

## THE CHANGES IN THE ORAL MUCOSA CAUSED BY CONTACT WITH RESTORATIVE MATERIALS

Adina Oana Armencia<sup>1</sup>, A. Nicolau<sup>1</sup>, Al. Călin<sup>2</sup>, Carina Balcos<sup>1\*</sup>,  
Ramona Feier<sup>4</sup>, Dana Baci<sup>4</sup>, Mihaela Monica Scutariu<sup>3</sup>

“Grigore T. Popa” University of Medicine and Pharmacy Iasi, Romania  
Faculty of Dental Medicine

1. Department of Dento-Alveolar Surgery And Maxilo-facial Surgery

3. Faculty of Medicine

2. Department of Implantology, Removable Dentures, Dental Technology

4. “Dimitrie Cantemir” University Târgu-Mureș

Faculty of Medicine

**THE CHANGES IN THE ORAL MUCOSA CAUSED BY CONTACT WITH RESTORATIVE MATERIALS (Abstract):** The clinical interpretation of mucosal changes upon contact with restorative materials still raises many questions, mainly due to the questionable biological qualities of these materials. **Material and method:** The study sample comprised 32 cases. The morphopathological examination involved analyzing the structural composition of mucosal material obtained from the oral mucosa. The biopsy fragments were processed for standard microscopic examination. **Results and discussion:** The number of cellular layers in the spinous layer was altered, with flattened cells and small intercellular spaces, often observed in long-standing restorations that compress the underlying mucosa. The histopathological image of the mucosa in contact with non-precious metal alloys veneered with ceramic showed minimal changes in both the epithelium and the connective tissue. Traumatic factors led to alterations in epithelial keratinization (parakeratinization, hyperkeratinization), resulting in thickening or, conversely, thinning of the epithelium. **Conclusions:** The anatomopathological examination highlighted morphological aspects characteristic of the etiological factor. **Key-words:** DENTAL MATERIALS, BIOCOMPATIBILITY, MUCOSAL REACTIONS, HISTOPATHOLOGY

### INTRODUCTION

Although the oral cavity is easily accessible for direct clinical examination, and the clinical diagnosis of mucosal lesions in the presence of prosthetic restorations may seem simple and easy to establish based on subjective and objective clinical signs (when present), certain details of pathological processes can escape regular clinical investigations and go unnoticed, hence the need for microscopic studies. Due to sometimes mild symptoms, a large portion of developed mucosal lesions are detected relatively late, often indicating the involvement of associated etiological factors. The biological integrity and reliability of dental restorations depend on multiple factors related to the dynamic balance of the arches, materials, execu-

tion conditions, as well as the oral environment (1, 2).

Besides mechanical qualities such as resistance to functional or parafunctional stresses, processability, and corrosion resistance, a restorative material should also possess biological properties, namely biocompatibility and the absence of toxic interactions with oral environmental factors affecting the structures of the stomatognathic system.

The occurrence of local complications has led the specialized literature in recent years to focus more on the complex process involved in their integration into organism biology and the oral cavity. The clinical interpretation of mucosal alterations in prosthetic patients, wearing prosthetic restorations made of metal alloys,

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either as they are or veneered with ceramic, still raises many questions, precisely due to the sometimes questionable biological properties of these materials. Mucosal reactions that occur in the oral cavity are often attributed to stress or the inadequate protection provided by local factors against the direct or indirect effects (through released by-products) of restorative materials (3, 4, 5). Since clinical manifestations are not always conclusive, the use of morpho-pathological examination in conjunction with clinical examination may provide some clarification.

For a long time, the research on oral mucosal changes in the presence of prosthetic restorations has been based on biopsy material without being correlated with clinical data and anamnestic information that is so useful in interpreting the results. The regularity of multiple histological variations may help identify the type of reactivity based on the involvement of factors related to the existence of prosthetic restoration, as well as the material and its components, which, when released into saliva, could induce varied tissue reactions.

For this reason, this study aimed to evaluate the clinicopathological reactions of mucosa upon contact with restorative materials, as well as their depth.

### MATERIAL AND METHOD

The study group consisted of 32 selected cases from private practice where prosthetic restorations needed to be replaced for various reasons (subjective complaints, mucosal reactions, restoration damage, decementation, etc). The age of the patients ranged from 48 to 64 years, with a mean age of 56 years. Inclusion and exclusion criteria were followed (age group, origin environment, socioeconomic level, cooperation level with the dentist, type of lesion, type of restoration material). Patients who provided informed consent and had coronal dental lesions, partial or complete edentulism, and prosthetic restorations made from various materials (acrylic restorations, Cr-Co alloy, Cr-Ni alloy, ceramic-plated Cr-Co alloy, or ceramic on a zirconia framework) were selected. Additionally, the presence or absence of systemic conditions that could influence the structural quality of the oral mucosa was considered during patient selection. The selected patients had restorative or prosthetic treatments with a duration of up to 10 years.

For comparison, a control group of 50 clinically healthy patients with similar age range (42-50 years, with a mean age of 46 years) was included in the study. These control patients had prosthetic or dental restorations made from the same materials in their oral cavities. Including individuals with lower age limitations in the study was necessary to exclude the influence of general conditions that can affect ion release, such as menopause, chronic systemic diseases, thyroid disorders, metabolic disorders, etc.

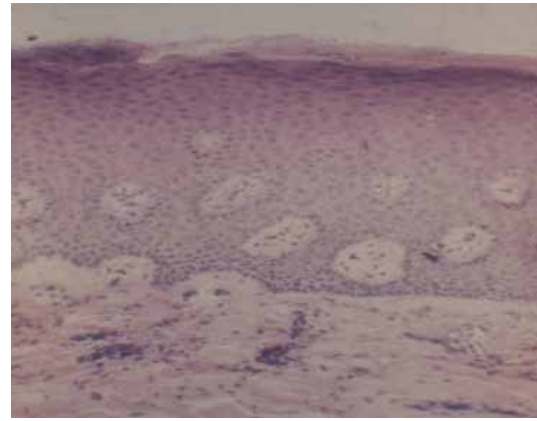
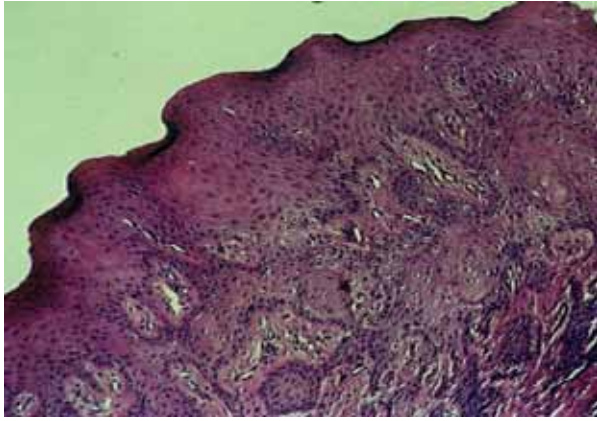
The data were collected after clinical and paraclinical examinations, and the information was recorded in the patients' observation forms. The characteristic parameters, such as age, origin environment, and sex, were quantified and represented. The presence or absence of subjective symptoms related to the characteristic pathology was also recorded.

The morpho-pathological examination involved the structural analysis of mucosal material taken from the underlying oral mucosa of the bridge or the gingival mucosa near the dental restorations. Biopsy specimens taken during pre-prosthetic surgical interventions were processed for standard examination under light microscopy, following the standard preparation and examination steps :

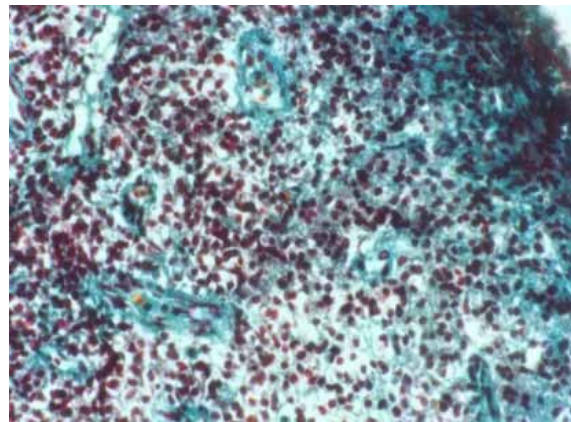
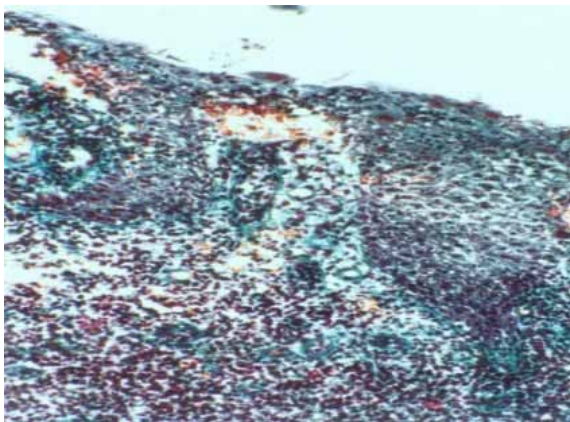
- Fixation for 24 hours in 10% formaldehyde solution in 0.1M phosphate buffer at a pH of 7.2 at 40°C (allowing preservation of the fragment)
- Embedding in paraffin
- Sectioning using the Reichart rotary microtome to obtain sections of 3-5  $\mu\text{m}$  for routine staining
- Mounting the sections on glass slides and drying them
- Actual staining, which included routine hematoxylin-eosin (HE) staining for general histological structure, and the Trichrome staining variant (Szekely) to highlight collagen fibers.
- Evaluation of mucosal changes was performed based on the morphological characteristics of epithelial and connective tissues, as well as the appearance of vascularity through microscopic examination.

### RESULTS

The microscopic examination of the oral mucosal samples obtained from biopsy and staining revealed that, in most cases, there were



**Fig. 1.** Inflammation of the mucosa due to mechanical irritation (col HE 100x): thickened gingival epithelium with elongated epithelial ridges



**Fig. 2.** Slightly ulcerated epithelium with lymphoplasmacytic infiltrate in the chorion and vasodilatation (col. Trichrome 100x)

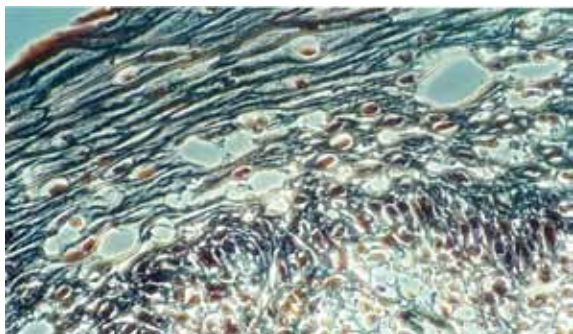
**Fig. 3.** Dystrophic lesions with dyskeratosis and lymphoplasmacytic inflammatory infiltrate with macrophages (col. Trichrome 200x)

subacute or chronic corio-epithelial inflammatory changes beneath the prosthetic restorations. The mucosa collected from the control patients, who did not exhibit clinical reactions to the prosthetic materials, showed varying degrees of epithelial thickening with elongated epithelial ridges, which were sometimes filiform and other times sinusoidal. These thickening and elongation of the epithelium can be considered as an adaptation to low-intensity mechanical irritations caused by food manipulation during the masticatory process. The superficial layers of the epithelium were well-represented, and there was no notable inflammatory infiltrate in the corion layer. It is important to note that not all mucosal reactions encountered in this study can be solely attributed to the prosthetic material used (fig. 1).

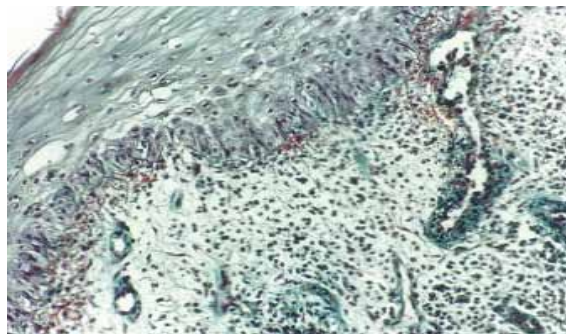
The presence of mechanical micro-irrigation exerted over time on the mucosa by Cr-Co-based dental restorations, without major differ-

ences compared to other alloys used, can be highlighted on histological preparations as images showing atrophic changes in the epithelial extensions. These extensions are reduced in number, flattened, and have a decreased height, attributed to a reduced number of cellular layers in the spinous layer. The cells appear flattened, and the intercellular spaces are small. On the other hand, the superficial layer is well-represented, while the underlying connective tissue (corion) appears densified with thickened and flattened papillae. This can make the corio-epithelial border appear blurred and flattened. However, the basal cells are well-organized and clearly demarcated from the superficial corion by a distinct basal membrane. In some clinical situations accompanied by inflammatory phenomena, the gingival epithelium may appear normal or slightly modified. Sometimes, there may be small discontinuities in the epithelial layer with minimal thickening of the epithelial





**Fig. 4.** Hypoplastic gingival epithelium. The basal layer with hyperchromic nuclei and mitotic figures (col. Trichrom. 200x)



**Fig. 5.** Degenerative aspect of the spinous layer with lymphoplasmacytic inflammatory infiltrate in the chorion. (col. Trichrome 200x)

layer, which can be attributed to irregular corial papillae located closer to the epithelial surface. Additionally, there may be vasodilation and an inflammatory infiltrate consisting of lymphocytes and plasma cells. Overall, the histological findings suggest that the presence of mechanical microirritations from Cr-Co-based dental restorations can lead to atrophic changes in the epithelial extensions and alterations in the corion and inflammatory responses in some cases (fig. 2, fig. 3).

A less common histopathological image is represented by a gingival mucosa specimen taken from a case with Cr-Ni restorations, in which significant changes are observed in the epithelium. The epithelium appears hypoplastic with pronounced dyskeratosis in the spinous layer, manifested by flattened cells, evident ballooning with clarification of the cytoplasm and intercellular spaces, and homogeneous acidophilic content. Parakeratinization is present in the superficial layer. The basal layer is composed of cells with hyperchromic nuclei and a few mitotic elements. The appearance is similar to that found in contact dermatitis, as a response to the restorative material releasing composition-derived products in the oral cavity (fig. 4).

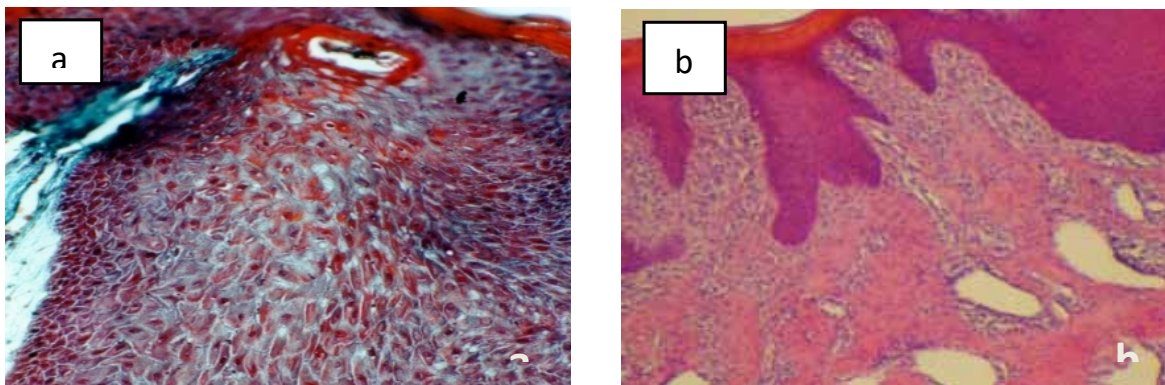
Based on the histopathological findings in the oral mucosa adjacent to acrylic restorations, degenerative changes have been observed. These changes are characterized by evident parakeratinization in the superficial layer and a dyskeratotic appearance with cytoplasmic clarification in the spinous layer of the epithelium. The basal layer appears clearly in the histological image, exhibiting a moderate number of mitotic figures, indicating a regenerative tendency compared to the degenerative changes seen in the spinous layer. Within the connective tissue

(corion), there is a diffuse infiltrate of lymphocytes and plasma cells, along with dilated venules and capillaries ( fig. 5)

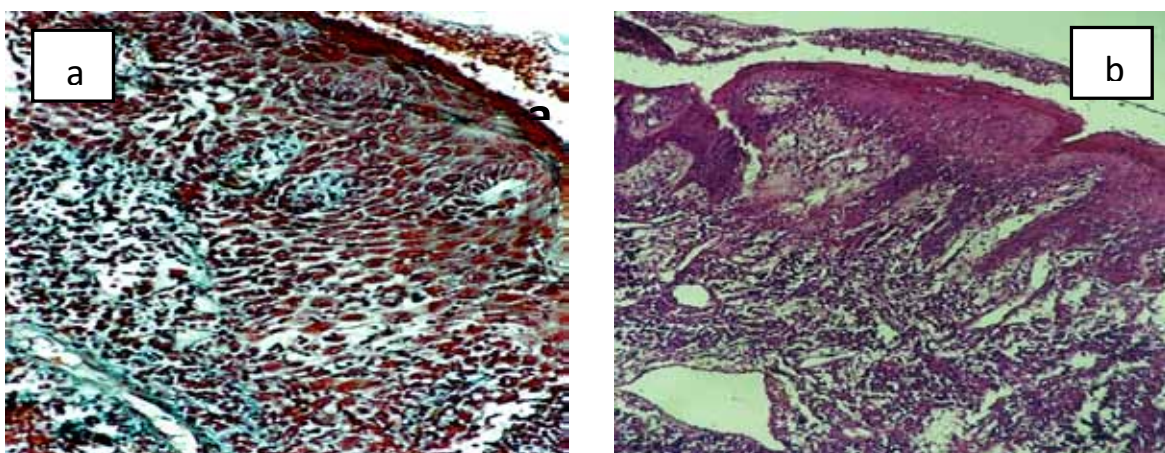
The reduced inflammatory phenomena clinically observed in the majority of cases with simple Cr-Co alloy restorations or ceramic-coated restorations, as well as those made from ceramic on a zirconia framework, can be justified by the morphological aspect of the epithelium in response to traumatic effects. The mentioned changes in the morphological aspect of the epithelium, such as thickening, ortho- or parakeratosis, irregular papillae, and proximity to the surface of the epithelium, are often observed around dental restorations, especially in cases where the restorations have been in place for a longer period. The underlying connective tissue usually does not show apparent changes (fig. 6a, fig. 6b).

The presence of a dyskeratotic epithelium with pronounced acantholysis in the spinous layer, parakeratinization, and a superficial layer of cellular debris caused by significant cell desquamation suggests an evident chemotoxic or allergic action from the Ni-based alloy. This finding may indicate a potential adverse reaction to the alloy, leading to tissue damage and compromised defense mechanisms. The cellular desquamation in patches indicates a decrease in the protective function of keratin. Moreover, the presence of a mononuclear, lymphoplasmacytic infiltrate in the superficial corion is associated with abundant vasodilation and desquamation of anucleated cells (fig. 7).

On preparations taken from edematous and often hypertrophic mucosa underneath the prosthetic works made from a Cr-Ni alloy, a hypertrophied epithelium with superficial erosions, larger intercellular spaces, and occasional ab-



**Fig. 6.** Gingival mucosa with epithelium of uneven thickness, with hypertrophic and atrophic areas with parakeratosis and chorial papillae approaching the surface (col. HE 100x)



**Fig. 7.** Gingival mucosa with a dyskeratotic epithelium, acantholysis and cellular desquamation, lympho-plasmacytic infiltrate in the chorion (a) ; hypoplastic epithelium, desquamation of anucleated cells, polymorphonuclear infiltrate and vasodilatation (b) (col. HE 100x).

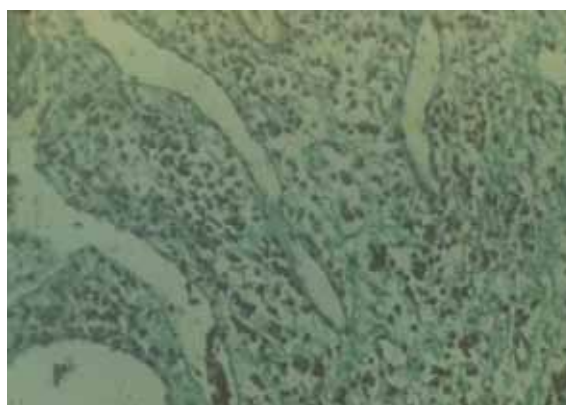
sence of the superficial layer is evident. The underlying connective tissue (corion) exhibits dilated blood vessels and abundant perivascular lymphoplasmacytic inflammatory infiltrate (fig. 8).

Within cellular polymorphism, plasma cells, which have the ability to develop specific antibodies against antigens present in the oral environment, are frequently encountered among immune cells. It appears that over 80% of IgA synthesized in the body is the result of plasma cells located in the mucosal stroma.

In some situations, we have observed a densification of the connective tissue, with thickening of connective fibers and few cellular elements, along with collagenization and fibrosis of the mucosal stroma. In certain limited areas, the fibrosis process seems to be quite accelerated.

**DISCUSSIONS**

The inflammatory characteristics of the observed soft tissue seem to be constant but var-



**Fig. 8.** Edema appearance of the gingival mucosa in Cr-Ni alloy (col. Trichrome 100x)

iable in intensity in the oral or gingival mucosa neighboring restorations made from nickel-based alloys or acrylic-veneered restorations, which are still quite frequently encountered in practice in recent decades. It is known that the threshold of sensitivity of the oral mucosa to toxic agents is much lower compared to the cutaneous epi-



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thelium, due to the anatomical and physiological characteristics of the oral mucosa (low representation of fatty tissue, influence of saliva flow, increased absorption capacity) (6, 7, 8).

The absence or partial absence of the stratum corneum can contribute to the rapid removal, degradation, or transformation of allergens, followed by hematogenous drainage of the resulting compounds (5, 9, 10). The present allergic reactions are contact reactions, with strictly localized symptoms in areas that come into direct contact with the salivary film.

The occurrence of neighboring reactions at the mucosal level depends not only on the pH value of saliva and buffering capacity but also on the potential for mucosal damage caused by the released ions. In this context, it should be noted that the capacity of ions released from dental restorations in the oral environment, as well as the level of salivary secretion, should be taken into account when estimating the risk of lesion formation or growth in patients, which contributes to increased ion release in the oral environment (11, 12).

Chromium-Cobalt (Cr-Co) alloys used rarely induce local allergic reactions, primarily attributed to chromium ions. However, the possibility of distant skin reactions cannot be ruled out. Nickel (Ni), which is present in a proportion of 1-20% in Ni-containing Cr-Co alloys, can induce allergic reactions in patients with increased sensitivity. Nevertheless, research indicates that due to their low solubility and high corrosion resistance, Cr-Co alloys have noble alloy characteristics. Studies show that in cases of allergy to chromium, cobalt, or nickel, the alloy formed by combining these elements is generally well-tolerated, with allergic reactions occurring exceptionally rarely, as demonstrated in our study (12, 13, 14).

As a consequence of the corrosion and degradation processes of dental restorations in the oral environment, older restorations can develop porosity that can harbor bacteria from dental plaque, leading to more or less severe inflammatory reactions. This can result in significant dystrophic changes in the neighboring mucosa, such as dyskeratosis, infiltration of mononuclear lymphoplasmacytic inflammatory cells, and a tendency for epithelial discontinuity (4, 15).

The presence of acantholysis at the cellular level, a consequence of micro-irrigation in the

epithelium, regardless of the restorative material used, allows for the penetration of bacterial toxins (10, 11). The abundant presence of leukocytes and plasma cells within the inflammatory infiltrate indicates a local defense response to constant microbial presence, typically observed in moderate quantities (as seen with Cr-Co restorations and ceramics) or a more pronounced inflammation in cases where a significant amount of microbial flora is retained (as observed with acrylic restorations or Cr-Ni restorations where surface degradation is more evident).

Nickel appears to be frequently implicated in the occurrence of significant reactions, particularly lichenoid reactions in neighboring tissues. This may be because all dental materials, especially monocomponent materials, have a certain solubility in saliva, as observed in the conducted study (16). The frequency of ulcers observed with Ni-based alloys may be attributed to the increased number of patients presenting with complaints, suggesting the involvement of corrosion products released into saliva. The most evident reaction of corrosion products from dental alloys on soft tissues is observed in contact with  $Ni^{2+}$  ions. Relatively reduced effects are observed on tissues exposed to  $Co^{2+}$  ions.

### CONCLUSION

The study of morpho-pathological preparations highlighted the occurrence of atrophic epithelial changes, with a reduction in its thickness, while the papillary ridges were reduced in number, thickened, and flattened, with a densified corium, leading to a blurred corio-epithelial boundary. Modifications occurring at the epithelial level were observed when traumatic factors intervened, with changes in epithelial keratinization (parakeratinization, hyperkeratinization), thickening or, on the contrary, thinning in cases of chronic micro irritations, integrity alterations affecting different depths, or alterations in interpapillary digitations with arborescent appearance. Additionally, bundles of more or less thick collagen fibers were observed in the corium, along with cellular elements, blood vessels, and active inflammatory reactions in the connective tissue, especially when microbial flora is retained in the remaining rough areas on the surface, accelerating plaque formation.

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### \* Corresponding authors

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Carina Balcos  
e-mail: carinutza2005@yahoo.com