

# Does My Mouth Show My Age?

## Aging of Oral Mucosa: Correlating underlying changes with clinical patient needs

A Peer-Reviewed Publication  
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## Educational Objectives

At the conclusion of this educational activity participants will be able to:

1. Explain why it is important to separate aging processes from disease processes.
2. Contrast the signs of aged oral mucosa with the aged skin and lips.
3. Relate how repair within the oral mucosa changes with age.
4. Describe the future prospects for controlling the effects of aging within the oral mucosa.

## Abstract

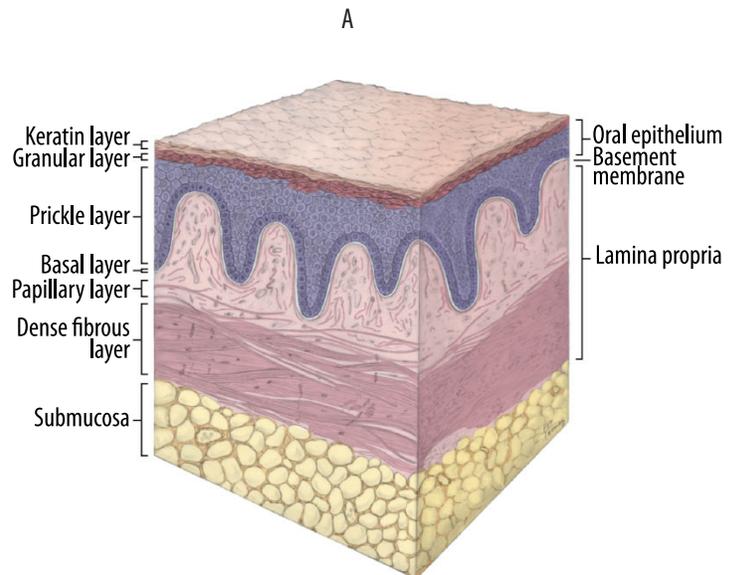
Geriatric individuals comprise the most rapidly growing population segment in the U.S. The unique needs of this subgroup will impact the oral health of our patient base. The goal of this course is to understand how the patients' aging oral mucosa affects their clinical needs. Clinicians need to distinguish aging processes from disease processes, and to examine the signs of aging within the oral mucosa as well as the underlying microscopic changes. This includes details concerning how the repair of the oral mucosa is affected. The basic histology of the oral mucosa will be reviewed as well as future prospects for controlling the effects of aging in the oral mucosa.

## Aged or Diseased Oral Mucosa?

The oral cavity has correctly been described as a mirror that reflects the health of the individual.<sup>1</sup> Changes indicative of disease can manifest as alterations in the oral mucosa lining the mouth. Thus the mouth can reveal systemic conditions such as diabetes or vitamin deficiency, or the local effects of tobacco or chronic alcohol use. Outside the realm of disease is the occurrence of aging and its impact on the oral mucosa. The novel approach to overall consideration of aging is to distinguish it from any disease states that can occur.

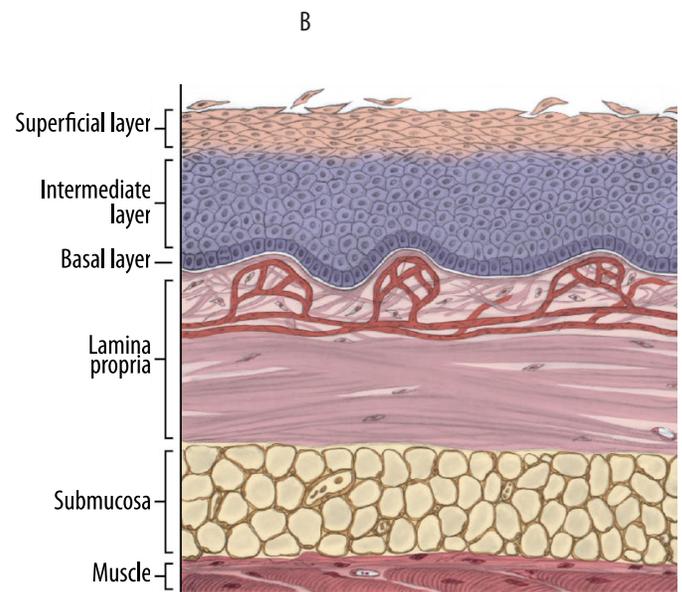
When disease states are separated from the consideration of aging, one may start to ask critical questions concerning the aging of the oral mucosa such as: What are the signs of aging of the oral mucosa that I may see in my patients of advanced age? Can the mouth really show the patient's exact age? How does the aging process of the oral mucosa affect their clinical care? Are there any interventions to stop or modify the aging process of the oral mucosa I can share with my patients? What does the future hold for subsequent generations as they age as indicated by their oral mucosa?

The geriatric population is the most rapidly growing segment of the general population, a fact which will have dramatic implications in the future for the systemic health and oral health of our patients.<sup>2</sup> Therefore the dental professional needs to be ready to meet the clinical needs of this new population of older patients.



Oral Mucosa  
(and underlying tissues)

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Nonkeratinized Stratified Squamous Epithelium  
(and deeper tissues)

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Figure 1: Microscopic view of layers of oral mucosa lining the oral cavity for both keratinized regions (A) and nonkeratinized regions (B) (From Fehrenbach, MJ and Popowics, T. *Illustrated Dental Embryology, Histology, and Anatomy*, ed 4, Saunders/Elsevier, 2015).

## Oral Mucosa Review

Microscopically, the oral mucosa almost continuously lines the oral cavity (Figure 1). The oral mucosa is composed of stratified squamous epithelium overlying a connective tissue proper, or lamina propria; these two tissue types are equivalent to the epidermis and dermis of the skin and lips, respectively.

Even though the entire oral cavity has these two basic tissue types, regional differences are noted throughout in the oral mucosa. For example, the oral mucosa is perforated in various regions by the ducts of salivary glands. Other regions have thinner or thicker layers of epithelium present and some regions of the lamina propria contain specialized elastic fibers.

The oral mucosa can be keratinized or nonkeratinized, depending on the region. All types of epithelium act as an environmental barrier to pathogenic invasion and mechanical irritation as well as offering protection against desiccation. These protective features are accentuated in the types of epithelium that contain keratin, which is like the callus formation over the skin or lips.

Keratinized oral mucosa is associated with masticatory mucosa and generally noted in the hard palate as well as the attached gingiva surrounding the roots of the teeth and most lingual papilla of the dorsal surface of the tongue.

Nonkeratinized oral mucosa is associated with lining mucosa generally noted in the buccal mucosa, labial mucosa, alveolar mucosa, floor of the mouth, ventral surface of the tongue, and soft palate. Nonkeratinized epithelium is the most common form of epithelium in the oral cavity. Unlike keratinized epithelium, nonkeratinized epithelium usually has no superficial layers showing keratinization. Nonkeratinized epithelium may, however, readily transform into a keratinizing type in response to frictional or chemical trauma, in which case it undergoes hyperkeratinization.

Both types of oral mucosa, masticatory and lining respectively, show many layers, with regeneration occurring within the tissue during its specific turnover times. Repair is possible within the oral mucosa with minor injuries and very little scarring is noted.

## Orofacial Signs of Aging With Underlying Changes

Aging is a complex, continuous, and slow process that gradually involves most if not all organs of the body, causing “abnormal functioning in both qualitative and quantitative terms, as well as morphological or structural changes”.

The signs of aging of the skin and lips are usually more conspicuous than that of the oral mucosa. An initial sign of aging in the skin and lips that can be noted by the dental professional during an extraoral examination is the increase in facial wrinkling and lines around the mouth (Figure 2). This includes the creasing and then cracking at the labial commissures. Measures can be taken to fill out the area with cosmetic fillers or the use of plastic surgery to smooth out the area.

However, these wrinkles and lines are primarily the result of a loss of vertical dimension (Figure 3). The resorption of the



Figure 2: Aging of skin and lips (A) with facial wrinkling and lines around the mouth is more conspicuous than that of oral mucosa. However, aging of oral mucosa (B) does reflect some of same changes observed in skin and lips such as gingival recession of the attached gingiva causing root exposure, possibly resulting in root caries and periodontal disease (as shown) (A from Durai PC, et al. *Aging in Elderly: Chronological Versus Photoaging*. *Indian Journal of Dermatology, Open-i Project, Library of Medicine*, 2012 at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3482795/>; B from Fehrenbach, MJ. *Personal Collection*).

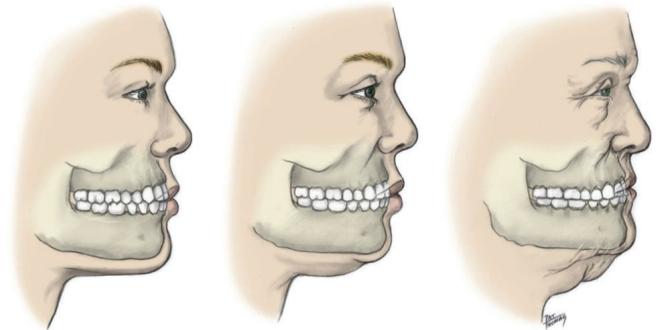


Figure 3: Loss of vertical dimension in lower third of the face in twenty-year increments (ages 20, 40, 60) as alveolar process resorbs. The dentition has also undergone a reduction in height by attrition from mechanical wear of masticatory surfaces. This results in facial wrinkles and lines around the mouth (From Fehrenbach, MJ and Popowics, T. *Illustrated Dental Embryology, Histology, and Anatomy, ed 4, Saunders/Elsevier, 2015*).



Figure 4: Fordyce spots (or granules) within buccal mucosa, a non-pathological oral variant that is increased in patients with advanced age (From Migliorati, CA, et al. *Diagnosis and Management of Oral Lesions and Conditions: A Resource Handbook for the Clinician, InTech, 2014*).

alveolar bone, coupled with usual attrition of the teeth, causes a loss of height of the lower third of the face when the teeth are in maximum intercuspation.<sup>1</sup> The extent of this loss is determined based on clinical judgment using the Golden Proportions. This part of the vertical dimension is important in determining the way in which the teeth and jaws function.

In addition, as the proper amount of height in the lower third of the face is reduced, the facial wrinkling around the mouth increases as the skin sags and loses its resilience with age. With the loss of vertical dimension, older patients can take on a cartoonish “Popeye” facial appearance that is esthetically displeasing and may result in diminished function of the teeth and jaws.

The loss of vertical dimension can be exacerbated by pathology such as tooth loss, severe periodontal disease or increased levels of attrition, as noted with the parafunctional habit of bruxism. The overall goal must be to protect the natural vertical dimension inherent in a patient’s face. Retention of the dentition by preventive maintenance, damage control for habits, and restorative care as well as replacement by prosthesis helps preserve the vertical dimension. Thus the patient is prevented from not looking older than their chronological years.

Also the exposure to the environment including solar damage must be taken into account along with facial aging since this can break down the deeper tissue of the dermis. In comparison, the oral mucosa is protected from the sun and its effects as opposed to the skin and lips. Other increased environmental toxicity, such as chronic alcohol and tobacco use, can also amplify the impact of aging on the skin and lips as both also break down the components of the facial dermis.<sup>1</sup>

Patients more easily note these facial signs of aging and seem intent on stopping its impact. However, it is up to the dental professional to tie these outward signs of aging to that which can occur to the inner oral mucosa. This will enable the patient to begin preventive methods to reduce the impact of the aging oral mucosa as well as their overall oral health.

### Aged Oral Mucosa With Underlying Changes

The effects of aging upon skin and lips have been considered in numerous studies as well as professional and over-the-counter treatments that patients are aware of, but the affect of aging on the oral mucosa has received comparatively little attention.

The aging of the oral mucosa does reflect some of the same changes observed within the skin and lips (Figure 2). As with any type of aging consideration, one’s perceived age is a better biomarker of skin and lip aging, as well as aging of the oral mucosa, than actual chronological age.

Similar to aging of the skin and lips, it is sometimes difficult to distinguish changes caused by aging in the oral mucosa from changes caused by disease or lack of oral care. Examples such as severe root exposure from gingival recession in the aged population can be more a sign of chronic periodontal disease than of



Figure 5: Varicosities within ventral surface of tongue, a non-pathological oral variant that is increased in patients with advanced age (From Chu CH, et al. *Oral health of Chinese people with systemic sclerosis. Clinical Oral Investigations, Open-i Project, Library of Medicine, 2010 at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3212684/>*)



Figure 6: Xerostomia causes inflammation of the oral mucosa as shown with the tongue. Hyposalivation is not directly due to aging but mainly due to medications taken by older individuals such as this patient, who was newly prescribed antidepressants (From Fehrenbach, MJ and Popowicz, T. *Illustrated Dental Embryology, Histology, and Anatomy, ed 4, Saunders/Elsevier, 2015*).

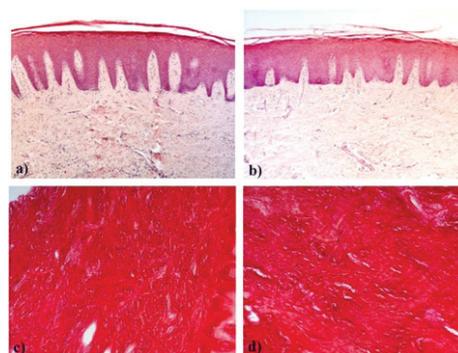


Figure 7: Microscopic view of both young oral mucosa (a, c) and old oral mucosa (b, d), with its epithelial thinning, loss of prominence of rete ridges, and blunting of underlying connective tissue papillae, as well as increased fibrosis of connective tissue of lamina propria (From Gagliano N, et al. *Effects of Aging and Cyclosporin A on Collagen Turnover in Human Gingiva. Open Dental Journal, Open-i Project, U.S. National Library of Medicine, 2009 at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817891/>*).

age. The exposed root surfaces increase the risk for root caries, another sign of disease rather than of aging.

The most commonly noted sign of aging in the oral mucosa is the increase of Fordyce spots (or granules), which represent ectopic lobules of sebaceous glands within the labial and buccal mucosa (Figure 4).<sup>1</sup> These multiple raised yellowish papules can concern older adults during self-examination of their mouths. Patients should be reassured that they are presenting with a non-pathological oral variant if the clinician is asked about them.

Varicosities are another common visible sign of aging, occurring in approximately 40-50% of the aged population (Figure 5). Varicosities are abnormally dilated veins, and are not limited to the oral cavity. In the oral cavity they may be present in any location, but often involve the lips, buccal mucosa and labial mucosa, and lateral and ventral surfaces of the tongue.<sup>1</sup>

The exact etiology of these varicosities is unknown, but it may be associated with weakening of the vessel wall as a consequence of aging. Again, the older adult patients may need to be reassured after self-examination that they are again presenting a non-pathological oral variant.

With aging, the number and overall size of each lingual papilla on the surface of the tongue and its associated taste buds are also reduced through hypertrophy. This hypertrophy primarily affects the foliate lingual papillae on the lateral surface of the tongue. The overall loss of lingual papillae leads to increased smoothness of the tongue surface that must be differentiated from pathology such as a vitamin deficiency. This situation may also be related to changes in taste perception as a person ages.

Elderly have been noted to experience a reduction in taste perception by up to 80%, primarily associated with sweet, salty, bitter and acid substances.<sup>3</sup> Usually salty and sweet taste perceptions are lost first, followed by bitter and sour tastes. At age 20, there are around 252 taste buds per papilla. After age 75, this number drops to 88 taste buds per papilla, leading to partial loss of taste function, in addition to changes in appetite. If there is also dry mouth present, it can also have an additive negative impact on the sense of taste as can loss of the sensation of smell.

Hyposalivation, the reduction in the production of saliva, makes the oral mucosa drier and thus less protective against trauma and infection. This is because dry mouth or xerostomia causes inflammation of the oral mucosa, which can especially be noted with the tongue (Figure 6). Dry oral mucosa becomes thin and friable and susceptible to minor trauma, increasing the likelihood of infection. Xerostomia can also lead to increased root caries, problems in speech and mastication, as well as bad breath (halitosis) in the aged population.<sup>1</sup> However, reduction in salivary volume is not directly due to aging but mainly a side effect of medications taken by older individuals or concurrent disease processes that affect the salivary glands.<sup>1,3</sup>

Thus it is now accepted that significant changes in salivary flow are not observed in healthy elderly persons when they are not taking drugs with anticholinergic side effects. In addition,

no age-related decreases in the secretion of certain salivary constituents (e.g., total proteins, proline-rich proteins, lactoferrin, sodium, and potassium) are observed in a healthy population.

Interestingly, a few studies are reporting “significant age-related alterations in salivary function that were associated with the amount of caloric intake levels in nonmedicated elders”. Thus it is possible that a reduced caloric diet that can be present in the institutionalized or low functioning elderly may consequently reduce salivary function. This shows the need for increased studies concerning the elderly and their high risk of a compromised nutritional status and its effect on the oral mucosa.<sup>6</sup>

Aging of the oral mucosa has classically been noted microscopically as a reduction of its epithelial thickness due to atrophy (Figure 7).<sup>3</sup> However, the accepted change with age to a thinner epithelium or tissue atrophy is beginning to be questioned since new reports are citing that it may be likely “linked to the effects of systemic disease, drug therapy, or both, rather than an intrinsic biologic aging process of the mucosa”. Future studies hopefully will be able to discern if this epithelial atrophy is due to aging or disease states as they remove confounding factors in the research.

There is also a reduction in stippling of the attached gingiva with age (Figure 8). Stippling is observed clinically as small pinpoint depressions in younger mouths, which usually gives the attached gingiva an orange-peel appearance, indicating the pull of the epithelium toward the lamina propria in these areas, a process that is analogous to the button tufting on upholstery.<sup>1</sup> The loss of stippling on the surface of the epithelium makes the tissue appear as if it were pulled smoother over the underlying lamina propria.

With these overall changes in both the epithelial thickness and stippling due to aging, the physical protection the epithelium provides for the deeper lamina propria and its components such as blood vessels and lymphatics could be compromised. This epithelial barrier serves as protection against mechanical,



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Figure 8: Reduction of surface stippling on attached gingiva is noted with increased age, which makes it appear smoother. In addition, the degree of keratinization starts to decline in the masticatory mucosa, giving the tissue a “satin-like” appearance. Increased fibrosis of underlying lamina propria making the tissue firmer with palpation. Slight to moderate gingival recession is also noted (From Fehrenbach, MJ and Popowicz, T. *Illustrated Dental Embryology, Histology, and Anatomy*, ed 4, Saunders/Elsevier, 2015).

thermal, chemical, and biological damage to these deeper layers. If compromised with aging, the risk of trauma and infection is increased.

At the same time, microscopically, the thickness and number of rete ridges in the epithelium diminishes and the underlying connective tissue papillae become blunted as the oral mucosa ages.<sup>1,2</sup>

In addition to the loss of usually prominent rete ridges, the degree of keratinization starts to decline in the masticatory mucosa. This primarily occurs in the attached gingiva, producing a “satin-like” appearance of the tissue. While cell division at the basal layer of the epithelium does not slow down, studies show that the turnover times do slow down for all regions of the oral cavity. As a result, the tissue of the oral cavity goes into an overall decline in its production of younger cells and fibers.

Usually noted during an intraoral examination of an elderly patient is recession of the attached gingiva (Figure 8). This withdrawal varies due to genetic, external, local and systemic factors. It can predispose the dentition to periodontal disease and root caries.

Like most tissues of the body, the oral mucosa usually undergoes regeneration as the individual cells die. Regeneration occurs through growth and differentiation of the same type of tissue that has been destroyed or from its precursor. It is a continuous physiologic process that occurs with most tissue types and in most organs within the body, with both injury and disease. The turnover time is the time it takes for the newly divided cells to completely replace the tissue or associated organ within a body system.<sup>1</sup>

The overlying epithelium within oral mucosa is usually capable of rapid cellular turnover. Thus younger epithelium is highly regenerative because its deeper germinal cells are capable of reproduction by mitosis in the basal layer. In fact, the epithelium of the oral mucosa generally has a faster turnover time than the epidermis of the skin and lips.<sup>1</sup> This difference becomes apparent when a superficial injury to the facial skin or lips lasts for weeks as opposed to the quicker healing after the patient accidentally bites down on their cheek.

But with the aging process, the overall ability of the oral mucosa to repair itself is reduced and the length of the repair time is increased.<sup>2</sup> Thus your patient may take longer to heal as they age. The ability to repair affects the deeper tissue of the oral mucosa as well such as the underlying periodontium that supports their dentition.

Microscopically, changes also occur in the composition of the matrix of the lamina propria and in the production of a less well defined division between its papillary and dense layers in older oral mucosa (Figures 7 and 8).<sup>1</sup> Collagen fibers appear thickened and are arranged into dense bundles resembling those found in tendons or ligaments.<sup>3</sup> This is related to the fibrosis of the lamina propria of aged attached gingiva with its noted increased firmness upon palpation.

Elastic fibers, if present in the lamina propria of the oral region, also appear changed to some extent, even though more of them are present. These elastic fibers show structural degenerative changes with aging. This change in elastic fibers may explain the loss of resiliency found in aged oral mucosa as well as the skin and lips, which reduces its rebound after force is applied. However, the relative changes with age in either elastic or collagen fibers have not been quantified even within other regions of the body.

Within the aged lamina propria, the fibroblasts are now decreased in quantity, appear smaller, and are less active in older oral mucosa. The entire lamina propria has a slower collagen turnover time. However, unlike the lamina propria of the attached gingiva, the nearby interwoven periodontal ligament does not show any significant changes related to aging alone.

Finally, Langerhan cells become fewer with age, which may contribute to a decline in cell-mediated immunity of the oral mucosa. These are stellate dendritic cells found within the oral mucosa, which are derived from precursors in the bone marrow. Langerhan cells reside in the epithelium of many oral regions, but the frequency in the buccal epithelium is considerably higher than the numbers in the attached gingiva and floor of the mouth, but not as high as the adjacent skin and lips.

These cells provide the oral mucosa with tolerance to antigens since they take up and process these foreign structures allowing cell-mediated immunity to occur. Cell-mediated immunity is an immune response that does not involve antibodies as does the humoral immunity, but rather involves the activation of phagocytes, antigen-specific cytotoxic T-lymphocytes, and the release of various cytokines in response to an antigen. Cell-mediated immunity is important in fighting certain disease states such as oral lichen planus and Sjögren syndrome, which are present in higher numbers within an older population.

Recently, to see how aging affects the immune system, the researchers have looked at Down syndrome. This is a chromosomal disorder resulting in various abnormalities, but most importantly to this discussion, it forces the person to age prematurely. Several studies have also focused on abnormalities of the immune system in individuals with this syndrome, demonstrating selective cell-mediated immunodeficiency, defective neutrophil polymorphonuclear leukocyte chemotaxis, and impaired antibody response to specific pathogens, low T-cell lymphocyte counts, and immature subsets of T-lymphocytes. This leads these individuals to have an increased risk of infection, including those of the oral mucosa.

Similar effects could be serious to the health of the oral mucosa since “age-related declines in immune function cause more susceptibility to infections” as noted in those with Down syndrome. For these individuals this frequently involves *Candida albicans*, which also has increased prevalence in the elderly. In aged patients, this fungal infection may result in denture stomatitis as well as candida angular cheilosis as op-

posed to thrush in young patients. It hypothesized that the susceptibility to mucosal infections is caused not only by an innate abnormal immune response brought on by chromosomal damage, but also by acceleration of aging in individuals with Down syndrome. Thus there must always be a concern for the risk of infection such as oral candidiasis due to a less effective immune system in the aged population.

Nerves and end organs in the oral mucosa may also be affected by increased age, brought about mainly by arteriosclerotic processes. These processes related to age affect the entire body by causing the progressive obliteration of smaller capillaries and the overall reduction of cell metabolism. The effects on the oral mucosa include a progressive loss of sensitivity to mechanical, thermal and chemical stimuli, while gustatory ability related to swallowing also declines with advancing age.

The type of reactions of the oral mucosa to placement of an oral prosthesis changes with increased age. In younger patients, mechanical irritation that may occur with a poorly placed oral prosthesis tends to give rise mainly to painful inflammation and swelling, while chronic atrophic processes involving oral ulcers are the predominant response in old age.<sup>3</sup>

### **Patient Clinical Needs Due to Aged Oral Mucosa**

With the increasing age of the patient population, the dental professional must consider the affects of aging on the oral mucosa during dental treatment, especially those dealing with longer healing times. Extended healing time must be discussed with the older patient since it can impact appointment scheduling. Appointments for dental procedures such surgery as well as nonsurgical periodontal therapy may need to be scheduled so less is done per appointment, thus allowing the healing process to catch up, reduce discomfort, and allow for the best patient outcomes.

Post dental treatment diet should be limited to lukewarm foods that are soft, moist, and easy to chew or thinned with liquids such as broth, milk, yogurt, or gravy. Foods that are crunchy, sharp, spicy or acidic that may cut or scrape the oral mucosa should be avoided. These temporary dietary changes will help prevent any further oral injury and provide comfort as well as maintain nutritional levels needed for healing.

It is also important to keep in mind that prolonged oral discomfort may prompt a change to a long-term “junk food” diet, thus increasing their caries risk. This is especially true of those patients having a negative experience with oral prostheses. The elderly should be monitored after placement of a dental prosthesis for any signs of discomfort or adverse tissue response such as atrophy.

Knowing that the epithelium of the mouth possibly has undergone generalized atrophy, your older patients need to be considered more fragile to the trauma that can occur during dental procedures. When looking at a specific dental procedure such as local anesthesia administration, excess pressure on the oral mucosa that can occur may produce bruising resulting in

an oral hematoma. Other commonly performed procedures such as prolonged use of either the rubber dam and high-speed suction as well as aggressive wiping of the tissue with gauze may also adversely affect the more fragile nature of their aged oral mucosa, causing oral ulcerations.

However, short-term use of the rubber dam and bite block may prevent issues dealing with the swallowing difficulties brought on by aging. Placing the patient upright during most of the dental appointment may also be necessary, as well as use of nitrous oxide to relax any gag reflex. Also giving the patient time to react to rinses, using less volume when flushing, and overall not rushing care may prevent any dramatic gasping moments.

Care must be taken with extreme changes in water temperature when flushing the mouth as well as any use of chemicals or lasers that may possibly burn tissue. This is due to the lack of neural sensitivity from the intrinsic changes in the nerves with age. Thus older patients may not pick up on any related early tissue response before irreversible tissue damage has occurred. Pre and post-treatment use of gentle antimicrobial oral rinses can reduce the higher risk of infection in the aged from a less effective immune system.

Noting any further thinning of the oral mucosa such as with oral ulcerations needs to an important part of the intraoral examination procedures in the elderly, such as that which occurs with ill-fitting prosthesis or accidental self-inflicted injury.<sup>12</sup> With these serious lesions, the more aggressive use of stronger oral rinses with chlorhexidine, or oral antibiotics, may be needed to prevent oral infection.

Discussion of the loss of taste perception may come up with your elderly patients. The general reasons on how age affects one's taste sensation need be explained to those who have this concern. However, this situation may need to be considered for medical consultation to a certified nutritionist if it affects the patient's overall health or an increased risk of caries is again noted along with a newly acquired “junk food” diet.

Prevention is key to aging gracefully and avoiding any tangle with systemic disease states and this certainly holds true for oral mucosa. Certain cases of trauma related gingival recession of the attached gingiva might be prevented by appropriate toothbrushing techniques or utilization of a mouthguard. Other cases may be multifactorial but still need to be part of the overall treatment plan.

Also support of a sound diet will keep your patients healthier regardless of their age, as well as avoiding use of tobacco and excessive alcohol consumption. Management of xerostomia must also be actively pursued in the aged population to prevent side effects as discussed. This may involve rinses, lubricating sprays or gels, and chewing special gums.<sup>12</sup>

Finally, reminders that regular dental maintenance visits are still a priority for long-term oral health may also need to be reinforced. Budget concerns for dental care may become an issue with retirement from jobs that offered insurance benefits.

However, self-care should be a number one priority since it can avoid many of the factors that add to the aging level of the oral mucosa and the risk of oral disease.

### Future for Aging Oral Mucosa

What does the future hold for controlling or even reversing the aging of oral mucosa? The answer to the age-old search for the “fountain of youth” in regards to aged oral mucosa may be the most common cell in all types of connective tissue, the fibroblast (Figure 9). Fibroblasts synthesize intercellular substances and certain types of protein fibers. They are needed to sustain the connective tissue of the body, including the lamina propria of the oral mucosa.<sup>1</sup>

Different types of protein fibers are found in various types of connective tissue. The main connective tissue fiber type found in the body, as well as the lamina propria, is the collagen fiber. Collagen fibers are composed of the protein collagen, including distinct types that have been shown by immunologic study to have great tensile strength. All collagen fibers are composed of smaller subunits, or fibrils, which are composed of microfibrils—similar to a strong, intact rope that is composed of smaller entwined strands of roping material.

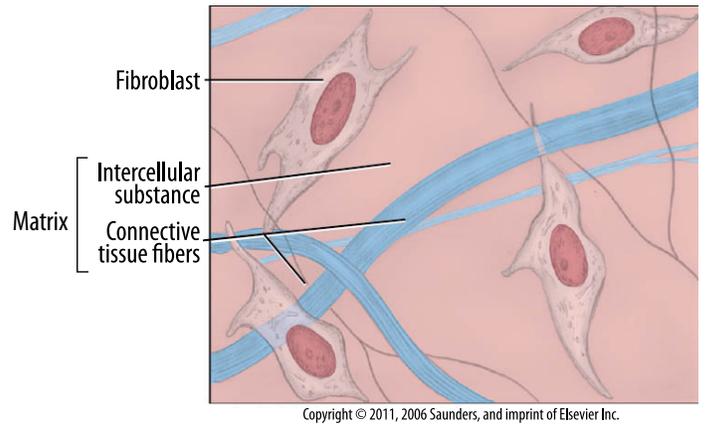
The elastic fibers are another type of protein fiber, composed of microfilaments embedded in the protein elastin, which results in a tissue that has the ability to stretch and then to return to its original shape after contraction or extension. Certain regions in the oral cavity, such as the soft palate, contain elastic fibers in the connective tissue of lamina propria to allow this type of tissue movement during mastication and speech.

Fibroblasts as a group appear as flat, elongated cells with cytoplasmic processes at each end. They are considered fixed cells in connective tissue, because they do not leave the tissue to enter the blood, as compared to mobile cells, such as white blood cells. Due to recent studies, we now know that subpopulations of fibroblasts may occur in connective tissue such as that of the lamina propria.

One of these fibroblast subpopulations are young fibroblasts that are actively engaged in the production of fibers and intercellular substance. However, as with all types of cellular aging, fibroblasts can become less active over time, with a resultant reduction in cytoplasm, mitochondria, and rough endoplasmic reticulum, which is also evident in the later stages of chronic advanced periodontal disease (Figure 10).

This cellular change in the older set of fibroblasts is considered a type of replicative senescence since there is less replication activity that drives fibroblasts to do their work.<sup>1</sup> Fibrosis and atrophy are now present within the connective tissue of the lamina propria in the oral mucosa as noted earlier with the obvious increased firmness of the attached gingiva upon palpation.

But what if the fibroblasts were adequately stimulated during repair, so that these formerly sluggish older fibroblasts could revert to a more active state? Producing more active fibroblasts could mean a youthful boost to the connective tissue of the



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Figure 9: Fibroblasts within young and healthy lamina propria of the oral mucosa surrounded by matrix of intercellular substance and connective tissue fibers they have produced (From Fehrenbach, MJ and Popowicz, T. *Illustrated Dental Embryology, Histology, and Anatomy*, ed 4, Saunders/Elsevier, 2015).

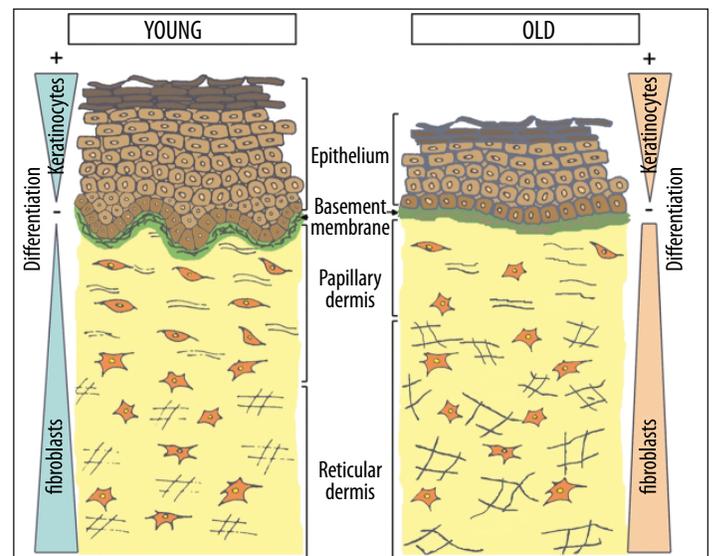


Figure 10: Young tissue of the skin and lips and old tissue, with its lower level of young fusiform fibroblasts and increased fibrosis of surrounding connective tissue as indicated by the crosshatched areas. Similar effects are noted in the oral mucosa. (From Mine S, et al. *Aging Alters Functionally Human Dermal Papillary Fibroblasts but Not Reticular Fibroblasts: A New View of Skin Morphogenesis and Aging*, PLoS ONE, Open-i Project, U. S. National Library of Medicine, 2008 at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2605251/>).

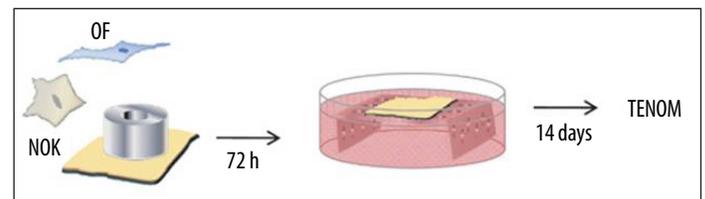


Figure 11: Methodology for producing full-thickness tissue-engineered “normal” oral mucosal models (TENOM): oral fibroblasts (OF) and “normal” oral keratinocytes (NOK) were seeded onto a scaffold within a steel ring and cultured (From Colley HE, et al. *Development of tissue-engineered models of oral dysplasia and early invasive oral squamous cell carcinoma*, British Journal of Cancer, Open-i Project, U.S. National Library of Medicine, 2011 at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3242522/>).

lamina propria. Thus the possibility of harnessing the power of fibroblasts to keep active within the underlying lamina propria may be another way to preserve the oral mucosa just waiting to be discovered. Also a more complete understanding of turnover time may be the future basis for how both the aging processes and disease processes in the body are delayed or fought, including aging and disease occurring in the oral mucosa.

Newer approaches for replacing injured oral mucosa include the use of autologous grafts and cultured epithelial sheets as well as the use of advanced healing agents such as platelet-rich plasma (PRP). Amelogenin proteins have been used for over 15 years to regrow hard and soft tissue, reversing gingival recession. Many of our patients may experience these newer approaches in their future dental procedures so we will need to keep up with technological advancements within dentistry. In a side note about technological advancements, oral mucosa from either the mandibular alveolar mucosa or buccal mucosa is now the primary donor tissue for the reconstruction of urethral defects.

However, even more fantastic in the future is the harnessing of the recent tissue engineering for our patients, which now includes that of oral mucosa. This advance combines cells and materials to produce a 3-D reconstruction of the tissue type so as to simulate its anatomic structure and function (Figure 11).<sup>1</sup> This shows promise for actual clinical use, such as the replacement of soft tissue defects in the oral mucosa that occur with severe gingival recession and even with a more serious disease state such as oral cancer.

In addition, future tissue engineering of the oral mucosa will have a direct impact on the approaches to biocompatibility of dental materials and oral healthcare products as well as therapies associated with implant or soft tissue interfaces. This new world technology may also be a reprieve for the aging oral mucosa in which we could virtually “prop up” the entire oral cavity to age more healthfully. That could take oral maintenance of our patients in dental practice to a whole new level.

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## Author Disclosure

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