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STUDY OF STRUCTURAL-PROLIFERATIVE CHANGES IN GINGIVAL EPITHELIUM ASSOCIATED WITH CHANGES IN THE PARODONTIUM STATE

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The summary: literature review of structural and proliferative changes in the epithelium of the gum associated with changes in parodontium status is presented.

Keywords: ***epithelium of the gum, proliferative processes.***

Clinical appearance of oral mucosa associated with comorbid internal conditions reflects its morphological restructuring and includes papillary hyperplasia, gingival hyperemia and stomatorrhagia, which corresponds to chronic gingivitis [15, 21, 22, 41, 44].

It's obviously related to vascular restructuring which may lead to revascularization with the growth of new arterioles and capillaries. Their walls however are not morphologically ready to deliver biologically active substances to the full extent [3, 6, 14, 24, 27, 29, 40].

There are data regarding a positive correlation between H. Pylori colonization of oral mucosa and gastrointestinal mucosa in patients with gastrointestinal disorders. The highest level of H. Pylori oral and gastrointestinal mucosal colonization is found in denture patients. A state of the parodontium, an oral hygiene state and a level of H. Pylori oral and gastrointestinal mucosal colonization are also correlated [4, 22].

It's been found that physiological regeneration in oral epithelium is characterized by three interrelated processes: cell migration, proliferation and differentiation. It must be noted that the label incorporated into DNA as early as 48 hours after DNA labeling. The labeled cells start passing to the surface in twenty-four hour period. The speed of epithelization is 0,27 mm/hand it overtakes the speed of granulation tissue formation (0,04 mm/h) [10, 11, 28].

Regenerating epithelium is characterized by the presence of glycogen granules in the cells' cytoplasm and increased amount of RNA and oxidation/reduction enzymes. During the processes of differentiation and multilayer epithelium formation these features are being lost. Despite number of studies there are not enough data regarding epithelial regeneration in dental patients with comorbid conditions [16, 17, 18, 19, 24, 31, 36].

There is a high correlation between epithelization and granulation tissue growth. Not only epithelium can stimulate the growth of granulation tissue but it also produces collagenase which participate in the tissue restructuring. Delay in epithelization results in early sclerosis of granulation tissue which, in turn, slows down epithelization of affected areas. Though epithelium may grow on any surface, a firm cellular layer forms only on granulation tissue of certain maturity. Regeneration of both epithelium and granulation tissue is regulated to a large extent by fibroblasts and hormonal factors, such as epidermal growth factors of different origin and growth inhibitors. Epithelial hyperplasia (inflammatory inserting growth) results from mechanisms similar to those seen in regenerative hypertrophy of internal organs [2, 6, 9, 26, 30, 32, 33, 43, 38].

Changes in proliferation activity of gingival epithelium and the lamina propria of the gingival are typical morphological presentations of their reaction to any internal abnormalities [13, 16, 18, 19, 23, 34].

Some authors believe that ^{3}H-thymidine radioautography provides the most reliable and accurate data on DNA synthesis [8, 16, 24].

In gingival epithelium ^{3}H-labeled cells are found in the stratum basale, much less often in the stratum spinosum. A cell uses ^{3}H-labeled thymidine during DNA synthesis. It accumulates in the nuclei which either undergo the S-phase or enter it during incubation [6, 16, 20, 35].

The absence of glycogen in the stratum basale and deep layers of the stratum spinosum of gingival epithelium reflects prevalence of Krebs cycles enzymes activity. That proves the fact mytoses, which occur mostly in this part of epithelial layer, require energy released by oxidation [37].

Mitotic activity of tissue is strongly influenced by exo- and endogenous factors, physical activity in particular. Some of these factors which influence cirdadian rhythm of cell division are functional cell activity and general functional activity of a body. Changes in metabolism are links in a complex chain of processes which drive a circadian rhyme in mitotic activity. In a natural 24-hour cycle in human body activity a negative correlation is seen between functional activity and cell division [1, 7, 16].

During intensive short-term physical load mitotic activity decreases dramatically due to increased adrenalin release. Long-term physical load results in increased mitotic activity. "Antagonism" between function and mitosis reflects the relationship between the processes [1, 16, 18, 19].

Denture use can be likened to long-term physical activity, which helps to explain the increase in epithelial mitotic activity under a denture base. Short-term denture use is associated with decreased mitotic activity while long-term denture use induces its increase [17, 25].

E.I. Gavrilov (1979) holds a different opinion. In his view, after 5 years of denture use a decrease in mitotic activity results from glycogen appearing in the cells of the basal layer and lower glucose uptake [5].

During the study of gastrointestinal epithelium by means of radioautography spontaneous circadian mitotic activity was found with a roughly 24± 4 hours cycle. There are two peaks in the cycle, though the second peak seen during evening and night hours is less evident [1, 19, 35, 42].

A study of cell proliferation in oral mucosa in female denture patients showed prevalence of average frequency of labeling, intensity of incorporation and mitotic index values. These data indicate higher intensity of regeneration in women than in men, due probably to sexual dimorphism and bad habits [17, 23, 24].

According to J.S.Rowat and C.A.Squier (1986), a mitotic index also correlates with the thickness of an epithelial layer, indicating higher speed of proliferation. Lining mucosa renews faster than masticatory mucosa [39].

Mitotic activity in gingival epithelium increases when epithelial keratinization slows down which happens in gingivitis and parodontitis [30, 39].

There is a correlation between severity of gingivitis, extent of morphological changes and intensity of cell division. This fact proves that gingival epithelium is still capable of an adequate adaptive response in the presence of increasing inflammatory and dystrophic changes. The growth of a mitotic index combined with a relatively stable frequency of labeling numbers indicate some disruption of cell differentiation and more rapid extrusion of cells associated with gingival inflammation. In the same time the increase in a mitotic index may represent lengthening the duration of mitosis, not a rise in the number of cells undergoing it [18, 19].

Some clinical forms of lichen planus is reported to be associated with increased number of parodontium inflammatory diseases [12].

Thus the analysis of the literature on morphology of parodontium in patients with comorbid internal conditions showed that changes in the state of the oral cavity occur due to metabolic, haemodynamic, immunological and neuroregulatory processes associated with a disease. The literary data indicate that gastrointestinal tract disorders coexist with changes in oral mucosa. This interrelation is produced through anatomical, physiological and humoral communications between different parts of the gastrointestinal tract.

Studies of the upper gastrointestinal tract in patients with comorbid internal conditions have shown that a type changes in oral mucosa depends on the form and duration of a main disease.

In the same time there are some changes of the oral cavity mucosa typical for different gastrointestinal conditions. Besides, patients with comorbid internal diseases may present with various inflammatory and destructive changes in the oral cavity mucosa. It should be noted, however, that there are not enough data on how a patient's age, their general health condition and the state of the oral cavity affect a morphological structure of denture base mucosa. The existing data are contradictory which may reflect different approaches to defining age groups and lack of a comprehensive morphological characterization of the oral cavity mucosa.

REFERENCES

1. Alov, I. A. Cytophysiology and pathology of mitosis [Text] / I. A. Alov. – M.: Medicine, 1982. – 263 p.
2. Apoptosis and cell proliferation as alternative forms of T-cells response to stimulation [Text] / A. A. Yarilin, M. M. Litvina, M. F. Nikonova [and col.] // Immunology. – 1999. – № 2. – P. 20 – 23.
3. Banchenko, G. V. Evaluation of epithelial cell differentiation in prints taken from different areas of oral mucosa in healthy adults [Text] / G. V. Banchenko, O. G. Akopyan, A. A.

Agadzhanyan // Dentistry. – 1997. – № 1. – P. 12 – 14.

4. Bibik, M. V. PCR-analysis of oral mucosa in peptic ulcer disease associated with H. Pylori infection [Text] : essay dissert. … cand. of med. Sci. / M. V. Bibik. – Novosibirsk, 2005. – 22 p.
5. Gavrilov, E. I. Denture and denture base [Text] / E. I. Gavrilov. – M., 1979. – 264 p.
6. The interrelationship between changes in oral mucosa and gastrointestinal conditions [Text] / G. I. Oskol'skiy, L. M. Nepomnyashchikh, E. L. Lushnikova, A. V. Yurkevich [and col.] // Far Eastern medical journal . – №3. – 2010. – P. 67-75 .
7. Gemonov, V. V. Epithelial morphogenesis of the cranial part of the gastrointestinal tract: abstracts of the 3-rd Congress of International Morphological Association [Text] / V. V. Gemonov, O. E. Cherep // Morphology. – 1996. – № 2. – P. 44.
8. Histoautoradiography in morpho-functional evaluation of the masticatory system [Text] / V. V. Panikarovskiy, A. S. Grigor'yan, G. M. Korobeynikov, V. M. Kiselev // Dentistry. – 1973. – № 1. – P. 4 – 8.
9. Grigoryan, A. S. Morphogenesis of early stages of inflammatory parodontium diseases [Text] / A. S. Grigoryan, O. A. Frolova, E. V. Ivanova // Dentistry. – 2002. – № 1. – P. 19 – 25.
10. Gulyamov, M. G. Quantity cytological parameters of the oral cavity epithelium in healthy people [Text] / M. G. Guliamov, V. I. Pol'skiy, A. A. Baybaev // Health Care in Tajikistan. – 1999. – № 4. – P. 108 – 109.
11. Danilevskiy, N. F. Osteogenic precursor cells and regeneration in dentistry [Text] / N. F. Danilevskiy, V. S. Astakhova, O. N. Romanenko // Dentistry. – 1998. – № 1. – C. 125 – 130.
12. Zagorodnyaya, E. B. Pathomorphological, immunohistochemical and cytological aspects of lichen planus of the oral cavity mucosa [Text] : essay. dissert. … cand. of med. sci. / E. B. Zagorodnyaya. – Novosibirsk, 2010. – 30 p.
13. Kapitonova, M. Yu. New criteria for evaluation of the functional state of cells by means of computer ultramorphometry [Text] / M. Yu. Kapitonova // Morphology. – 2000. – № 3. – P. 54.
14. Matsyupa, D. V. Morphological changes in gingival mucosa in peptic ulcer disease [Text] : essay. dissert. cand. of med. sci. / D. V. Matsyupa. – Novosibirsk, 2005. – 22 p.
15. Mikhaleva, L. M. Apoptosis and ultrastructural changes in plasmocytes of gingival mucosa in patients with parodontitis [Text] / L. M. Mikhaleva, V. D. Shapovalov // Immunology. – 2002. – № 2. – P. 83 – 87.
16. Oskol'skiy, G. I. Pathomorphological, clinical and functional evaluation of the masticatory

system in cases of a changed interalveolar distance [Text] : essay dissert. … cand. of med. sci. / G. I. Oskol'skiy. – Novosibirsk, 1995. - 14 p.

17. Oskol'skiy, G. I. Radiographic evaluation of gingival epithelium in denture patients with gastrointestinal conditions [Text] / G. I. Oskol'skiy, V. A. Kravchenko // Current issues of health care and clinical medicine development.: materials from regional sci. and pract. conf. – Birobidzhan, 1997. – P. 267 – 270.
18. Oskol'skiy, G. I. Radiographic evaluation of gingival epithelium proliferation in chronic gingivitis [Text] / G. I. Oskol'skiy, M. I. Radivoz, A. Ya. Astakhova // Bulletin of experimental biology and medicine. – 1997. – № 10. – P. 473 – 476.
19. Oskol'skiy, G. I. Proliferative processes in gingival epithelium in humans [Text] / G. I. Oskol'skiy, S. S. Timoshin, L. I. Utkina // Dentistry. – 1993. – № 3. – P. 14 – 16.
20. Superficial structure of the hard palate mucosa evaluated by means of focused-beamed electronic microscopy [Text] / Kh. I. Irsaliev, A. A. Zufarov, S. A. Fayzullaev, R. T. Khabiev // Materials of VIII All-Union Congress of Dentists. - M., 1987. – T. 1. – P. 170 – 171.
21. Tsepov, L. M. Cytologic parameters and electrokinetic mobility of buccal epithelium cells' nuclei in evaluation of parodontium [Text] / L. M. Tsepov, E. V. Vasileva, A. I. Nikolaev // Dentistry. – 1999. – № 3. – P. 7 – 8.
22. Tsimbalistov, A. V. A state of the oral in patients with H. Pylori infection [Text] / A. V. Tsimbalistov, N. S. Robakidze // Current problems in dentistry: collection of abstracts. – M., 1999. – P. 250 – 252.
23. Yurkevich, A. V. Structural and morphological aspects of gingival mucosa in diabetes mellitus type 2 [Text] : dissert. … cand. of med. science / A. V. Yurkevich. – Novosibirsk, 1999. – 22 p.
24. Yurkevich, A. V. Pathomorphological aspects of gingival mucosa in diabetes mellitus and peptic ulcer disease and peptic ulcer disease [Text] : dissert. PhD (med. science). / A. V. Yurkevich. – Novosibirsk, 2005. – 36 p.
25. Abdel Razek, M. K. Histochemical and histopathologic studies of alveolar mucosa under complete dentures [Text] / M. K. Abdel Razek, N. A. Shaaban // J. Prosthet. Dent. – 1971. – Vol. 39, № 1. – P. 29 – 36.
26. Apoptosis of oral epithelial cells in oral lichen planus caused by upregulation of BMP-4 [Text] / S. G. Kim, C. H. Chae, B. O. Cho [et al.] // J. Oral. Pathol. Med. – 2006. – Vol. 35. – P. 37 – 45.
27. Carmeliet, P. Blood vessels and nerves: common signals, pathways and diseases [Text] / P. Carmeliet // Nature Rev. Genet. – 2003. – № 9. – P. 710 – 720.

28. Coates, P. J. The association between cell proliferation and apoptosis: studies using the cell cycle-associated proteins Ki-67 and DNA polymerase [Text] / P. J. Coates, S. A. Hales, P. A. Hall // J. Pathol. – 2001. – Vol. 1, № 78. – P. 71 – 77.
29. Corbet, E. F. Oral mucosal lesions in 65-74-year-old Hong Kong Chinese [Text] / E. F. Corbet, C. J. Holmgren, H. P. Philipsen // Community Dent. Oral. Epidemiol. – 2004. – Vol. 22, № 5. – P. 392 – 395.
30. Evidence that human oral epithelium reconstituted in vitro and transplanted onto patients with defects in the oral mucosa retains properties of the original donor site [Text] / M. de Luca, E. Albanese, M. Megna [et al.] // Transplantation. – 1990. – Vol. 50. – P. 454 – 459.
31. Dourmishev, L. A. Dermatomyositis associated with malignancy. 12 case reports [Text] / L. A. Dourmishev // Adv. Exp. Med. Biol. – 1999. – Vol. 45, № 5. – P. 193 – 199.
32. Gasparoni, A. Intercellular junctions in oral epithelial cells: ultrastructural and immunological aspects [Text] / A. Gasparoni, C. A. Squier, L. Fonzi // Ital. J. Anat. Embryol. – 2005. – Vol. 110. – P. 83 – 91.
33. Gerson, S. L. Drug resistance gene transfer: Stem cell protection and therapeutic efficacy [Text] / S. L. Gerson // Exp. Hematol. – 2000. – Vol.28. – P.1315 – 1324.
34. Silver-binding nucleolar organizer regions (AgNORS) in beniqn and maliqnant brest lesions: Correlations with ploydy and growth phase by DNA flow cytometry [Text] / D. D. Giri, J. F. Nottinqham, J. Lawry [et al.] // J. Path. – 1989. – Vol. 157. – P. 307 – 313.
35. Kirschner, H. Autoradiographic studies of periodic new cell formation in the human oral epithelium [Text] / H. Kirschner, L. Rehling // Dtsch. Zahnarztl. Z. – 1982. – Vol. 37, № 4. – P. 384 – 387.
36. Kratochvil, F. J. Partial removable prosthodontics [Text] / F. J. Kratochvil // Community. Dent. Oral. Epidemiol. – 2003. – Vol. 23, № 6. – P. 214 – 217.
37. Kvidera, A. Rates of clearance of the epithelial surfaces of mouse oral mucosa and skin [Text] / A. Kvidera, I. C. Mackenzie // Epithelial. Cell. Biol. – 1994. – Vol. 3. – P. 175 – 180.
38. Morphological changes in oral mucosa and their connective tissue cores regarding oral submucous fibrosis [Text] / K. Yoshimura, U. B. Dissanayake, D. Nanayakkara [et al.] // Arch. Histol. Cytol. – 2005. – Vol. 68. – P. 185 – 192.
39. Rowat, J. S. Rates of epithelial cell proliferation in the oral mucosa and skin of the tamarin monkey (Saguinus fuscicollis) [Text] / J. S. Rowat, C. A. Squier // J. Dent. Res. – 1986. – Vol. 65, № 11. – P. 1326 – 1331.
40. Scardina, G. A. Morphologic changes in the microcirculation induced by chronic smoking

habit: A videocapillaroscopic study on the human gingival mucosa [Text] / G. A. Scardina, P. Messina // Am. J. Dent. – 2005. – Vol. 18. – P. 301 – 304.

41. Stohler, C. Etiology and occurrence of denture stomatitis. A review of literature [Text] / C. Stohler // Schweiz. Mschr. Lahnmed. – 1984. – Vol. 94, № 2. – P. 187 – 189.
42. Viljamoa, P. Mitotic activity in the craniofacial cartilages IV. Circadium variation in mitotic activity in the cranial base cartilages of 20-day rats [Text] / P. Viljamoa // Proc. Finn. dent. Soc. – 1987. – Vol. 87, № 4. – P. 171 – 174.
43. Walter, B. Ultrastructural relationship of denture surfaces, plaque and oral mucosa in denture stomatitis [Text] / B. Walter, R. M. Frank // J. Biol. Buccale. – 2003. – № 2. – P. 145 – 166.
44. Watson, J. B. Oral mucosa and complete dentures [Text] / J. B. Watson, D. Gordon // J. Prosth. Dent. – 1982. –Vol. 47, № 2. – P. 133 – 140.

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