ADITUM
Enrich your Research

Ophthalmology and Vision Care

Research Article

How Mandibular Movement Intersects with Ocular Lacrimation: A Literature Synthesis

Reza Rastmanesh[1,2]
[1]The Nutrition Society, London, UK.
[2]The American Physical Society, College Park, MD, USA.

Article Info

Received: March 20, 2025
Accepted: April 01, 2025
Published: April 15, 2025

***Corresponding author:** Reza Rastmanesh, School of Animal and Range Sciences, Haramaya University, Ethiopia.

Citation: Reza Rastmanesh, (2025). "How Mandibular Movement Intersects with Ocular Lacrimation: A Literature Synthesis" Ophthalmology and Vision Care, 5(1); DOI: 10.61148/2836-2853/OVC/045.

Abstract

The COVID-19 epidemic has led to the widespread use of face masks in an effort to reduce disease transmission. Face masks may contribute to the severity of dry eye disease. Possible mechanisms have been proposed, including leakage of air from the superior edge of the mask, passing over the eyes. There may be other factors as well.

There is a direct association between the salivary flow rate and the jaw muscle activity during speaking, chewing and mastication. There is also a positive association between dry mouth and dry eye. Agents that stimulate salivary gland secretions may concomitantly alleviate dry eye symptoms. This may provide a therapeutic opportunity that has not been explored in the past. Results of a recent experiment showed that chewing gum or candy alleviated dry eye. We hypothesize that chewing, mastication or speaking may have stimulated ocular lacrimation. We also suggest that impeded mandible jaw movement while wearing face masks may contribute to reduced lacrimation, leading to a worsening of dry eye disease. Face masks can additionally inhibit contagious yawning in community settings through impairment of both face recognition and emotion recognition and thereby can diminish yawning-mediated tear production. We discuss in this paper the role these mechanisms may play in the worsening of preexisting dry eye disease, as a result of face mask wearing. This may have implications for pharmaceutical and nutraceutical industries aiming to relieve dry eye and mouth and may provide ideas for improvements in face mask design that might reduce their impact jaw motion, and secondarily on dry eye disease.

Keywords: COVID-19; dry eye; face mask; mandibular movement; facial nerve

Introduction

Ocular problems due to face mask use during COVID-19 pandemic were first reported by Moshirfar et al [1]. Regular face mask wearing is accompanied with an increase in dry eye symptoms among some people [2-6] including contact lens wearers [2 ,7], negatively impacting visual quality. This phenomenon is especially important since it is expected that face mask use will continue for the foreseeable future. Many people including the young, are already at increased risk of dry eye disease because of increased screen time, as a result of the shift to online education [8], and other activities such as online shopping, web surfing and the use of mobile phones [9]. Since the beginning of the pandemic, people spend more time looking at screens which may exacerbate dry eye symptoms [5].

Factors contributing to dry eye are not homogenous. Thus, it is important to elucidate the underlying mechanism(s) in order to determine the best strategy to prevent and/or alleviate dry eye symptoms. We categorized possible mechanisms by which use of face masks may negatively impact dry eye disease, which led to our complementary hypothesis regarding the various factors affecting this problem.

Currently Proposed Explanations and Mechanisms:

Mechanical Explanation:

This explanation mainly focuses on poor fit of the mask or looseness of mask apposition against the face and nose, so that some airflow is directed towards the eyes. The face mask may also interfere with lubricating agents reaching the eyes, because of fears patients may have about potential contamination from hands and drug containers during mask wear [10]. Other mechanical ventilation factors may possibly intensify and exacerbate airflow effects as well.

Recent experiments by Ding et al [11] (using infrared thermography with measurement of maximum interblink period and ocular surface temperature) support this hypothesis and provide a pathway by which faster tear evaporation leads to a faster onset of ocular discomfort and thereby shortens the amount of time one can refrain from blinking [12]. Enhanced tear evaporation leads to thinner localized areas of the tear film and thereby localized tear hyperosmolarity, which in turn activates the inflammation pathway associated with dry eye disease [13]. Inflammation then results in stimulation of polymodal and mechanonociceptor nerve endings and enhances activity of cold thermoreceptors to evoke sensations of ocular dryness and pain [11].

This study [12] provides a mechanistic explanation of this concept. A similar mechanism was described by Hayirci et al [14] in the setting of continuous positive airway pressure for patients with obstructive sleep apnea syndrome.

In nurses working in ICUs wearing sealed goggles during COVID-19, dehydration has been proposed as a mechanism for Meibomian oil hardening and chalazion formation [15].

Eyelid/Ocular Microbiota Explanation:

Just as the term microbiome or microbiota refers to all types of microorganisms present in or on the human body, the term ocular microbiota refers to all types of microorganisms present in or on the eyes. It has been shown that commensal microbiota play a critical and fundamental role in regulating host physiology, including the induction and development of the immune system and host defense mechanisms against the invasion of pathogens. In this regard, dysbiosis (referred as unbalanced microbiota) could lead to pathogenic microbial overgrowth and cause local or systemic inflammation [16]. The ocular surface is directly exposed to the outside environment, and can be affected by numerous pathogenic microorganisms [17].

Meibomian glands located in the eyelids are in charge of secretion of oily components for the tear film to protect the ocular surface from overt dryness, discomfort, or damage. Dysfunction of Meibomian glands often leads to evaporative dry eye syndrome. Despite some inconsistencies in the literature, mostly due to technical issues, it has been shown that altered ocular microbial species can sometimes be associated with dry eye syndrome and dysfunction of Meibomian glands [18-20]. Corynebacterium, as ocular surface "resident microbiota", is possibly associated with dry eye syndrome. However, it might be argued that alteration in the ocular surface microbiota may not be a cause, but rather it might be a corollary to ocular surface disorders.

Chalazion development, though primarily caused by a non-infectious obstruction of eyelid Meibomian glands, may also be associated with multiple specific bacterial isolates related to changes to the gut microbiome [21;22]. It is worth remembering that oral flora (including bacterial pathogens and normal flora) can easily be incorporated into expired droplets capable of reaching the ocular surface, while talking, sneezing, or coughing [23]. Therefore, as Silkiss et al [24] have nicely explained, mask wear can provide a funnel for enhanced bacterial exposure to the eyelids and cheeks, which in turn may promote inflammation. This is because an unbalanced ocular microbiota may lead to pathogenic microbial overgrowth, which may then cause local or systemic inflammation [17].

Frequent hand washing or use of hygienic/alcoholic disinfectants drastically changes the microbiome of hands [25-27]. This might lead to facial, eyelid or ocular surface microbiota alterations during the COVID-19 pandemic. There is currently no direct empirical evidence to support this hypothesis. However, an altered skin surface or gut microbiota community might theoretically be transmitted to the face, cheeks and eyelids, because mask wearers frequently manipulate their masks. This, in turn, may increase the chances of transferring bacteria from the hands to the face.

This is especially important in people who are already at increased risk of dry eye. In diseases such as Sjögren's syndrome (SS), there is a combination of Meibomian gland dysfunction and dry eye syndrome, with changes in ocular surface microbiota [28-30]. An altered gut-eye-lacrimal gland-microbiome axis has been previously implicated in dry eye in SS [31]. It might be conjectured that in addition to altered ocular/facial microbiota, unbalanced gut microbiota due to obsessive hand washing and sanitizing/cleaning practices in the home, and more specifically in the kitchen, may be partially responsible for dry eye. This may exacerbate pre-existing dryness, caused by wearing a face mask.

Causal Explanation:

A recent systemic review by Nasiri et al [32] concluded that the mechanism of dry eye or foreign body sensation is unclear in COVID-19 patients and may not be directly associated with the SARS-CoV-2 virus. After an extensive search in PUBMED, SCOPUS and Scholar using the terms 'dry eye', 'COVID-19', 'SARS', and 'SARS-CoV-2', there was no record of a causal association between COVID-19 infection and dry eye. Below, we will summarize some very recent evidence to show that the possibility exists that damage to lacrimal and Meibomian glands may occur due to COVID-19.

Recently, Grajewski et al [33] demonstrated the presence of angiotensin converting enzyme 2 (ACE2) expression in the conjunctiva by immunohistochemistry. This was previously shown to be present by Sungnak et al [34] on an RNA level. This was also observed in other pioneering studies, which demonstrated high expression of ACE2 mRNA in the conjunctiva and cornea of the human eye. [35;36]. A review of SARS-CoV-2-related English language articles from December 2019 through mid-April 2020 found in online databases, has concluded that ACE2 receptors and their expression on the ocular mucosal surface may explain the development of conjunctivitis in COVID-19 patients, although it may go unnoticed due to its mild nature [37]. ACE2 expression has been reported in the lacrimal glands of animal models such as mice [38] and rhesus monkeys [39]. However so far, we are unaware of any human study that has reported the presence or absence of ACE2 expression or ACE2 receptors in lacrimal glands and/or Mebomian glands. Hong et al [40] studied 56 subjects before and after the development of COVID-19. It was found that 6 patients (11%) had ocular redness before the onset of respiratory symptoms. Scores on the OSDI (Ocular Surface Disease Index) and SEEQ (Salisbury Eye Evaluation Questionnaire) tests, both of which assess dry eye symptoms, were significantly worse after contracting COVID-19, even in patients without visible conjunctivitis. Similar studies confirm a worsening in ocular symptomatology following onset of COVID-19 in nearly all patients [41]. The worsening of dry eye symptoms in these patients suggests that the possibility of a direct causal association between COVID-19 infection and dry eye, via direct damage to the lacrimal and Meibomian glands. Conversely, healthy individuals without COVID-19 generally remain asymptomatic.

Alternatively, it is possible that worsening of dry eye symptoms is mediated via salivary gland dysfunction caused by COVID-19. Recent evidence revealed ACE2 expression in human salivary glands, in patients reporting oral symptoms such as dry mouth and amblygeustia, due to damage to the salivary gland caused by the COVID19 [42]. There is evidence showing a direct anatomical association between salivary glands and lacrimal glands and that treatment of salivary hypofunction, improves dry eye symptoms [43-45]. Targeted AQP1 gene therapy of the submandibular glands in a murine model of SS not only improved salivary flow, but also lacrimal gland function [43], suggesting existence of a direct uni- or bilateral interaction between these two secretory glands. In fact, salivation improves lacrimal gland function in dry eyes. Upon stimulation, the seventh cranial nerve aids in the secretion of tears from the lacrimal glands and creates a sense of relief from mild dryness of the eyes [45]. The facial nerve contains fibers for both the lacrimal gland and the submandibular salivary gland. After the facial nerve passes through the geniculate ganglion, the parasympathetic secretomotor nerve fibers for the submandibular salivary gland travel with the main nerve trunk. The secretory nerve fibers for the lacrimal gland separate from the facial nerve to join the greater petrosal nerve. These secretory nerve fibers then pass through the sphenopalatine ganglion before innervating the lacrimal gland [44]. For a full anatomical description, see these references: [44;45]. Briefly, it there are evidences showing a direct damage to the lacrimal glands by the COVID-19 virus [46;47].

Novel Mechanism:

There is a direct association between the salivary flow rate and jaw muscle activity during mastication [48-51], i.e., the higher the chewing rate, the higher the saliva secretion. There is also a positive association between dry mouth and dry eye in humans (in normal adults [52], in subjects with and without symptoms of dry mouth and/or eyes, in patients with primary SS [53], in the elderly [54], and in patients with dry eye symptoms [55]).

It is not surprising that agents that stimulate salivary gland secretions, such as pilocarpine [56] and cevimeline [57], stimulate lacrimal gland (and/or Meibomian gland) secretion and alleviate dry eye symptoms. However, it was surprising to find that simply chewing gum or candy also alleviated dry eye symptoms, without involvement of receptors, antagonist(s) or agonists(s). Higher salivary secretion brought about by chewing gum or candy led to significantly lower dry eye scores [58], with no drug-receptor interactions involved.

In the only published trial with a double-blinded crossover design, Asakawa et al [58] evaluated eye dryness with the RT-7000 Auto Ref-Topographer and Tear Stability Analysis System (TSAS) (Tomey, Nagoya, Japan). Briefly, healthy participants experiencing eyestrain (n=46, 23 male and 23 female, 20-59 yrs old) were instructed to keep their eyes open for 10 seconds. Severity of eye dryness was then evaluated by measuring ring break-up time (RBUT). The RBUT was measured by analyzing break-up of the tear layer within a 6-mm radius of the center of the cornea and its deformation over time, and measuring the number of seconds required to reach the cut-off value of –0.5 D, in accordance with the algorithm provided by Tomey. Each 10-year age group cohort included 12 subjects, with the exception of the 30s group, which included 10 subjects. A visual task was performed on reading material displayed on a computer screen at a fixed distance for 60 min. Participants were asked to chew gum or candy (two pieces for two 15-min periods) starting 15 and 45 min after starting to read. Subjects chewed gum on Day1 and candy on Day2, and vice versa. With regard to the visual analogue scale, there were no significant difference between scores of subjective eye fatigue between chewing gum and chewing candy ($P = 0.397 - P = 0.909$). Those scores of eye heaviness and eye tiredness were significantly longer in duration before and after the visual task with candy ($P = 0.013$ and $P = 0.025$, respectively), but not with chewing gum. The changes of subjective accommodation were significantly lower after the visual task, after chewing candy or chewing gum ($P = 0.043$).

Most importantly, before and after the visual task, the RBUT values showed a significant trend (i.e., 10.0 sec and 9.6 sec, respectively, $P = 0.053$) only with chewing gum but not with chewing candy ($P = 0.132$) 58. It is very important to note that participants were asked to chew gum or candy only for two 15-min periods, while in real-world setting; wearing a face mask lasts very long.

Their experiment provides the first experimental evidence supporting our novel hypothesis that salivary secretion can (either directly or indirectly) enhance ocular secretions, possibly via a mechanism involving mandibular jaw movement.

Wearing a face mask meanwhile can substantially impair the jaw movement during daily activities such as speaking, chewing, and swallowing [59;60]. For instance, normal yawning which is a physiological behavior could be deregulated due to the restriction of mandibular jaw movement by face mask wearing [59]. It worth to remind that tears can be described as of two types: reflex tears, which are induced by a range of stimuli (eg. yawning, as a very important stimulus), and basal tears, which are the non-stimulated lacrimation of the tear glands [61]. Yawning –i.e., powerful stretching of the mandible jaw– is contagious and can be both conscious and unconscious. Face masks can additionally inhibit contagious yawning in community settings through impairment of both face and emotion recognition [60;62;63] and thereby can diminish yawning-mediated tear production. It is also interesting that even self-induced yawning stimulates aqueous tear [64], and saliva production [65]. Most interestingly, during yawning, muscle sympathetic nerve activity is inhibited [66] and a marked increase of cerebral blood flow [67], and significant increase in blood flow through the ophthalmic veins occurs [68], all of which contribute to normal tear production.

We use these facts to support the mechanism we propose: Decreased salivary flow rate and to a lesser extent, insufficient lower jaw movement due to the restriction of mandibular jaw movement by face mask wear, may represent a new mechanism by which dry eye is exacerbated in face mask wearers.

Hypothetical Pathway:

Chewing/mastication [69] and speaking [70;71] both of which are activities that entail mandible movement, increase cerebral blood flow (rCBF). Chewing also increases actions of the autonomic nervous system (sympathetic and parasympathetic nerves) [72-74]. Chewing gum also increases blood flow to the eyes and to the parasympathetic nerves which predominantly act to contract the iris sphincter muscle [58]. On the other hand, certain physical activities or psychological situations can alter patterns of rCBF. For example, walking [74], experiencing social phobia during stressful speaking tasks [75], and social phobia treated with citalopram or cognitive-behavioral therapy [76] differentially change the pattern of rCBF. An rCBF pattern of relatively enhanced cortical, as opposed to subcortical perfusion is seen in the nonphobic subjects, showing that cortical evaluative processes are taxed by public performance. Conversely, the social phobia symptom profile is associated with an altered cerebral blood flow, i.e., increased subcortical activity [75] which amazingly is similar to altered cerebral blood flow in patients with SS [77-80] in which dry eyes and dry mouth are clinical hallmarks [81;82]. Altered rCBF patterns are reported in patients with COVID-19 [83-87]. This may be due to a possible neuroinvasive action of SARS-CoV-2, or it may be a partial manifestation of an altered pattern of mandible movement, resulting from the wearing of a face mask.

As for direct association between impaired jaw movement and dry eye, current evidence comes mainly from case series reports of patients with impaired jaw movement 88-90, which all share in the facial nerve impairment and hypofunction of lacrimal component of the nervus intermedius function [91].

There is currently no report to directly link facemask-induced dry eye with lacrimal gland aquaporins (AQPs) expression in humans, however, there is huge amount of evidence to establish this notion in submandibuar glands [92-95]. For instance, pigs fed with different dietary treatments –based on different grinding intensities and compactions of the same diet– showed significantly different AQP5 expression in mandibular gland, with highest AQP5 expression in those fed with coarsely ground pelleted diets compared to other softer diets [92], clearly suggesting that higher jaw movement is positively associated to AQP5 expression in a rate dependent manner. In another recent experiment, Saito et al examined the impact of the decline and recovery of masticatory function on expression and localization of AQP5 in the Wistar rat submandibular salivary gland by inserting and removing an incisor bite plate. Attachment of incisor bite plate resulted in a decrease in the expression of AQP5. Alterations in the localization of AQP5 were confirmed between two weeks and four weeks in the same rats. Conversely, alteration in the expression and localization of AQP5 were not seen in the recovery group. These findings suggest that a loss of molar occlusion and jaw movement decreases AQP5 expression and alters its localization in the rat submandibular salivary gland. Interestingly, removal of the bite plate permitted the recovery of both AQP5 expression and its normal localization in the submandibular salivary glands [94].

Thus, higher jaw movement is associated with higher AQP5 expression in submandibular salivary glands [92-95]. It however remains to be explored whether face mask-induced dry eye is mediated via altered AQPs expressions in lacrimal glands.

AQPs are a group of water channel proteins which mediate the passage of water molecules through membranes [96]. The Meibomian and lacrimal glands are rich in AQPs [97-99]. Altered cerebral blood flow homeostasis results in dysfunction of AQPs both in the brain and secretory glands [13;100-104] which, like the lacrimal and Meibomian glands, are rich in AQPs. [105-107].

There is empirical evidence supporting the hypothesis that these effects are eventually mediated by modulation of parasympathetic nerve and muscarinic receptors 108;109. See reviews [110;111]. In support of this conclusion, in a counterfactual reasoning model, the function of sympathetic and parasympathetic nerves during gum chewing is in harmony with autonomic nerves [112]. The submandibular gland AQP5 is degraded by parasympathetic denervation and is recovered by cevimeline, which is an M3 muscarinic receptor agonist [113].

These observations could have deep implications regarding the effect of social distress and the limitation of physical activity brought about by the COVID-19 pandemic. Social phobia negatively impacts verbal communications, resulting in a further decrease in mandibular jaw movement, possibly adding to the problem of dry eye disease.

Conclusions:

We hypothesize that prolonged wearing of face masks might reduce movement of the mandible. Less frequent face-to-face verbal communication (pre-COVID-19 pandemic vs. post-COVID-19), and possibly impeded yawning, might have further contributed to altered patterns of blood flow to the eyes and rCBF, due in part to social distress and physical confinement. This, in turn, may theoretically have affected modulation of parasympathetic nerve and muscarinic receptors through AQPs in the lacrimal and Meibomian glands. Face masks, meanwhile, can impair contagious yawning in community settings through impairing the performance of both face and emotion recognition and thereby can diminish yawning-mediated tear production. At present this remains a hypothesis that needs to be tested.

Perspective and Suggestions for Future Studies:

In order to come to a better understanding of how COVID-19 might affect dry eye disease, the possible interaction or modification effect between confounding variables should be considered in future studies. This might facilitate the discovery of better preventive measures and therapeutic agents for the management of dry eye symptoms experienced by patients suffering from this pandemic. As an example, a future study might look at whether higher rates of verbal communication by women as compared to men has an impact on the potential effect of face mask wearing on the development of dry eye disease, including the issues of proper versus improper mask fitment, and continuous versus intermittent mask wear. Another study might seek to compare different types of face masks such as surgical masks versus N95 masks, to see if the relative degree of leakage from the edge of the mask affects eye dryness. Retrospective data collection methods are subject to respondent memory bias, self-bias and self-rating bias. To diminish the memory bias in relation to dry eye, proper web-based registries or online surveys can be utilized. In this regard, there are validated questionnaires such as Standardized Patient Evaluation of Eye Dryness (SPEED) questionnaire, which can be used to evaluate the symptomatology of patients. The SPEED questionnaire could be compared to the more diffuse Ocular Surface Disease Index (OSDI) questionnaire [41]. The SPEED questionnaire can discriminate between asymptomatic and symptomatic individuals in relation to dry eye disease [114]. Occupational and prior health history, such as a history of prior refractive surgery, computer professionals with high levels of screen time, and history of systemic conditions such as SS, rheumatoid arthritis or symptoms of dry mouth should be explored. Milder cases can be handled over teleconsultation [115].

It would be interesting to look at dry eye prevalence in a number of categories, such as obsessive people who strictly quarantined at home (which may result in less or no use of a face mask, and reduced exposure to COVID-19), those with high levels of screen exposure, those with little or no viral exposure, and those who strictly observed face mask wearing protocols, versus those who did not.

If it can be shown that COVID-19 adversely impacts ocular lacrimation, this might provide us with an explanation for the magnitude of dry eye disease seen during this pandemic, even among those with mild cases of COVID-19.

Suggestions for Affected Patients:

Individuals wearing a face mask should be instructed to blink more often and to avoid mask displacement or incorrect fitting, which might contribute to air leaking above the mask, increasing dry eye symptoms [116]. Mask designs that permit transparent and freer mandibular movement may also help in this regard.

Disclosure Statement:

The author has nothing to disclose. No outside funding/support was received for this study.

Declaration of Competing Interest:

There is no conflict of interest.

Acknowledgement:

The author extends his sincere gratitude to Michael W Gaynon MD (Byers Eye Institute at Stanford University, Palo Alto, California) for critical appraisal and invaluable comments.

References:

1. Moshirfar M, West WB, Jr., Marx DP. Face Mask-Associated Ocular Irritation and Dryness. Ophthalmol Ther 2020; 9(3):397-400.
2. Boccardo L. Self-reported symptoms of mask-associated dry eye: A survey study of 3,605 people. Cont Lens Anterior Eye 2021;101408.
3. Krolo I, Blazeka M, Merdzo I et al. Mask-Associated Dry Eye During COVID-19 Pandemic-How Face Masks Contribute to Dry Eye Disease Symptoms. Med Arch 2021; 75(2):144-148.
4. Mastropasqua L, Lanzini M, Brescia L et al. Face Mask-Related Ocular Surface Modifications During COVID-19 Pandemic: A Clinical, In Vivo Confocal Microscopy, and Immune-Cytology Study. Transl Vis Sci Technol 2021; 10(3):22.
5. Pandey SK, Sharma V. Mask-associated dry eye disease and dry eye due to prolonged screen time: Are we heading towards a new dry eye epidemic during the COVID-19 era? Indian J Ophthalmol 2021; 69(2):448-449.
6. Scalinci SZ, Pacella E, Battagliola ET. Prolonged face mask use might worsen dry eye symptoms. Indian J Ophthalmol 2021; 69(6):1508-1510.
7. Martinez-Perez C, Monteiro B, Soares M et al. Influence of Face Masks on the Use of Contact Lenses. Int J Environ Res Public Health 2021; 18(14).
8. Talens-Estarelles C, Garcia-Marques JV, Cervino A et al. Online Vs In-person Education: Evaluating the Potential Influence of Teaching Modality on Dry Eye Symptoms and Risk Factors During the COVID-19 Pandemic. Eye Contact Lens 2021.
9. Barthakur R. Computer vision syndrome. Internet Journal of Medical Update 2013; 8(2):1-2.
10. Sun CB, Wang YY, Liu GH et al. Role of the Eye in Transmitting Human Coronavirus: What We Know and What We Do Not Know. Front Public Health 2020; 8:155.
11. Hirata H, Meng ID. Cold-sensitive corneal afferents respond to a variety of ocular stimuli central to tear production: implications for dry eye disease. Invest Ophthalmol Vis Sci 2010; 51(8):3969-3976.
12. Ding JE, Kim YH, Yi SM et al. Ocular surface cooling rate associated with tear film characteristics and the maximum interblink period. Sci Rep 2021; 11(1):15030.
13. King-Smith PE, Nichols JJ, Nichols KK et al. Contributions of evaporation and other mechanisms to tear film thinning and break-up. Optom Vis Sci 2008; 85(8):623-630.
14. Hayirci E, Yagci A, Palamar M et al. The effect of continuous positive airway pressure treatment for obstructive sleep apnea syndrome on the ocular surface. Cornea 2012; 31(6):604-608.
15. ȷgarbane B, Tadayoni R. Cluster of chalazia in nurses using eye protection while caring for critically ill patients with COVID-19 in intensive care. Occupational and environmental medicine 2020; 77(8):584-585.
16. McDermott AM. Antimicrobial compounds in tears. Exp Eye Res 2013; 117:53-61.
17. Li JJ, Yi S, Wei L. Ocular Microbiota and Intraocular Inflammation. Front Immunol 2020; 11:609765.
18. Dong X, Wang Y, Wang W et al. Composition and Diversity of Bacterial Community on the Ocular Surface of Patients With Meibomian Gland Dysfunction. Invest Ophthalmol Vis Sci 2019; 60(14):4774-4783.
19. Li Z, Gong Y, Chen S et al. Comparative portrayal of ocular surface microbe with and without dry eye. J Microbiol 2019; 57(11):1025-1032.
20. Zhang Y, Liu ZR, Chen H et al. Comparison on conjunctival sac bacterial flora of the seniors with dry eye in Ganzi autonomous prefecture. Int J Ophthalmol 2013; 6(4):452-457.
21. Cui Y, Song L, Li X et al. A study of the correlation between chalazion and intestinal flora in chinese children. 2020.
22. Nemet AY, Vinker S, Kaiserman I. Associated morbidity of

chalazia. Cornea 2011; 30(12):1376-1381.
23. Ibrahimi OA, Sharon V, Eisen DB. Surgical-site infections and routes of bacterial transfer: which ones are most plausible? Dermatol Surg 2011; 37(12):1709-1720.
24. Silkiss RZ, Paap MK, Ugradar S. Increased incidence of chalazion associated with face mask wear during the COVID-19 pandemic. Am J Ophthalmol Case Rep 2021; 22:101032.
25. Fierer N, Hamady M, Lauber CL et al. The influence of sex, handedness, and washing on the diversity of hand surface bacteria. Proc Natl Acad Sci U S A 2008; 105(46):17994-17999.
26. Mukherjee PK, Chandra J, Retuerto M et al. Effect of alcohol-based hand rub on hand microbiome and hand skin health in hospitalized adult stem cell transplant patients: A pilot study. J Am Acad Dermatol 2018; 78(6):1218-1221.
27. Rocha LA, Ferreira de Almeida E Borges, Gontijo Filho PP. Changes in hands microbiota associated with skin damage because of hand hygiene procedures on the health care workers. Am J Infect Control 2009; 37(2):155-159.
28. de Paiva CS, Jones DB, Stern ME et al. Altered Mucosal Microbiome Diversity and Disease Severity in Sjogren Syndrome. Sci Rep 2016; 6:23561.
29. Tsigalou C, Stavropoulou E, Bezirtzoglou E. Current Insights in Microbiome Shifts in Sjogren's Syndrome and Possible Therapeutic Interventions. Front Immunol 2018; 9:1106.
30. Zaheer M, Wang C, Bian F et al. Protective role of commensal bacteria in Sjogren Syndrome. J Autoimmun 2018; 93:45-56.
31. Moon J, Choi SH, Yoon CH et al. Gut dysbiosis is prevailing in Sjogren's syndrome and is related to dry eye severity. PLoS One 2020; 15(2):e0229029.
32. Nasiri N, Sharifi H, Bazrafshan A et al. Ocular Manifestations of COVID-19: A Systematic Review and Meta-analysis. J Ophthalmic Vis Res 2021; 16(1):103-112.
33. Grajewski RS, Rokohl AC, Becker M et al. A missing link between SARS-CoV-2 and the eye?: ACE2 expression on the ocular surface. J Med Virol 2021; 93(1):78-79.
34. Sungnak W, Huang N, Becavin C et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat Med 2020; 26(5):681-687.
35. Hikmet F, Mear L, Edvinsson A et al. The protein expression profile of ACE2 in human tissues. Mol Syst Biol 2020; 16(7):e9610.
36. Hui KPY, Cheung MC, Perera RAPM et al. Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures. Lancet Respir Med 2020; 8(7):687-695.
37. Kharel SR, Khatri A, Janani MK et al. Unfolding COVID-19: Lessons-in-Learning in Ophthalmology. Clin Ophthalmol 2020; 14:2807-2820.
38. Zhang BN, Wang Q, Liu T et al. [A special on epidemic prevention and control: analysis on expression of 2019-nCoV related ACE2 and TMPRSS2 in eye tissues]. Zhonghua Yan Ke Za Zhi 2020; 56(6):438-446.
39. Deng W, Bao L, Gao H et al. Rhesus macaques can be effectively infected with SARS-CoV-2 via ocular conjunctival route. BioRxiv 2020.
40. Hong N, Yu W, Xia J et al. Evaluation of ocular symptoms and tropism of SARS-CoV-2 in patients confirmed with COVID-19. Acta Ophthalmol 2020.
41. Meduri A, Oliverio GW, Mancuso G et al. Ocular surface manifestation of COVID-19 and tear film analysis. Sci Rep 2020; 10(1):20178.
42. Chen L, Zhao J, Peng J et al. Detection of SARS-CoV-2 in saliva and characterization of oral symptoms in COVID-19 patients. Cell Prolif 2020; 53(12):e12923.
43. Lai Z, Yin H, Cabrera-Perez J et al. Aquaporin gene therapy corrects Sjogren's syndrome phenotype in mice. Proc Natl Acad Sci U S A 2016; 113(20):5694-5699.
44. Modi P, Arsiwalla T. Crocodile Tears Syndrome. 2021.
45. Pramanik T, Ghising R. Salivation induced better lacrimal gland function in dry eyes. Nepal Med Coll J 2009; 11(4):258-260.
46. Dermarkarian CR, Chilakapati M, Hussein M et al. Bilateral orbital inflammation in a 6-month old with SARS-CoV-2 infection. Orbit 2021;1-4.
47. Shen J, Wu J, Yang Y et al. The paradoxical problem with COVID-19 ocular infection: Moderate clinical manifestation and potential infection risk. Comput Struct Biotechnol J 2021; 19:1063-1071.
48. Iguchi H, Magara J, Nakamura Y et al. Changes in jaw muscle activity and the physical properties of foods with different textures during chewing behaviors. Physiol Behav 2015; 152(Pt A):217-224.
49. Pereira LJ, Gaviao MB, Engelen L et al. Mastication and swallowing: influence of fluid addition to foods. J Appl Oral Sci 2007; 15(1):55-60.
50. Simione M, Loret C, Le RB et al. Differing structural properties of foods affect the development of mandibular control and muscle coordination in infants and young children. Physiol Behav 2018; 186:62-72.
51. van der BA, Engelen L, Pereira LJ et al. Oral physiology and mastication. Physiol Behav 2006; 89(1):22-27.
52. Jacobsson L, Hansen BU, Manthorpe R et al. Association of dry eyes and dry mouth with anti-Ro/SS-A and anti-La/SS-B autoantibodies in normal adults. Arthritis Rheum 1992; 35(12):1492-1501.
53. Hakansson U, Jacobsson L, Lilja B et al. Salivary gland scintigraphy in subjects with and without symptoms of dry mouth and/or eyes, and in patients with primary Sjogren's syndrome. Scand J Rheumatol 1994; 23(6):326-333.
54. Schein OD, Hochberg MC, Munoz B et al. Dry eye and dry mouth in the elderly: a population-based assessment. Arch Intern Med 1999; 159(12):1359-1363.
55. Koseki M, Maki Y, Matsukubo T et al. Salivary flow and its relationship to oral signs and symptoms in patients with dry eyes. Oral Dis 2004; 10(2):75-80.
56. Wu CH, Hsieh SC, Lee KL et al. Pilocarpine hydrochloride for the treatment of xerostomia in patients with Sjogren's syndrome in Taiwan--a double-blind, placebo-controlled trial. J Formos Med Assoc 2006; 105(10):796-803.
57. Ono M, Takamura E, Shinozaki K et al. Therapeutic effect of cevimeline on dry eye in patients with Sjogren's syndrome: a randomized, double-blind clinical study. Am J Ophthalmol 2004; 138(1):6-17.
58. Asakawa K, Kanno S, Ando T et al. The Effects of Chewing Gum in Preventing Eyestrain. Biomed Res Int 2020; 2020:2470473.

59. Cappa CD, San Francisco Opera Costume Department, Ristenpart WD et al. A highly efficient cloth facemask design. Aerosol Science and Technology 2021;(just-accepted):1-21.
60. Saeidi R, Huhtakallio I, Alku P. Analysis of Face Mask Effect on Speaker Recognition. 2016: 1800-1804.
61. Ruud Buijs, Dick Swaab. Autonomic nervous system. In: Pierre Vinken, George Bruyn, editors. Handbook of Clinical Neurology. Amsterdam: Elsevier, 2021.
62. Gori M, Schiatti L, Amadeo MB. Masking Emotions: Face Masks Impair How We Read Emotions. Front Psychol 2021; 12:669432.
63. Grundmann F, Epstude K, Scheibe S. Face masks reduce emotion-recognition accuracy and perceived closeness. PLoS One 2021; 16(4):e0249792.
64. Rooney SM, Gehlbach PL. Self-induced yawning stimulates aqueous tear production. ASSOC RESEARCH VISION OPHTHALMOLOGY INC 9650 ROCKVILLE PIKE, BETHESDA, MD_بG_2000, خ: S67.
65. Telford JI. Effects of contagious yawning on saliva production and swallowing in adults with traumatic brain injuryG_ôa possible treatment method. 2020.
66. Askenasy JJ, Askenasy N. Inhibition of muscle sympathetic nerve activity during yawning. Clin Auton Res 1996; 6(4):237-239.
67. Askenasy JJM. Is yawning an arousal defense reflex? The Journal of psychology 1989; 123(6):609-621.
68. Hirashita M, Shido O, Tanabe M. Blood flow through the ophthalmic veins during exercise in humans. European journal of applied physiology and occupational physiology 1992; 64(1):92-97.
69. Momose T, Nishikawa J, Watanabe T et al. Effect of mastication on regional cerebral blood flow in humans examined by positron-emission tomography with (1)(5)O-labelled water and magnetic resonance imaging. Arch Oral Biol 1997; 42(1):57-61.
70. Formby C, Thomas RG, Halsey JH, Jr. Regional cerebral blood flow for singers and nonsingers while speaking, singing, and humming a rote passage. Brain Lang 1989; 36(4):690-698.
71. Knopman DS, Rubens AB, Klassen AC et al. Regional cerebral blood flow patterns during verbal and nonverbal auditory activation. Brain Lang 1980; 9(1):93-112.
72. Hasegawa Y, Ono T, Hori K et al. Influence of human jaw movement on cerebral blood flow. J Dent Res 2007; 86(1):64-68.
73. ISHIYAMA I, SUZUKI M. Blood pressure and cerebral blood flow volume responses to mastication of food. Journal of Japanese Society for Mastication Science and Health Promotion 2005; 15(1):24-36.
74. Kanno S, Shimo K, Ando T et al. Gum chewing while walking increases fat oxidation and energy expenditure. J Phys Ther Sci 2019; 31(5):435-439.
75. Tillfors M, Furmark T, Marteinsdottir I et al. Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study. Am J Psychiatry 2001; 158(8):1220-1226.
76. Furmark T, Tillfors M, Marteinsdottir I et al. Common changes in cerebral blood flow in patients with social phobia treated with citalopram or cognitive-behavioral therapy. Arch Gen Psychiatry 2002; 59(5):425-433.
77. Chang CP, Shiau YC, Wang JJ et al. Abnormal regional cerebral blood flow on 99mTc ECD brain SPECT in patients with primary Sjogren's syndrome and normal findings on brain magnetic resonance imaging. Ann Rheum Dis 2002; 61(9):774-778.
78. Huang WS, Chiu PY, Kao A et al. Detecting abnormal regional cerebral blood flow in patients with primary Sjogren's syndrome by technetium-99m ethyl cysteinate dimer single photon emission computed tomography of the brain--a preliminary report. Rheumatol Int 2003; 23(4):174-177.
79. Kao CH, Ho YJ, Lan JL et al. Regional cerebral blood flow and glucose metabolism in Sjogren's syndrome. J Nucl Med 1998; 39(8):1354-1356.
80. Lass P, Krajka-Lauer J, Homziuk M et al. Cerebral blood flow in Sjogren's syndrome using 99Tcm-HMPAO brain SPET. Nucl Med Commun 2000; 21(1):31-35.
81. Bowman SJ. Primary Sj__gren's syndrome. Lupus 2018; 27(1_suppl):32-35.
82. Cornec D, Saraux A, Jousse-Joulin S et al. The differential diagnosis of dry eyes, dry mouth, and parotidomegaly: a comprehensive review. Clinical reviews in allergy & immunology 2015; 49(3):278-287.
83. Mahajan A, Mason GF. A sobering addition to the literature on COVID-19 and the brain. J Clin Invest 2021; 131(8).
84. Qin Y, Wu J, Chen T et al. Long-term microstructure and cerebral blood flow changes in patients recovered from COVID-19 without neurological manifestations. J Clin Invest 2021; 131(8).
85. Soldatelli MD, Amaral LFD, Veiga VC et al. Neurovascular and perfusion imaging findings in coronavirus disease 2019: Case report and literature review. Neuroradiol J 2020; 33(5):368-373.
86. Sonkaya AR, Oztrk B, Karadas O. Cerebral hemodynamic alterations in patients with Covid-19. Turk J Med Sci 2021; 51(2):435-439.
87. Ziai WC, Cho SM, Johansen MC et al. Transcranial Doppler in Acute COVID-19 Infection: Unexpected Associations. Stroke 2021; 52(7):2422-2426.
88. Kalra HK, Magoon EH. Side effects of the use of botulinum toxin for treatment of benign essential blepharospasm and hemifacial spasm. Ophthalmic Surg 1990; 21(5):335-338.
89. Mancini P, Bottaro V, Capitani F et al. Recurrent Bell's palsy: outcomes and correlation with clinical comorbidities. Acta Otorhinolaryngol Ital 2019; 39(5):316-321.
90. May M, Hardin WB. Facial palsy: interpretation of neurologic findings. Laryngoscope 1978; 88(8 Pt 1):1352-1362.
91. Tamura M, Murata N, Hayashi M et al. Injury of the lacrimal component of the nervus intermedius function after radiosurgery versus microsurgery. Neurochirurgie 2004; 50(2-3 Pt 2):338-344.
92. Dall'Aglio C, Mercati F, De FE et al. Influence of Different Feed Physical Forms on Mandibular Gland in Growing Pigs. Animals (Basel) 2020; 10(5).
93. Mizumachi-Kubono M, Watari I, Ishida Y et al. Unilateral maxillary molar extraction influences AQP5 expression and distribution in the rat submandibular salivary gland. Arch Oral Biol 2012; 57(7):877-883.
94. Saito E, Watari I, Mizumachi-Kubono M et al. Occlusional Modifications Reversibly Alter Aquaporin 5 Expression and Localization in Rat Salivary Glands. Front Physiol 2020;

11:528.
95. Xu H, Shan XF, Cong X et al. Pre- and Post-synaptic Effects of Botulinum Toxin A on Submandibular Glands. J Dent Res 2015; 94(10):1454-1462.
96. Kordowitzki P, Kranc W, Bryl R et al. The Relevance of Aquaporins for the Physiology, Pathology, and Aging of the Female Reproductive System in Mammals. Cells 2020; 9(12).
97. Delporte C. Aquaporins in secretory glands and their role in Sjogren's syndrome. Handb Exp Pharmacol 2009;(190):185-201
98. Delporte C. Aquaporins and Gland Secretion. Adv Exp Med Biol 2017; 969:63-79.
99. Soyfoo MS, Chivasso C, Perret J et al. Involvement of Aquaporins in the Pathogenesis, Diagnosis and Treatment of Sjogren's Syndrome. Int J Mol Sci 2018; 19(11).
100. Jullienne A, Badaut J. Molecular contributions to neurovascular unit dysfunctions after brain injuries: lessons for target-specific drug development. Future Neurol 2013; 8(6):677-689.
101. Kovacs R, Heinemann U, Steinhauser C. Mechanisms underlying blood-brain barrier dysfunction in brain pathology and epileptogenesis: role of astroglia. Epilepsia 2012; 53 Suppl 6:53-59.
102. Liu X, Zhang W, Alkayed NJ et al. Lack of sex-linked differences in cerebral edema and aquaporin-4 expression after experimental stroke. J Cereb Blood Flow Metab 2008; 28(12):1898-1906.
103. Zador Z, Stiver S, Wang V et al. Role of aquaporin-4 in cerebral edema and stroke. Handb Exp Pharmacol 2009;(190):159-170.
104. Zhang Y, Xu K, Liu Y et al. Increased cerebral vascularization and decreased water exchange across the blood-brain barrier in aquaporin-4 knockout mice. PLoS One 2019; 14(6):e021841
105. Ding C, Huang J, Veigh-Aloni M et al. Not all lacrimal epithelial cells are created equal heterogeneity of the rabbit lacrimal gland and differential secretion. Current eye research 2011; 36(11):971-978.
106. Tsai PS, Evans JE, Green KM et al. Proteomic analysis of human meibomian gland secretions. British Journal of Ophthalmology 2006; 90(3):372-377
107. Yu D, Thelin WR, Randell SH et al. Expression profiles of aquaporins in rat conjunctiva, cornea, lacrimal gland and Meibomian gland. Experimental eye research 2012; 103:22-32.
108. Berggreen E, Nylokken K, Delaleu N et al. Impaired vascular responses to parasympathetic nerve stimulation and muscarinic receptor activation in the submandibular gland in nonobese diabetic mice. Arthritis Res Ther 2009; 11(1):R18.
109. Waterman SA, Gordon TP, Rischmueller M. Inhibitory effects of muscarinic receptor autoantibodies on parasympathetic neurotransmission in Sjogren's syndrome. Arthritis Rheum 2000; 43(7):1647-1654
110. Ekstrom J. Autonomic control of salivary secretion. Proc Finn Dent Soc 1989; 85(4-5):323-331.
111. Proctor GB, Carpenter GH. Regulation of salivary gland function by autonomic nerves. Auton Neurosci 2007; 133(1):3-18.
112. ISHIYAMA I, SUZUKI M, MATSUBARA S et al. Function of sympathetic and parasympathetic nerves during gum chewing with CVRR, wave height of plethysmogram and plasma catecholamine concentration as functional indices of autonomic nerves. Journal of Japanese Society for Mastication Science and Health Promotion 1998; 8(1):42-52.
113. Li X, Azlina A, Karabasil MR et al. Degradation of submandibular gland AQP5 by parasympathetic denervation of chorda tympani and its recovery by cevimeline, an M3 muscarinic receptor agonist. Am J Physiol Gastrointest Liver Physiol 2008; 295(1):G112-G123.
114. Asiedu K, Kyei S, Mensah SN et al. Ocular Surface Disease Index (OSDI) Versus the Standard Patient Evaluation of Eye Dryness (SPEED): A Study of a Nonclinical Sample. Cornea 2016; 35(2):175-180.
115. Murthy SI, Das S, Deshpande P et al. Differential diagnosis of acute ocular pain: Teleophthalmology during COVID-19 pandemic - A perspective. Indian J Ophthalmol 2020; 68(7):1371-1379.
116. Giannaccare G, Vaccaro S, Mancini A et al. Dry eye in the COVID-19 era: how the measures for controlling pandemic might harm ocular surface. Graefes Arch Clin Exp Ophthalmol 2020; 258(11):2567-2568.