

The Impact of COVID-19 on the Faces of Frontline Healthcare Workers

Shino Bay Aguilera DO FAAD,^a Irene De La Peña MD,^b Martha Viera MD FAAD,^c
Bertha Baum DO FAAD FAOCD,^d Brian W. Morrison MD FAAD,^e
Olivier Amar MD ASPS BAPRAS SOF, CPRE,^f Matthieu Beustes-Stefanelli MD MBA,^g Mehreen Hall DO^h

^aShino Bay Cosmetic Dermatology, Fort Lauderdale, FL

^bAesthetic Medicine and Laser Therapy, Department of Aesthetic Medicina Universidad del Rosario, Bogotá, Colombia

^cDoral Dermatology Group, Doral, FL

^dHollywood Dermatology, Hallandale, FL

^ePhillip Frost Department of Dermatology & Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL

^fPlastic Reconstructive and Aesthetic Surgeon, London, United Kingdom

^gPlastic Surgery Unit, Maison Lutetia, Paris, France

^hLarkin Community Hospital Palm Springs Campus, Hialeah, FL

ABSTRACT

As the coronavirus epidemic continues, a host of new cutaneous complications is seen on the faces of frontline healthcare workers wearing personal protective equipment on a daily basis. To minimize the risk of COVID-19 infection, healthcare workers wear tight-fitting masks that lead to an excessive amount of pressure on the facial skin. Mechanical pressure, mask materials, and perspiration can all lead to various types of cutaneous lesions such as indentations of the face, skin tears, post-inflammatory hyperpigmentation, ulceration, crusting, erythema, and infection. The objective of this article is to provide effective and straightforward recommendations to those health care providers using facial masks in order to prevent skin-related complications.

J Drugs Dermatol. 2020;19(9):858-864. doi:10.36849/JDD.2020.5259

INTRODUCTION

The worldwide pandemic of the novel and highly infectious Coronavirus disease 2019 (COVID-19) originated in Wuhan, China in December 2019.¹ The etiology of this disease is due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which as of April 14, 2020, has affected more than 1.9 million people and taken the lives of more than 119,000 worldwide. Currently, it is speculated that the source of this infection is from bat-derived coronavirus, which spread to humans via an unknown intermediate mammal host.

The most frequent routes of transmission are airborne droplets containing viable viruses, and direct/indirect contact with contaminated surfaces.² Mucosal membranes that line various facial orifices are the most susceptible to viral transmission. Once the virus enters the body in any of the aforementioned routes, the single-stranded RNA-enveloped (ss-RNA) SARS-CoV-2 virus binds to the angiotensin-converting enzyme 2 (ACE-2) receptor. Once the virus makes contact with the target cell receptor, it enters the cell using the cell endosomes. This mechanism of action is facilitated by the cell's type 2 transmembrane serine protease, TMPRSS2 interacting with the virus S-spike protein. Once inside the cell, the virus takes over the cell's machinery by first transmitting the ss-RNA into the cell's cytoplasm. Later, the cell is forced to translate the ss-RNA in-

side the cell's ribosome into viral polyproteins that encode for the replicase-transcriptase complex. Viral structural proteins are created inside the cell cytoplasm with the help of proteinase enzymes. At the same time, the virus makes the infected cell synthesize RNA via its RNA-dependent RNA polymerase. These components are created inside the cell for assembly and release of new viral particles.³

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a beta coronavirus now known to cause illness in humans. Since SARS-CoV-2 proteins bind to gastrointestinal and respiratory cells, they cause mild to severe respiratory and gastrointestinal symptoms.⁴ The incubation period is believed to be two to fourteen days following exposure. The signs and symptoms of COVID-19 infection range from asymptomatic to mild symptoms to severe respiratory symptoms and mortality. Risk factors for this infection include: adults older than forty or fifty years of age, male gender, pre-existing medical conditions, and lifestyle. Common initial symptoms of infection are fever, non-productive cough, shortness of breath, difficulty breathing, malaise, and fatigue. Less common symptoms are myalgias, headaches, confusion, diarrhea, and rhinorrhea. Twenty percent of individuals with COVID-19 may have a critical presentation of this infection. These symptoms range from pneumonia, renal

failure, acute respiratory distress syndrome (ARDS), multiple organ failure leading to death.⁴

The current Center for Disease Control and Prevention and the World Health Organization guidance states that in order to decrease the rate of transmission of the virus, it is imperative to social distance, practice self-imposed isolation, protect mucous membranes with masks and glasses, and to wash hands properly before touching the face. Worldwide, millions of people are adhering to these recommendations to prevent exposure and infection by voluntary self isolation, a prerogative that frontline health care providers cannot have. As the pandemic accelerates, there is an increasing concern for health care providers who take care of infected individuals in hospitals to contract the infection themselves or infect family members at home. In order to protect themselves and their loved ones, health care providers must use protective devices such as eye protection goggles, full face visors, and fluid repellent surgical masks.⁵ A tight seal must be created between the mask in use and the skin in order for it to be effective. However, the prolonged use of these masks, the material of the masks, facial perspiration, and the pressure utilized to achieve the seal is causing moderate to severe skin damage in health care providers on the frontlines.⁵ In this document, some simple and easy-to-follow guidelines are discussed and recommended to help prevent or treat personal protective equipment (PPE) induced skin damage and lesions.

Overview of Cutaneous Complications

During the COVID-19 world-wide health crisis, health care workers are obligated to use protection devices to prevent infection. Devices like fluid repellent surgical masks, eye protection goggles, full face shields, or visors are part of the PPE arsenal. Long working hours in healthcare facilities and a high risk of contamination forces frontline workers to use protective equipment for long periods of time. Here, we discuss the skin injuries caused by the prolonged or repetitive use of surgical face masks and how those injuries can be prevented and treated.

In the healthcare setting, The World Health Organization recommends the use of a particulate respirator such as the USA health-certified N95 mask, European Union standard FFP2, or equivalent to prevent droplet exposure to COVID-19.⁶ These masks should be worn over the nose and mouth as a physical barrier to prevent droplets and splashes from reaching facial mucosa.⁷ The pressure that the mask exerts on the skin is key to achieving its protective purpose, but when the masks are worn repetitively and for a long time, this external force can cause a variety of skin injuries.

Prolonged use of the masks generates pressure, friction, and shearing, which, in turn, causes tissue deformation, inflammatory edema, and in severe cases, tissue ischemia. These factors

can lead to pressure ulcers especially on bony anatomical sites such as the nose and frontal bone. All of these lesions cause pain, visible pigmentary changes, and scars. Additionally, there is a change in the skin's microclimate and microbiota that can lead to infections, including folliculitis and acne.

Skin Injuries Due to Protective Mask Pressure

The skin-seal required by protective masks is the principal location of the facial injury. Additional to the increase of temperature and humidity inside the mask, prolonged pressure, and shear forces in the sealing area generates a direct deformation of the tissue, vascular occlusion, edema, and inflammatory reaction leading to the production of a device-related pressure ulcer.⁸ The protective mask may act as an irritant or allergenic agent that can lead to contact or allergic dermatitis.

1. Mask-related pressure ulcer

The skin-mask interface generates three important changes in the skin homeostasis that lead to a reduction of the epidermal barrier function and dermis biomechanical and biochemical tolerance. (1) There is an increase in transepidermal water loss (TEWL) associated with blood and lymph vessel occlusion because of the deformation of the extracellular matrix (ECM) where they are located. (2) Relative temperature and humidity increase, generating a change in the skin's microbiome. As a consequence, there is an inflammatory response and risk of infection. (3) The production of inflammatory mediators, infiltration of neutrophils and monocytes and the increment of reactive oxygen species (ROS).⁸

The evolution and magnitude of the lesions depends on the repetitive use, time and the amount of pressure on the same skin. For healthcare workers working in health facilities with COVID-19 patients, removing the mask is not an option. Limited access to personal protective equipment (PPE) further exacerbates the situation through its uninterrupted use.

Classification

We can classify cutaneous lesions according to their clinical presentation into 4 stages:

Stage 0:

Normal skin

Stage 1:

- a. Erythema in the nose bridge that disappears in the first 24 hours. Skin and tissue misshaping in the malar area with or without erythema that resolves in 24 hours or less. This is related to the use of face masks for less than 6–8 hours and not consecutive days. There can be some burning sensation in the affected area but there is no pain.
- b. Persistent nonblanchable erythema on the nasal bridge

and malar areas that persists more than 24 hours. There is edema and induration of the tissue particularly of the nasal bridge where pain and heat can be experienced. This is related to the use of face masks for more than 6 straight hours of use or everyday compression of the same skin areas.

Stage 2:

The persistent non blanchable erythema is accompanied with shearing lesions because of the increased friction factor. The lesions are characterized by crust formation associated with edema and induration. The wound compromises the dermal layer of the skin.

Stage 3:

Superficial ulcer, primarily on the bony prominence of the nose or any other pressure site clinically visible as an abrasion or a blister. The wound compromised the subcutaneous fat layer of the skin.

Stage 4:

If the pressure exposure continues without any prevention measure or treatment a deep full thickness pressure ulcer will appear. Bone, muscle and tendon may be exposed. The wound bed may be covered by slough.

Table 1 outlines the aforementioned classification system and their associated clinical manifestations.

Prevention Recommendations

Prolonged pressure of PPE to areas of bony prominence with thin overlying skin, such as the orbital rim and nasal bone, is the chief culprit of these facial lesions. Offloading techniques that minimize this pressure on the skin are the most effective means of prevention. Cushioning the infraorbital cheek and nasal bridge help protect the underlying skin from damage. Products such as surgical tape (ie, 3M Microfoam Surgical Tape™) and/or hydrocolloid dressing (ie, DuoDERM™) are effective. Additionally, positioning non-mask PPE, like face shields, in a way that does not put additional pressure on the mask is also beneficial.

It is critical that the seal of the mask is maintained when in use. Some products and application techniques may interfere with this seal, putting the user at risk for infection. If possible, cushioning products should be applied as one continuous strip to help minimize the risk of seal compromise of the mask. If two or more strips of a product are used, they should overlap and be applied firmly in place (Figure 1). A demonstrational video is also available online.⁹ Application of moisturizer to the face immediately before donning PPE can also interfere with the adherence of tape to the skin and compromise the seal of the mask. Instead, we recommend washing the face with a gentle cleanser prior to applying cushioning products. A seal check should always be done after donning a mask. Additional infor-

TABLE 1.

Clinical Stages of Injury	
Stages of Injury	
Stage 1 a	
	
Stage 1 b	
	
Stage 2	
	

FIGURE 1. Example of application of 2 strips of hydrocolloid dressing overlapping midline on the nasal bridge.



mation on how to properly perform a seal check is available through the Center for Disease Control (CDC) and National Institute for Occupational Safety and Health (NIOSH).¹⁰ Repetitive application and removal of these adhesive products can result in worsening erythema and irritation of the skin. Cushing adhe-

sive tape and/or dressing should be left in place for as long as possible. Ideally, it would only be applied once daily.

Treatment Recommendations

Once the lesions appear, treatment will be necessary to slow the process and also reverse the damage. An adequate routine that entails cleaning, moisturizing, and improving the skin's barrier function is imperative in the initial stages of the lesions. The use of a healing ointment of any type applied twice daily to the open sores and/or antibacterial ointment two times per day should be the intervention if any signs of infection are noted. For ulcers, consider using duoderm thin application daily. The best time to use the treatments recommended is at the end of the shift to make sure there is no effect on the seal of the masks. Treatment recommendations are described in Table 2.

TABLE 2.

Treatment Recommendations for Protective Mask Pressure Ulcers		
Stage	Treatment Recommendations	Prevention Recommendations
STAGE 0	No treatment needed	Use Sun Protection Daily SFP 30 - 50+ to prevent post inflammatory hyperpigmentation
STAGE 1 a	Moisturizer and aloe vera dressing after using the protective mask	Before using the mask apply a hydrocolloid dressing or foam surgical tape in the sealing area of the mask where there is pressure on the skin as described in the prevention section (check for a correct seal after applying)
STAGE 1 b	Solution of hyperoxygenated fatty acids with moisturizer should be applied before and after using the mask.	Silicone scar sheets can be used as an alternative if the hydrocolloid dressing is not available Daily massage the area to stimulate the skin vascularity and lymphatic flow. Ideally before and after using the face mask (only stages 1a-1b)
	Crusts: Restorative cream with copper sulfate and zinc sulfate in the crust twice a day. Cover the lesion with hydrocolloid patch	
	Consider growth factor dressing, Biafine, Cutagenix, and others such as Stratamed are excellent products to be used amongst others.	
STAGE 2	Open sores: Healing ointment of any type applied BID to the open sores, antibacterial ointment BID if any signs of infection are noted. Abrasions: Consider using a thin layer of duoderm daily	
STAGE 3	Pressure superficial ulcers: consider consulting a plastic surgeon. Treatment with dressing to accomplish healing by secondary intention. If there in failure, debridement / flap may be needed Deep pressure ulcer: consulting a plastic surgeon is needed.	According to plastic surgeon's considerations in each particular case
STAGE 4	Direct surgical debridement may be necessary. Flap surgery may be needed according to the plastic surgeon's assessment.	According to plastic surgeon's considerations in each particular case

FIGURE 2. Acne lesions in the lower third of the face after N95 mask use in a healthcare worker with acne-prone skin.



Acne exacerbations in predisposed individuals or de novo has been one of the most common adverse reactions reported to the N95 mask. In a study by Foo CC1 et al, over 35% of the staff who used masks regularly reported adverse skin reactions. Acne was the most frequent condition representing almost 60% of the patients in this study. All those who had skin reactions developed them while using N95 masks for an average duration of 8 hours a day and over a mean period of 8.4 months.¹¹

The most common adverse reaction reported to the N95 mask was acne, and this has 2 plausible explanations. First, a hot and humid microclimate is created in regions of the face covered by the mask, which predisposes a flare-up of acne. Secondly, occlusion of pilosebaceous ducts due to local pressure on the skin from the close-fitting mask could result in an acne flare.¹⁵

Pathophysiology

The appearance of acne with the use of N95 has many possible explanations. Acne occurs in sites dominated by *Cutibacterium acnes* (formerly *Propionibacterium acnes*) and *Malassezia* species, both of which can function either as commensal or pathogenic.

Skin microbiota provides the first line of protection against environmental factors and pathogens. The microbiota consists of both 'resident' and 'transient' microbes, and is constantly in flux, changing alongside environmental and host factors such as ultraviolet exposure, environmental microbes, personal hygiene and consumer care products, host hormone levels, sebum, and sweat. 'Microbiota' refers to microorganisms on the skin, and the 'microbiome' represents the total genomic component, measured by DNA analysis.¹² A complex interaction between skin and its commensal microflora safeguards skin from day-to-day environmental influence. Occasionally, because of imbalanced relationships, the skin commensal microbiota may shift to harmful communities in noninfectious skin-related pathologies such as atopic dermatitis, psoriasis, rosacea, and acne.^{13,14} This imbalance is thought to potentiate epithelial dysfunction, immune dysregulation, or overgrowth of pathogenic microbes. Several factors, such as hygiene and

environment, may involve changes in the microbiota composition among healthy and acneic skin. Acne tends to be more comedonal in preadolescents. Given this, it has been hypothesized that the microbiome of preadolescents or people with overproduction of sebum (hyperactive sebaceous glands) might be different.¹⁵

Factors that affect patients wearing long-term N95 masks may include the following: a hot and humid microclimate that is created in regions of the face covered by the mask, which predisposes to a flare-up of acne. Secondly, occlusion of pilosebaceous ducts due to local pressure on the skin from the close-fitting mask could result in an acne flare. Itch and rash were reported frequently as well with most cases probably due to irritant contact dermatitis from components of the mask.¹¹ Third, stress has long been suspected to induce acne flares by anecdotal observations but more recently has been scientifically proven. In a student examination stress study, increased acne severity is significantly associated with stress levels (Figure 2).¹⁶

The role of skin and the peripheral hypothalamic-pituitary-adrenal (HPA) axis has been studied in the pathogenesis of acne. Corticotropin releasing hormone (CRH) and its receptors have been detected on sebocytes. CRH promotes lipogenesis in sebocytes through up-regulation of key enzymes.¹⁷ Other hormones including ACTH and α -MSH also contribute to sebum production and possibly worsen the acne.¹⁸

Treatment Recommendations

Patients with acne prone skin should avoid pump-bottle lotions. These tend to contain more alcohol and can burn and sting when applied to skin that is dry, cracked, or peeling. Avoid retinol-containing anti-aging products, hydroxy acids, scrubs, and peels that can irritate the skin even more.

Further recommendations include: washing face daily or twice a day with gentle cleansers (avoid daily salicylic acid, with high percentage or benzoyl peroxide). Introduce an oil-free, hypoallergenic, and non-comedogenic, balanced-PH, cleanser. Adequate ingredients to use: moisture-rich soy, glycerin, sulfur 4–5% which is anti-inflammatory, natural alpha-hydroxy acid (AHA) such as lactic acid, glycolic acid, citric acid, and malic acid from blueberry extract, mandelic acid, pomegranate antioxidant cleanser, licorice extract, and zinc technology (to soothe irritated skin), bromelain enzymes, and cocoyl apple amino acids found to be safe and less irritating in acne prone skin.

For long shifts, healthcare workers may use gentle facial wipes cleansers with ingredients such as:

- Mild salicylic acid and witch hazel
- Lipo-hydroxy acid (LHA), a derivative of salicylic acid, used

to help exfoliate the surface of the skin and lift away dead skin cells, pore-clogging dirt, oil, and makeup.

- Zinc pidolate, which targets excess oil and further helps clear congested pores
- Grapefruit seed oil, which serves as a natural astringent

Moisturizers for acne prone sensitive skin:

- Avoid comedogenic products
- Include oil free, hypoallergenic products
- Moisturizers rich in ceramides, hyaluronic acid, glycerin, jojoba, marine complex, green tea
- Barrier creams with silicone-related ingredients
- Cosmetics free of dyes, fragrance, lanolin, parabens, and formaldehyde
- Moisturizer with minerals and ingredients that stabilize microbiota of the skin with prebiotic thermal water, selenium
- Topical pre and postbiotic, including prebiotic oat extract

Prescription treatment:

- Avoid high strength retinoid acids such as tazarotene, high percentage tretinoin; use low potency retinoic acid such as adapalene once or twice a week if needed. Newer versions of retinoids in lotion form can be used as alternatives.
- Azelaic acid 15% gel or foam two times a day will help with acne and post-inflammatory hyperpigmentation
- Mandelic acid 5% pads, improves acne and post-inflammatory hyperpigmentation
- Erythromycin ointment will help with inflammatory papules and irritation of the skin
- Avoid antibiotic solutions with alcohol
- Minocycline foam formulation which contains coconut oil in the vehicle and helps with moisturization.
- Oral antibiotics if patients present with moderate to severe acne

In cases of Isotretinoin treatment, utilize non-comedogenic moisturizers and the use of emollients before applying the mask.

The use of hydrocolloid bandages is practical for inflammatory papules and to prevent picking at certain lesions. These bandages absorb excess fluid, (ie, oil and pus) and can speed healing time for excoriated inflammatory lesions. They can help prevent scarring and post-inflammatory hyperpigmentation. This bandage can be left on for a few hours and have ingredients such as salicylic and hyaluronic acids.

II. Allergic Dermatitis, Contact Dermatitis, and Postinflammatory Hyperpigmentation

The aforementioned lesions include abrasions, pressure ulcers, edema, crusts, long term erythema and acne and folliculitis. Important consideration should be given to the possibility of

some patients developing an irritant contact dermatitis secondary to the equipment. True allergic contact dermatitis may occur to adhesives, rubber, or metal used in the masks. Patch testing may be prudent in those cases. The N95 masks are made of polypropylene fabric, a nonwoven technology.

Postinflammatory hyperpigmentation is mainly caused by pressure-related effects of mask use, especially on bony protrusions. Due to the long-term inflammatory reaction generated by the pressure changes in the affected tissues, melanocytes increase their melanin production and a localized brown patch can appear days after the initial signs of inflammation (ie. edema and erythema). This adverse effect can affect all skin phototypes, particularly Fitzpatrick skin types III, IV, and V.

Early implementation of emollients and topical corticosteroids in patients suspected of having contact dermatitis is useful for alleviating pruritus. For post-inflammatory hyperpigmentation, consider the use of azelaic acid, retinol, and other treatment options including short term hydroquinone in combination with fluocinonide 0.05% cream once the active lesions have cleared.

CONCLUSION

In general, when evaluating frontline healthcare workers with skin lesions, the clinical assessment as well as a full review of symptoms may be of guidance towards the correct treatment and resolution of the chief complaint. Prevention is key for the use of PPE during this pandemic, as well as any future instances that require N95 respirators on a daily basis.

This article reviews current reported facial lesions secondary to daily mask use seen in frontline healthcare workers working against COVID-19. When patients and providers have an astute understanding of this novel virus, its replicative nature, the dire need for PPE for those treating affected patients, and the short and long term effects of PPE on the skin barrier, we are able to elucidate a wide variety of treatments and recommendations to prevent long term effects on the skin. This is an ongoing and rapidly developing situation that as dermatologists we will continue to investigate and report any new lesions developed by the frontlines health workers. By imparting these therapies to the general public as well as to physicians treating COVID-19 skin conditions, we aim to provide comprehensive and effective recommendations in maintaining proper skin barrier protection, a crucial component of containing this virus.

DISCLOSURES

None of the other authors listed has any commercial associations or financial disclosures that might pose or create a conflict of interest with the methods applied or the results presented.

REFERENCES

1. ZhuN, Zhang D, Wang W, et al. China Novel Coronavirus Investigating and

- Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733.
2. Bridges C.B. Kuehnert M.J. Hall C.B. Transmission of influenza: implications for control in health care settings. *Clin Infect Dis*. 2003; 37: 1094-1101
 3. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol*. 2020;92(4):418-423. doi:10.1002/jmv.25681
 4. Wang R, Pan M, Zhang X, Fan X, et al. Epidemiological and clinical features of 125 Hospitalized Patients with COVID-19 in Fuyang, Anhui, China. *Int J Infect Dis*. 2020 April 11. Pii: S1201-9712(20)30203-4. doi: 10.1016/j.ijid.2020.03.070
 5. Advice on the use of masks in the context of COVID-19, World health organization Interim guidance April 6, 2020 https://apps.who.int/iris/bitstream/handle/10665/331693/WHO-2019-nCov-IPC_Masks-2020.3-eng.pdf?sequence=1&isAllowed=y
 6. World Health Organization. Advice on the use of masks in the context of COVID-19 (accessed 6 April 2020) https://apps.who.int/iris/bitstream/handle/10665/331693/WHO-2019-nCov-IPC_Masks-2020.3-eng.pdf?sequence=1&isAllowed=y
 7. National services scotland. Transmission Based Precautions Literature Review: Surgical Masks, Version 2.0 (October 2017) https://hpspubsrepo.blob.core.windows.net/hps-website/nss/1723/documents/1_tbp-lr-masks-v2.0.pdf
 8. Gefen A, Alves P, Ciprandi G, et al. An international consensus on device-related pressure ulcers: SECURE prevention. *Br J Nurs*. 2020 Mar 12;29(5):S36-S38. doi: 10.12968/bjon.2020.29.5.S36. <https://doi.org/10.12968/bjon.2020.29.5.S36>
 9. https://www.youtube.com/watch?v=kmdbyyha5ng&list=PLUCiA4BWx2zG5Ytn-eNCHTtMSpM7n_iIN&index=3&t=0s
 10. [NIOSH [2010]. How to properly put on and take off a disposable respirator. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2010-133 <https://www.cdc.gov/niosh/docs/2010-133/pdfs/2010-133.pdf>.)
 11. Foo CC1, Goon AT, Leow YH, Goh CL. Adverse skin reactions to personal protective equipment against severe acute respiratory syndrome—a descriptive study in Singapore. *Contact Dermatitis*. 2006 Nov;55(5):291-4.
 12. Rocha MA, Bagatin E Arch. Skin barrier and microbiome in acne. *Dermatology Res*. 2018 Apr;310(3):181-185.
 13. Barnard E, Dawson TL Ramasamy S. The role of the skin microbiota in acne pathophysiology. *Br J Dermatol*. 2019 Oct;181(4):691-699.
 14. Balato A, Cacciapuoti S, Di Caprio R, et al. Human microbiome: composition and role in inflammatory skin diseases. *Archivum Immunologiae et Therapiae Experimentalis*. (2019) 67:1–18
 15. Chen Y, Lyga J. Inflamm Brain-Skin Connection: Stress, Inflammation and Skin Aging. *Allergy Drug Targets*. 2014 Jun; 13(3): 177–190.
 16. Chiu A, Chon SY, Kimball A B. The response of skin disease to stress: changes in the severity of acne vulgaris as affected by examination stress. *Arch Dermatol*. 2003;139 (7):897–900.
 17. Zouboulis C C, Seltmann H, Hiroi N, Chen W, Young M, Oeff M, Scherbaum W A, Orfanos C E, McCann S M, Bornstein S R. Corticotropin-releasing hormone: an autocrine hormone that promotes lipogenesis in human sebocytes. *Proc Natl Acad Sci USA*. 2002;99 (10):7148–7153.
 18. Boesten D M, de Vos-Houben J M, Timmermans L, den Hartog G J, Bast A, Hageman G J. Accelerated aging during chronic oxidative stress: a role for PARP-1. *Oxid Med Cell Longev*. 2013. 2013:680414

AUTHOR CORRESPONDENCE

Mehreen Hall DO

E-mail:..... maysheikh@gmail.com