20 ° C in the freezer until the time of the study. The HSP70 level in the oral fluid was determined by enzyme immunoassay (IEA) (Enzo Life Science, EKS - 715) nitrotyrosine concentration (ELISA Kit «Hycult biotechnology b.v»), the result was expressed in ng / ml and nmol / g. All the patients received a set of basic medical measures.

**Results.** The study of dental status has revealed a low level of the oral hygiene in 38 (80.9%) patients. In all the patients, concomitant carious lesions of teeth with different severity degree, chronic generalized parodontitis of the 1st and the 2d degrees were diagnosed. In 31 (65.9%) patients the pathology of the occlusion was detected, 42 (89.4%) investigated patients had dentoalveolar anomalies, 23 (48.9%) had orthopedic constructions in the oral cavity. We studied the oral liquid of the patients with parodontitis (ChGP) by nitrotyrosine concentration (Ntz) (ELISA Kit «Hycult biotechnology b.v») and HSP 70 (Enzo Life Science, EKS - 715). Immunoenzymatic determinations of these markers have demonstrated a close relationship between the dynamics of their concentration in the oral fluid and the intensity of the pathological process.

As shown in the 1st Figure, at a primary examination of the patients with parodontitis (ChGP) was marked a considerable increase of nitrotyrosine concentration nearly at 8 times in relation to the healthy persons (control group) on the background of a sharp decrease of the HSP 70 protein in oral fluid, responsible for the implementation of molecular mechanisms of protecting macromolecules from oxidative stress. Such a pathobiochemical shift, in our opinion, indicates the development of oxidative stress and the disruption of the compensatory mechanisms of the cells. In conditions of oxidative stress significant development, HSP 70 is unable to perform its chaperone function and «correct» oxidatively damaged functionally active protein molecules, which in turn leads to an increase of the pathobiochemical processes in the periodontitis. On the 10th day of the observation, after the treatment, a decrease in the nitrotyrosine content and a normalization of the HSP 70 proteins concentration was recorded, which occurred on the background of the overall clinical picture parodontitis improvement: good hygienic state of the oral cavity, arrest of the inflammatory process, normalization of the circulation and resumption of the gingival relief.

Conclusions. Thus, the conducted studies have demonstrated that the HSP 70 and Ntz have been able to utilize as biological markers in prognosis and screening efficacy for performed treatment in dentistry. This type of clinical diagnostic study is a minimally invasive and informative method. Further studies in this direction are promising and relevant in modern dentistry and clinical laboratory diagnostics. The technical improvement of the laboratory determination of biomarkers, its transfer to the level of quantitative testing is the most important task of dentistry, because it allows not only to make accurate and timely diagnosis of the disease, but also to predict its progression, complications and outcomes. From this point of view, modern methods of laboratory diagnostics and their capabilities deserve special attention.

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### DYNAMICS OF MARKERS OF BONE RESORPTION IN ORAL FLUID IN PATIENTS WITH GENERALIZED PARODONTITIS DURING TREATMENT

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The topicality of this study is due to the considerable prevalence of periodontal diseases, which is 20-50% of the total world population[1]. It is known that the most indicative of the inflammatory-destructive process in the periodontal tissues is an X-ray examination, the results of which can be demonstrated to stabilize the pathological process as a result of treatment. However, to conclude about the state of alveolar bone is only possible in six months after treatment, which makes it impossible to monitor in its process for the purpose of correction. In this regard, the necessary task is the search for new non-invasive and informative methods of diagnosis, which may include biochemical examination of oral fluid[2]. It is proved that the main cause of inflammation in periodontal tissues is the microbial factor, namely, qualitative and quantitative changes in the microflora of the oral cavity, in particular the activation of parodontopathogenic microorganisms[3]. At the same time, inflammation causes the destruction of the connective tissue of the periodontal complex, characterized by collagen and proteoglycan metabolism disorders, and, consequently, resorption of bone[4]. In this case, the development of inflammatory process in the periodontal tissues leads to increased secretion of proinflammatory cytokines such as interleukin-1 $\alpha$ , -1 $\beta$ , -6, tumor necrosis factor- $\alpha$ . Neutrophils produce a large number of enzymes and inflammatory mediators. An increase in their concentration in saliva is a diagnostic sign of inflammatory processes in oral cavity. Therefore, in the search for diagnostic criteria, special attention should be paid to increasing the concentration of collagenases, which include matrix metalloproteinases. They should be considered key in describing the periodontal status, since type I collagen is in the vast majority in the extracellular matrix of the periodontal tissues. Among them matrix metalloproteinase-8 (MMP-8) is the main one in periodontitis, because 90-95% of collagenolytic activity falls on it[5]. All of the above has allowed us to formulate the purpose of the investigation as the study of the level of MMP-8 in oral fluid in patients with generalized periodontitis in the dynamics of the treatment.

**Materials and Methods.** 30 patients aged 37 - 45 years were included into the study. 15 of patients were diagnosed generalized periodontitis of the I degree of severity, 15 – the II degree of severity. As a control, indicators from a group of 8 persons with intact periodontal tissues, selected similarly for the gender and age characteristics of the observation group, were used. To assess the periodontal condition, a traditional clinical examination, supplemented by the results of an X-ray study, was used. All patients with generalized periodontitis received comprehensive treatment[3]. The content of MMP-8 in the oral fluid was studied using the immune enzyme method (BCM Diagnostics, DMP800, Total MMP8). The research was conducted before and immediately after treatment. The data of the conducted clinical and laboratory studies were to be processed using the «STATISTICA® for Windows 6.0» (StatSoft Inc., № AXXR712D833214FAN5).

**Results.** As a result of the conducted biochemical studies, it was proved an increase in the level of MMP-8 in the oral fluid in patients with generalized periodontitis ( $0.4 \pm 0.1$  ng / ml under the I degree of severity,  $0.7 \pm 0.2$  ng / ml – under the II degree against  $0.1 \pm 0.03$  ng / ml of control,  $p < 0.05$ ). At the same time, after a complex treatment, the level of this indicator decreased to  $0.2 \pm 0.07$  ng / ml under the I degree of severity and to  $0.5 \pm 0.1$  ng / ml – under the II degree ( $p < 0.05$ ). However, it should be noted that the results obtained after the course of treatment outweighed the control ( $p > 0.05$ ), which, in our opinion, suggests only about inhibition of the pathological process, rather than its complete elimination. Thus, according to the results of the studies, we found that the level of MMP-8 in the