

Functional and integrative approach to dermatology: Useful tips for your practice

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INTRODUCTION

The functional and integrative approach to dermatology is of great interest to both patients and clinicians, especially since many dermatologic conditions are reflections of systemic inflammation. It is important for the dermatologist to understand the intertwined relationships between the gut and skin microbiome and how it impacts skin health—the gut-skin-immune and endocrine system axis—and the importance of modifying lifestyle factors to prevent and treat inflammation as we seek to manage our patients in a more holistic manner. Likewise, patients are becoming more discerning and seek approaches other than traditional Western medical options. Our group is pleased to share our best practices and tips substantiated by evidence found in the literature.

WHAT IS FUNCTIONAL MEDICINE?

Functional medicine (FM) is a systems biology-based approach that focuses on identifying and addressing the root cause of disease. It incorporates the latest in genetic science, systems biology, and understanding of how environmental and lifestyle factors influence the emergence and progression of disease. FM practitioners spend time listening to patients and gathering their medical history. Information gathered is intended to identify the root causes of the illness, including triggers such as poor nutrition, stress, toxins, allergens, genetics and microbiome. Upon identification of the triggers and performing a nutrient oriented physical examination wherein all areas of the skin are inspected, a PERSONALIZED HEALTH CARE PLAN is given to the patient.¹ The plan will address many aspects of the patient's life, from physical needs, includ-

ing nutrition, exercise and sleep, to mental and emotional stressors related to social, work, and community life. This enables physicians to practice proactive, predictive, personalized medicine and empowers patients to take an active role in their own health. Hence, through this approach, dermatologic conditions can be addressed holistically in close partnership with the patient.

SKIN-GUT-BRAIN AXIS AND ACNE

Western type diets play a significant role in dysfunction of the gut microbiome by causing the release of several neurotransmitters that may play a role in skin inflammation.

New and established data suggested that gut microbiome dysbiosis may trigger or aggravate acne vulgaris.² Alteration and impairment of the gut microbiome has been speculated to cause significant changes such as an increase in Bacterioides species. High levels of *Cutibacterium acnes* (*C. acnes*) and *Cutibacterium granulosum* (*C. granulosum*) are found abundantly in pustules and comedones of acne patients,^{3,4} as well as *Malassezia* species, which are hypothesized to promote inflammation due to its chemoattraction to neutrophils, which then release cytokines and other pro-inflammatory mediators.^{4,5} Consumption of a Western diet comprised of refined carbohydrates, saturated fat, dairy products, and chocolates has been shown to cause gut imbalance by impairing the normal intestinal microflora, Bifidobacterium species, and Lactobacillus species.⁶ This gut dysbiosis leads to the production of acetylcholine, norepinephrine, and serotonin, which raises levels of insulin-like growth factor-1 (IGF-1)⁷ resulting in systemic inflammation in-

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DAIRY ELIMINATION AND SKIN CONDITIONS AMONG PREGNANT AND BREASTFEEDING MOTHERS

Consider eliminating cow's milk and other dairy products from the diet of pregnant and breastfeeding mothers with a history of acne and eczema.

Currently, mothers are advised by health professionals to drink cow's milk as a source of calcium during pregnancy and breastfeeding. However, a large body of evidence now exists that demonstrates how certain foods and food substances such as cow's milk may adversely influence hormones and cytokines that then cause acne and eczema.^{3,10} Milk and other dairy products have been identified by US law and the US Food and Drug Administration as a major food allergen.^{9,11} For pregnant and breastfeeding patients, it is recommended to eliminate cow's milk and other dairy products from their diet, and instead provide them with a list of calcium-rich foods that are abundant in the country and readily-available like malunggay, saluyot and beans. Patients may also be referred to a board-certified nutritionist.

PROBIOTICS, ANTIBIOTICS AND ACNE

Gut and skin microbiota are shifted in acne patients. Probiotics work synergistically with tetracycline antibiotics by improving the acne and increasing short chain fatty acids, which are anti-inflammatory and may diminish lipid secretion. When considering systemic antibiotics for an acne patient, the addition of a probiotic may provide better results and to decrease potential side effects of chronic antibiotic use.

Patients with acne have been found to have altered skin microbiota compared to healthy controls and show increased numbers of *C. acnes*, *C. granulosum*, *Staphylococcus epidermidis*, *Proteobacteria* and *firmicutes*, *Streptococcus*, and fungal *Malassezia*.¹² At the gut level, acne patients are found to have decreased Actinobacteria and increased Proteobacteria, with low levels of Bifidobacterium, Butyricoccus, Coprobacillus, Lactobacillus, and Allobaculum.¹³ Tetracycline class antibiotics are a standard of care for acne and work by inhibiting bacterial protein synthesis and are bacteriostatic but may cause gastrointestinal disturbances.

A small randomized controlled trial (RCT) by Jung et al in 2013 compared 3 groups of acne patients: Group A with probiotics alone, group B with minocycline alone, and Group C received both probiotics and minocycline.¹⁴ Clinical and subjective assessments showed a significant improvement in all groups in total lesion counts at 4 weeks after treatment initiation ($p < .001$), with continued improvement seen with each subsequent

follow-up visit ($p < .01$). At the 8- and 12-week follow-up visits, group C had a significant decrease in total lesion count versus groups A ($p < .001$) and B ($p < .01$). The probiotic given had a combination of *Lactobacillus acidophilus* (5B CFU), *Lactobacillus delbrueckii* (5B CFU) and *Bifidobacterium bifidum* (20B CFU).¹⁴

PREBIOTICS AND PROBIOTICS IN ATOPIC DERMATITIS

Atopic dermatitis (AD) is characterized by immune dysregulation and altered skin and gut microbiome. Improving nutritional status, nutrient digestion and dietary habits promote beneficial effects in the gut and the skin and regulate immune response. Prebiotics support the growth of "good bacteria" on the skin and in the gut, while probiotics supplement the gut with "good bacteria". These common immune regulators of the gut microbiota help reduce AD clinical symptoms.

Changes of microbial composition and function, termed dysbiosis, in the gut and the skin have been linked to alteration of immune responses and development of AD. The leaky gut or the damage of gut epidermal integrity permits the penetration of various foreign particles, such toxins, microbes and food particles into the systemic circulation, which may contribute to skin inflammation.¹⁵

Prebiotics are non-digestible components, mainly fiber and carbohydrates, that positively create an intestinal environment in which the good bacteria may thrive.¹⁶ Prebiotics were found to improve immune function and Th1/Th2 ratio in AD.¹⁷ Prebiotics also augment the production of short-chain fatty acids (mainly acetate, butyrate, and propionate), which have an anti-inflammatory effect.¹⁸ On the other hand, probiotics are living microorganisms that are either the same as or similar to the microorganisms naturally found in a healthy human. They are deemed beneficial to the host when they are given on acceptable amount.¹⁹ Probiotics reduce the severity of AD through its immunomodulatory effects. They lessen inflammation by reducing proinflammatory cytokines, IL-4, IL-6 and tumor necrosis factor- α (TNF- α).²⁰

Although mechanisms between gut microbiota and skin need to be further explored, improving nutritional status by supporting gut health can reduce immune activation and lead to overall improved health beyond reducing the clinical manifestations in AD.

OMEGA-3 FATTY ACIDS AND ITS USE IN DERMATOLOGY

Nutraceuticals or oral supplements may be useful adjuvants to skin health. Of this, Omega-3 fatty acid supplements may significantly improve cutaneous inflammatory diseases by ex-

erting strong anti-inflammatory actions against immune and epithelial cells. When managing patients with inflammatory skin conditions such as acne vulgaris, atopic dermatitis and even psoriasis, consider giving Omega-3 fatty acid supplementation as adjuvant treatment to decrease inflammation and help improve disease outcome.

Current evidence shows the increasing therapeutic benefits of nutraceuticals in the form of diet and supplements in maintaining healthy skin. Among these, Omega-3 fatty acid supplementation has been associated with significantly improving various dermatologic conditions by decreasing inflammation.²¹ Omega-3 fatty acid and its metabolites (resolvin E1, resolvin D1-5, and maresin 1) have demonstrated strong anti-inflammatory action thru phagocytosis and downregulation of inflammatory cytokines, hence its therapeutic potential in inflammatory cutaneous diseases.²² In a study by Koch et al., docosahexaenoic acid (DHA) supplementation significantly improved atopic dermatitis disease severity, dryness, and pruritus scores compared to saturated fatty acid control at 8 weeks ($p < .02$).²³ For untreated mild-to-moderate acne, a 10-week supplementation of 2000 mg/d EPA + DHA and gamma-linoleic acid, significantly reduced inflammatory and non-inflammatory acne lesions compared to the control group ($p < .05$).²⁴

Omega-3 fatty acid supplementation in the form of dietary modification with the incorporation of omega-3 fatty acid-rich foods was also proven to be beneficial. In an open-label study by Guida et al., 44 obese patients with mild-to-severe plaque psoriasis on various immunosuppressive drugs, a greater than 50% reduction in Psoriasis and Severity Index (PASI) scores and 74% improvement in Dermatology Life Quality Index (DLQI) was seen versus control ($p < 0.02$) after 6 months of being on a low-calorie diet (20kcal/kg/ideal body weight/day) supplemented with omega-3 fatty-rich foods.²⁵ However, in a double-blind study by Soyland et al., 145 patients with moderate-to-severe plaque type psoriasis, no statistically significant reduction in PASI was noted despite 4 months of supplementation of Omega-3 fat eicosapentaenoic acid + docosahexaenoic acid 5000mg/d.²⁶

Although its therapeutic benefits need further conclusive evidence, Omega-3 fatty acid supplementation may be an option to improve or maintain skin health in particular as a possible adjuvant treatment for inflammatory skin diseases such as atopic dermatitis, acne and psoriasis.

PERSONALIZED AND PRECISION MEDICINE: PSORIASIS & NUTRITION

In managing psoriasis, always explore multivariate treatment approaches. These include lifestyle and nutrition. The immunopathogenesis through -omics technology has expanded our understanding of psoriasis. We have different treatment options that specifically targets inflammatory media-

tors, such as biologics. This is good for both physicians and patients in managing this chronic condition. Dermatologists should use knowledge regarding the stimulatory or regulatory effects of nutrition on psoriasis. Therefore, personalized nutrition should be added in how psoriasis (and other chronic skin conditions) is managed.

Psoriasis has a strong association with genetic, environmental and immunological drivers. The new “-omics” technologies have made it possible to unravel different biomarkers that are ushering us into an era of personalized medicine.²⁷ Having sufficient information about the underlying immunopathogenesis of psoriasis would make management more holistic. Patients living with psoriasis often show unbalanced habits, including higher intake of fat and simple carbohydrates, and lower intake of fish and dietary fibers.²⁸ This nutritional difference was shown to be clearly associated with increased severity of psoriasis and cardiometabolic risk. Saturated fatty acids, red meat, simple sugars and alcohol have been shown to activate the following pro-inflammatory pathways: nucleotide-binding domain, leucine-rich repeats containing family, pyrin domain-containing-3 (NLRP3) inflammasome cascade, TNF-alpha/IL-23/IL-17 axis, generation of reactive oxygen species (ROS), gut dysbiosis, and suppression of regulatory T cells (Tregs).²⁹ Dermatologists can evaluate the diet of patients with psoriasis and monitor their nutritional status, suggesting dietary changes that complement the current standard therapies for psoriasis and address other associated comorbidities (e.g. cardiometabolic disease). Therefore, exploring and modifying the patient's nutrition provide a personalized framework for managing psoriasis.

CIRCADIAN RHYTHM, LIFESTYLE, AND SKIN HEALTH

Many patients need lifestyle interventions to address mood, stress, and metabolic health which all greatly impact the skin. Dermatologists can support their patients by starting a conversation on sleep-wake cycle, how it affects hormone secretion, and how aligning daily activities of feeding and physical activity with the body clock can downregulate inflammation at the cellular level to improve chronic skin diseases as well as slow down aging.

The skin as an organ contains and produces hormones that are important in maintaining homeostasis locally and systemically, as it is involved in complex neuroendocrine pathways that are directed by circadian rhythmicity. Melatonin, a highly circadian clock-dependent hormone, may be a key agent in the skin's ability to neutralize both endogenous and exogenous oxidative stress-generating molecules³⁰ and to maintain mitochondrial function in ultraviolet (UV)-exposed keratinocytes.³¹ If synchronized, the circadian clock allows for a faster and more

efficient defensive response of transcription factor nuclear factor-erythroid factor 2 (Nrf2) against environmental insults and cellular damage from chronic inflammation.³² Aside from environmental light as the primary synchronizer of the master clock in suprachiasmatic nucleus, the timing of our feeding and exercise are potent synchronizers as well. For example, it is better to perform high-intensity workout earlier in the day, as doing it at night can delay the onset of melatonin secretion which can lead to sleep dysregulation.³³ Acute sleep deprivation and chronic circadian misalignment can affect cortisol level and the balance of pro- and anti-inflammatory markers.³⁴ Although the impact of the sleep-wake cycle on specific skin diseases needs further studies, improving the overall health of patients is always a good place to start.

BARRIER REPAIR AND BROAD-SPECTRUM ANTI-MICROBIAL EFFECTS OF VIRGIN COCONUT OIL IN COVID-19 STUDIES

Use Virgin Coconut Oil (VCO) as a skin disease adjunctive topical treatment for barrier repair, antimicrobial and anti-inflammatory effect.

Antimicrobial lipid studies in the 1880s halted when the antibiotics era was started by penicillin.³⁵ Released in 1941, resistant *Staphylococcus aureus* strains were already reported in 1942. Antimicrobial resistance (AMR) has become a global problem for many bacteria, viruses, fungi and parasites.³⁶ The rise of more superbugs implicates the high usage now of disinfectants at medical, other facilities, homes, and for personal use against COVID-19.^{37,38} Continuing antimicrobial lipid studies rank the top Fatty acids (FAs) and their Monoglycerides at #(1) Lauric (C12:0); #(2) Capric (C10:0); #(3) both Caprylic (C8:0) and Myristic (C14:0). All are saturated medium chains, found highest in virgin coconut oil (VCO).³⁹ Their mechanism of action includes destruction of microbial lipid cell membranes and biofilms, innate immunity and anti-inflammatory effects. This differs from the mechanism of action of antibiotics which target proteins of microbes, that microbes in turn can readily mutate.⁴⁰ A comparison review of skin barrier repair, antibacterial, antifungal, wound healing, and skin ageing on 19 plant oils found in VCO had a therapeutic benefit and met all functions, except skin cancer prevention.⁴¹ Another review on plant oils to treat psoriasis

found VCO was the best humectant and occlusive oil.⁴² Half-way analysis in a mild to moderate COVID-19 infection, found significant outcome ratings in the VCO adjunctive care group.⁴³ More randomized controlled trials for asymptomatic to mild, another for severe and critical COVID-19 cases, and a blended learning workshop on why and how to use VCO in adjunctive care in three tertiary hospitals are close to Philippine Council for Health Research and Development to approval. Since VCO use in these studies continue to show significant results, it is recommended to use topical VCO for barrier repair, antimicrobial and anti-inflammatory effects, as it is functional and evidence-based.

PRURITUS AND ACUPUNCTURE

Pruritus is a common complaint of dermatology patients. Acupuncture may serve as an adjunct treatment to standard therapy.

Pruritus is commonly associated with dermatologic diseases such as atopic dermatitis, psoriasis, eczema, and urticaria. Acupuncture, through stimulation of A γ and C fibers and release of vasoactive mediators from inflammatory cells, can reduce pruritus.⁴⁴ Additionally, a recent study, showed that the parasympathetic activity and functional connectivity of the putamen and posterior part of the midcingulate cortex could be associated with antipruritic response to acupuncture.⁴⁵ Furthermore, a local study in 2021 showed acupuncture as a promising adjunct treatment in atopic dermatitis, significantly reducing pruritus, disease severity and implement of quality of life.⁴⁶

CONCLUSION

This paper summarizes new information on the interplay of skin diseases and the interplay with the immune system, environment, and the gastrointestinal system. This concludes that the health of an individual not only focuses on a single organ, but different organs can also cause an imbalance in other systems of the body that can lead to alteration of bodily functions. The approach of functional and integrative medicine to overall health is treating all aspects of the body, which also includes the microbiome. Finally, by better understanding the root cause of the condition, a personalized treatment can be formulated that can help control disease and prevent it from progressing.

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