

Skin Manifestations of Gluten Intolerance

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My Particular Interests

My approach to the skin

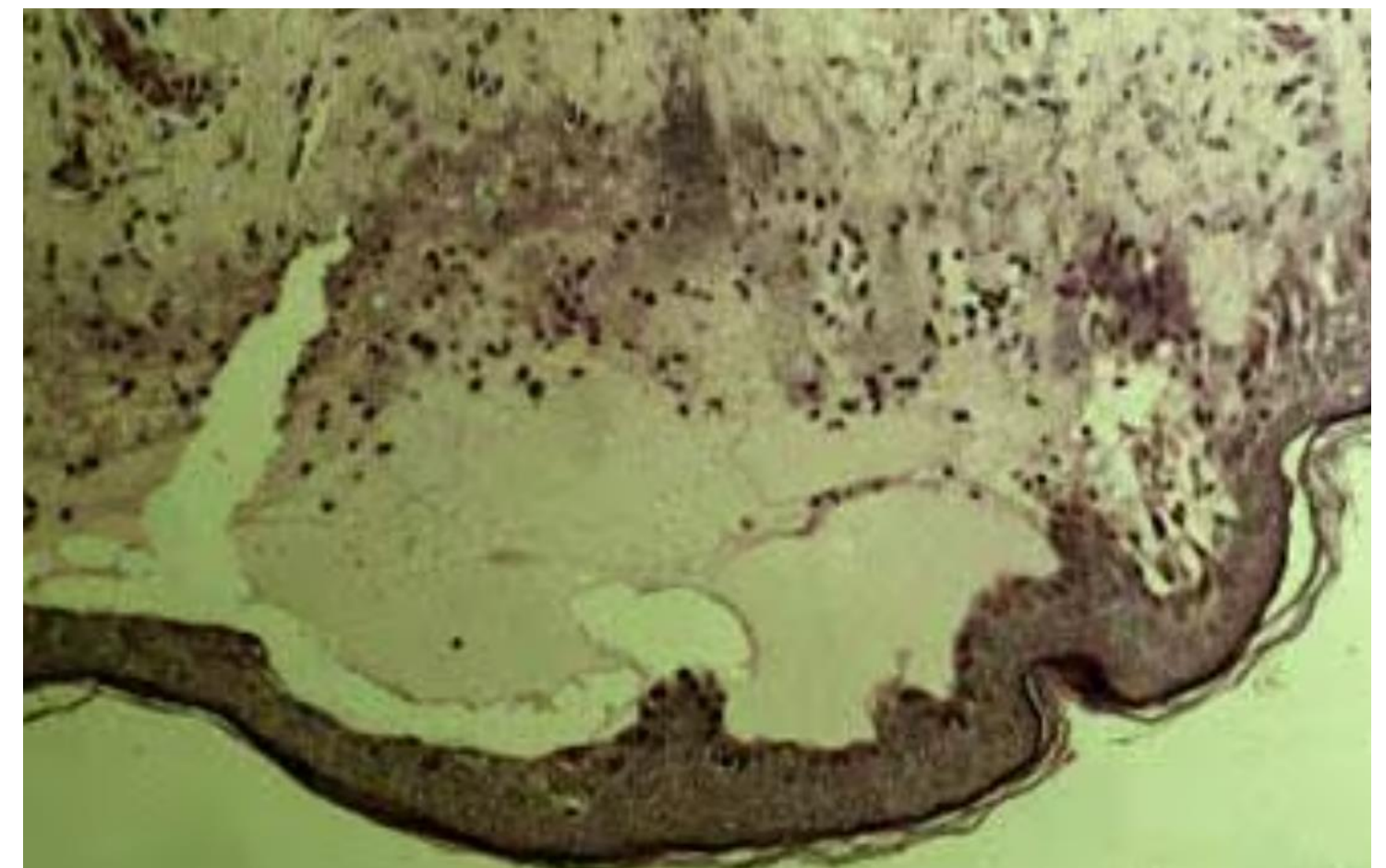
- Son of a physician who was gifted at seeing the patient as a whole
- Lifestyle interventions for autoimmune disease
- Psychodermatology - spent 13 years studying with Gerald Epstein, MD and the American Institute for Mental Imagery, phenomenology and non-deterministic psychology
- Conventional and Integrative dermatology
- Photobiology
- Circadian biology
- Health Food Entrepreneur

Dermatitis Herpetiformis (1/3)

The main direct skin manifestation

This is the most directly connected skin manifestation of gluten sensitivity, often considered the skin expression of celiac disease. It features intensely itchy and blistering skin eruption commonly on the elbows, knees, buttocks, and back.

- Among patients with celiac disease, 15-25% develop dermatitis herpetiformis.
- 10-15% of their first-degree relatives also have dermatitis herpetiformis or celiac disease.
- Co-existing diseases : thyroid abnormalities in 50% in patients, dermatomyositis, type 1 dm, rheumatoid arthritis, lupus



Dermatitis Herpetiformis (2/3)

Treatment

- Dapsone - the primary medication used to treat dermatitis herpetiformis. The exact mechanism of action is unknown
- Improvement can occur in hours after taking the medicine
- Tests include G6PD, CBC, Liver Function Tests, but generally well tolerated
- Does not affect the disease course of celiac whatsoever
- Can lower dose slowly once on strict gluten free diet

Dermatitis Herpetiformis (3/3)

Leading Theory

1. Usually appears later in people who have celiac disease without obvious symptoms initially.
2. When someone with this sensitivity eats gluten-rich foods, their body produces a specific type of antibody called IgA against a substance in the gut known as tissue transglutaminase (t-TG or TG2).
3. These IgA antibodies can travel through the bloodstream and mistakenly interact with a similar substance in the skin called epidermal transglutaminase (e-TG or TG3). Because these two substances are structurally similar, the antibodies intended to target the gut enzyme can also bind to the skin enzyme.
4. This mix-up leads to the accumulation of IgA and e-TG complexes in a layer of the skin called the papillary dermis. This accumulation triggers an immune response, which causes the skin lesions characteristic of dermatitis herpetiformis.

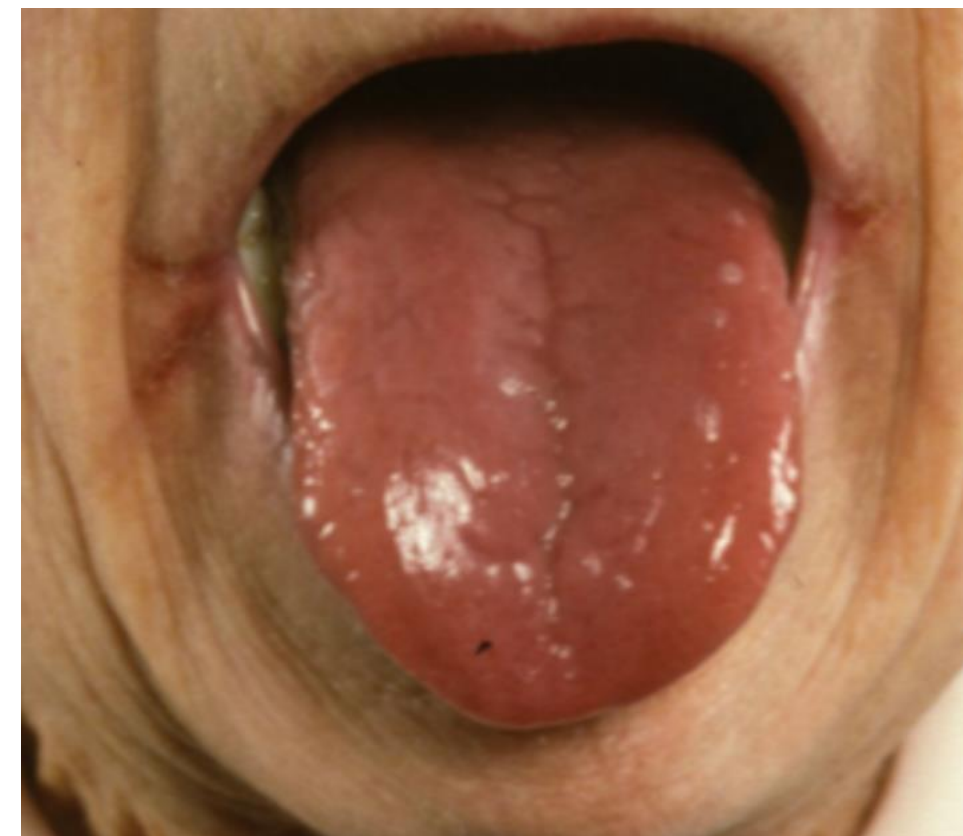
Essentially, the body's misguided attack against gluten ends up affecting the skin due to a case of mistaken identity between proteins in the gut and the skin.

- **All DH patients in one study showed signs of intestinal permeability with upregulation of zonulin and leaky gut**

Cutaneous Signs of Nutrient Deficiencies

Found in CD

- Ecchymoses (bruising) - Deficiency in Vitamin K
- Follicular Hyperkeratosis - Vitamin A
- Angular Chelitis - iron, zinc, and B vitamins (especially riboflavin, B2)
- Glossitis - iron and B vitamins, b12



Psoriasis

14% of psoriasis patients displayed elevated anti-gliadin IgA antibodies (AGA) (Kolchak, 2018)

- Gluten free diet has shown some improvement in patients with psoriasis.
- Psoriasis patients higher risk of metabolic disease - also high inflammatory markers with aortic inflammation being shown (Gelfand, University of Pennsylvania)



Palmoplantar Pustulosis

18% had IgA antibodies against gliadin and 10% against tTG (Micheallsson 2007)

- Most common in women smokers, association with psoriasis and stress
- Patients with this should be screened for celiac



Aphthous Stomatitis - canker sores

A meta-analysis showed that patients with CD had a significantly higher frequency of aphthous stomatitis compared to healthy subjects (Nieri M, 2017)

- Ferguson et al. recommended screening for deficiencies in folate, B12, and iron in patients with recurrent aphthae, with jejunal biopsy reserved for cases showing evidence of malabsorption (Ferguson M, 1980)



Alopecia Areata

2% of the general population,

- Ertekin et al. found that 41.7% of pediatric AA patients tested positive for IgA anti-tG Ab, and these patients exhibited total villous atrophy (Marsh type-IIIc) on intestinal biopsy. Eliminating gluten restored hair growth, suggesting CD screening for pediatric AA patients.
- Anti-gliadin Ab is linked to more extensive disease



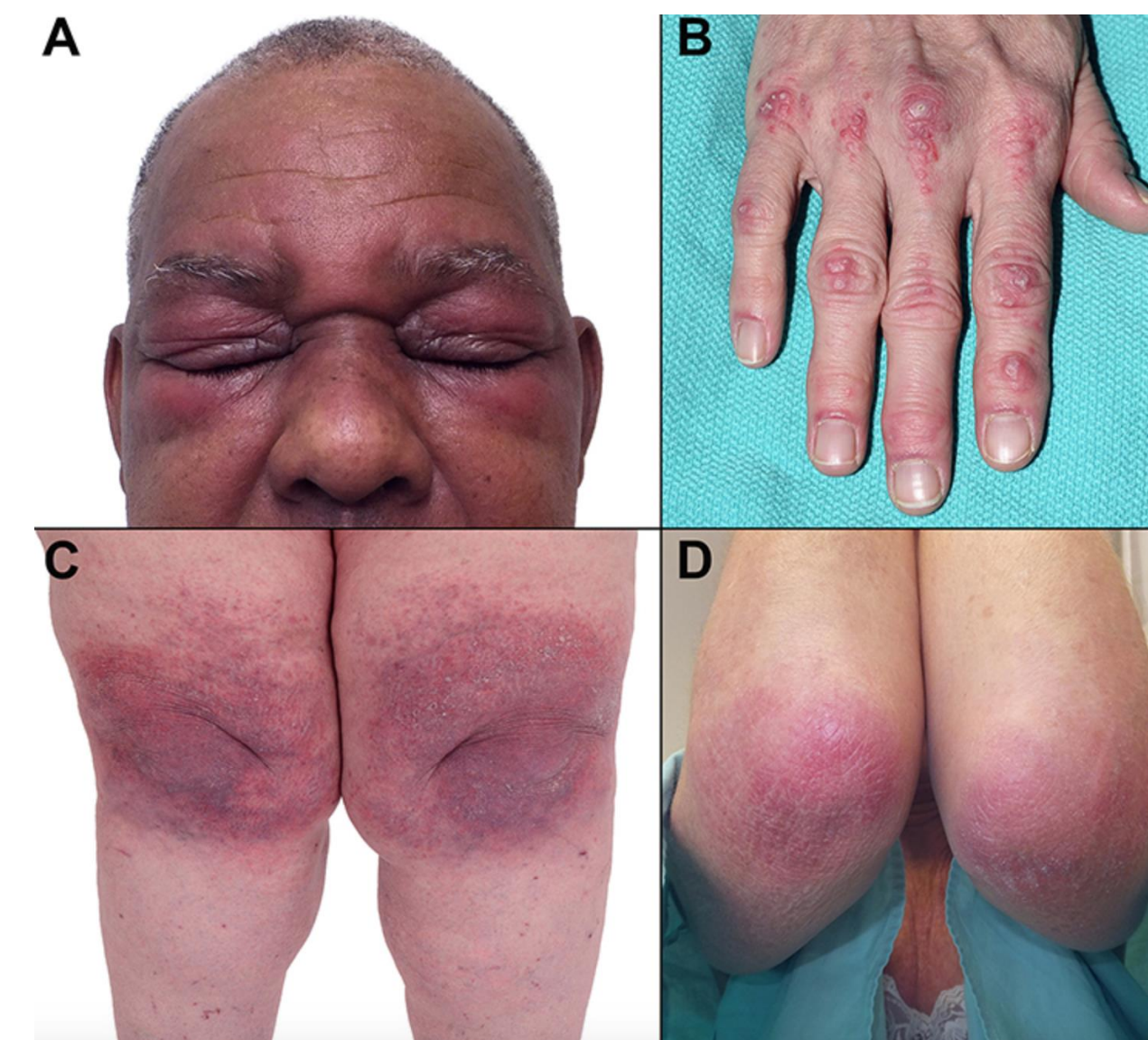
Dermatomyositis

In a study examining the link between CD and IM, IgA class AGA antibodies were found in 11% of DM patients, 44% of PM patients (Selva-O'Callaghan A, 2007)

Autoimmune Disease: Dermatomyositis is an inflammatory autoimmune disease primarily affecting the skin and muscles. It is characterized by distinctive skin rashes and progressive muscle weakness. Common skin manifestations include a heliotrope rash (purple or red rash around the eyes) and Gottron's papules (red or purple bumps over the knuckles).

Systemic Involvement: While primarily known for its effects on skin and muscles, dermatomyositis can also impact other body systems, including the lungs, heart, and gastrointestinal tract, potentially leading to more severe complications such as interstitial lung disease and cardiac issues.

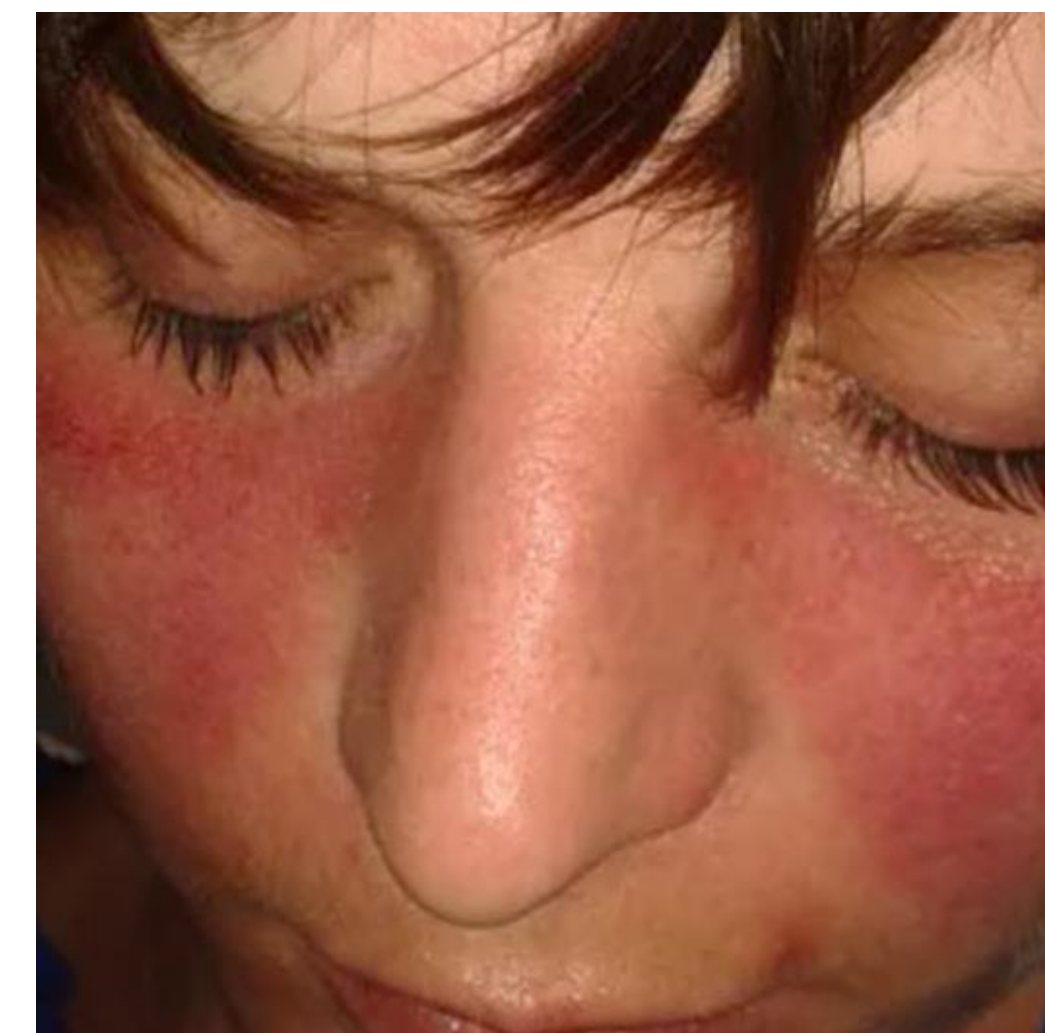
Treatment and Management: Treatment typically involves immunosuppressive medications, such as corticosteroids and disease-modifying antirheumatic drugs (DMARDs), to control inflammation and manage symptoms. Physical therapy is also crucial to maintain muscle strength and functionality. Additionally, managing exposure to sunlight is recommended due to photosensitivity associated with the disease.



Lupus

Low Risk Overall

In the research study titled "Increased Risk of Systemic Lupus Erythematosus in 29,000 Patients with Biopsy-Verified Celiac Disease," the case presented demonstrates that individuals diagnosed with CD faced a noteworthy threefold increase in the risk of developing SLE compared to the general population. However, the study consistently highlights that the absolute risks of developing lupus within this cohort remain low (Ludvigsson JF, 1980)



Atopic Dermatitis, Vitiligo, and Rosacea

All have associations



Gut Skin Axis

Interrelationship between Microbial Dysbiosis and Skin Conditions

Interrelationship between Microbial Dysbiosis and Skin Conditions

- The skin has its own microbiome, it is not a surprise that when the skin microbiome is altered, so is the gut microbiome
- Dysbiosis in both is related to altered immune signaling which promoted various skin diseases we discussed already, in addition to increasing the risk for skin cancer
- Skin estimated to have 10^{12} and the gut has 10^{14} microbial cell
- Gut and Skin Microbiome similar - both are the interplay between you and the environment

Psoriasis vs IBD

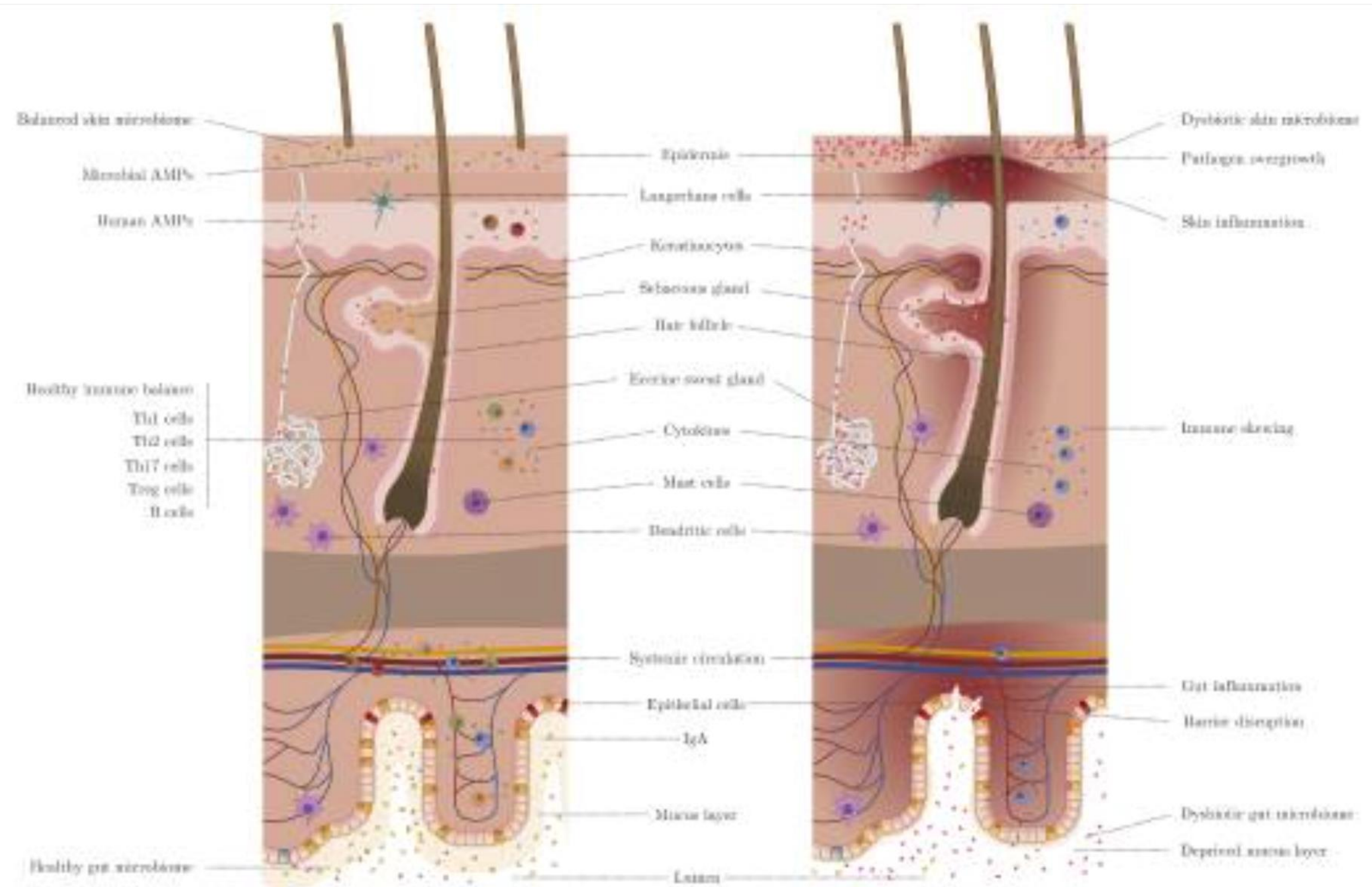
Similarities and a way to understand the interactions by example

- Epithelial barrier dysfunction
- Increased permeability of the epidermal skin and intestinal barrier is due to the augmented interaction of allergens and pathogens with inflammatory receptors of immune cells
- Both diseases have an analogous immune response and involve phagocytic, dendritic, and natural killer cells along with a range of cytokines and AMPs that induce a T cell response
- Both diseases are characterized by dysbiosis in the microbiome composition that covers the respective interface linings
- Is it surprise then that numerous studies provide evidence for a profound bidirectional link between gastrointestinal health and skin homeostasis through modification of the immune system

Additional Interesting Connections

More interplay

- Skin exposure to ultraviolet B (UVB) and therefore indirectly to serum vitamin D levels increase the diversity of the gut microbiome
- Food allergies may result from an impaired skin barrier: atopic dermatitis sensitizes to peanut allergy due to peanut protein exposure in household dust, leading ultimately to immunoglobulin E (IgE)-mediated mast cell expansion in the gut
- The gut–skin axis may be viewed as an integral part of the gut–brain–skin axis



Molecules with potential a modulatory effect on skin and gut either directly or indirectly.

Molecule	Documented/Possible effect in gut	Documented/Possible effect on skin	Reference
Bacterial metabolites			
SCFAs *	Anti-inflammatory effects	Anti-inflammatory effects	[132]
Vitamin D	Suppress inflammation in IBD*	Not reported	[133]
Urocanic Acid	Suppress inflammation in IBD*	Not reported	[134]
GABA *	Neurotransmitter modulation	Itch restriction	[135,136]
Dopamine	Neurotransmitter modulation	Inhibition of hair growth	[135,137]
Serotonin	Neurotransmitter modulation	Melatonin modulation	[135,138]
Acetylcholine	Neurotransmitter modulation	Barrier function	[135,139]
Phenol and p-cresol	Biomarker of gut dysbiosis	Impaired epidermal barrier function	[140]
Dietary components			
Catechins	Anti-inflammatory effects	Anti-inflammatory effects	[141]
Polyphenols	Anti-inflammatory effects	Anti-inflammatory effects	[142]
Lycopene	Selectively utilized by host microbiota	Protection against photodamage	[143,144]
Prolamin	Not reported	Protection against AD *	[145]
Phytomolecules	Not reported	Anti-ageing	[146]
Gluten	Coeliac disease	Skin Rashes	[58,59]

* Abbreviations: Atopic dermatitis (AD), gamma-aminobutyric acid (GABA), inflammatory bowel disease (IBD), and short chain fatty acids (SCFAs).

A Brief Note about GABA

What makes for good levels

- Depletion associated with anxiety and depression.
- Good sleep
- Deep breathing and relaxation
- Regular Exercise
- **Fermented Foods:** Foods like yogurt, kefir, tempeh, and kimchi can contain GABA and promote the growth of GABA-producing bacteria in the gut.
- **GABA-Enriched Foods:** Certain foods naturally contain GABA or its precursors, such as whole grains, fava beans, soy, lentils, and other beans; seeds like sunflower seeds; and nuts like almonds and walnuts.
- **Complex Carbohydrates:** Eating complex carbohydrates can increase the production of serotonin, which can be converted to melatonin and affect GABA indirectly
- Herbs - Passionflower, Valerian Root, Ashwaghandha, and Lemon Balm

The 4 pillars of health

By Dr. Robert Rhondell Gibson

- 1. Environmental Influences - Circadian biology, temperature, sun
- 2. Nutrition
- 3. Mental State
- 4. Movement / Mechanics
- Your mission should you choose to accept it is to hyper-optimize your health in all of these areas to overpower and influence your health in other areas of your life.

Environmental Influences

Circadian Biology

Award Recipients: The Nobel Prize in Physiology or Medicine 2017 was awarded jointly to Jeffrey C. Hall, Michael Rosbash, and Michael W. Young for their discoveries of molecular mechanisms controlling the circadian rhythm.

Key Discoveries: Their research uncovered the genetic basis of circadian rhythms, demonstrating how specific genes within cells create a self-sustaining loop of protein production that rises and falls over a 24-hour cycle, aligning physiological processes with the Earth's day-night cycle.

Key Points

1. You need morning AM sunlight into your retina to reset your circadian clock
2. There are other factors as well - that set this, when you eat. Eating late at night can alter this
3. LED and Fluorescent Lights and screens have blue light in them that can affect your circadian clock
4. You can get premature aging from these lights
5. These lights can interfere with your natural release of melatonin interfering with your sleep

The Sun and You

SHIFTING COLORS OF DAYLIGHT



1000 2000 3000 4000 5000 6000 7000 8000 9000 10000 11000 12000

COLOR TEMPERATURE IN KELVIN

Movement / Mechanics

A body in motion stays in motion

- Studies on walking in cities show that when a cities average steps increase to about 7000 steps, chronic diseases drop dramatically.
- Direct impact own gut permeability - extreme exercise opens the floodgates so to speak, moderate exercise does the opposite
- **Exercise and Gut Microbiota:** Regular physical activity, which helps increase or maintain muscle mass, can also alter the composition of the gut microbiota, promoting the growth of beneficial microbial species that contribute to overall health.
- **Enhanced Nutrient Absorption:** Regular exercise not only increases muscle mass but can also enhance gut motility and the absorption efficiency of nutrients, which are vital for muscle repair and growth.

G-BOMBS

By Joel Fuhrman, MD

- G- Greens
- B- Beans
- O- Onions
- M- Mushrooms
- B- Berries
- S - Seeds
- Most concentrate on what you should avoid, perhaps its time to give a think to what we should include.

Mental State

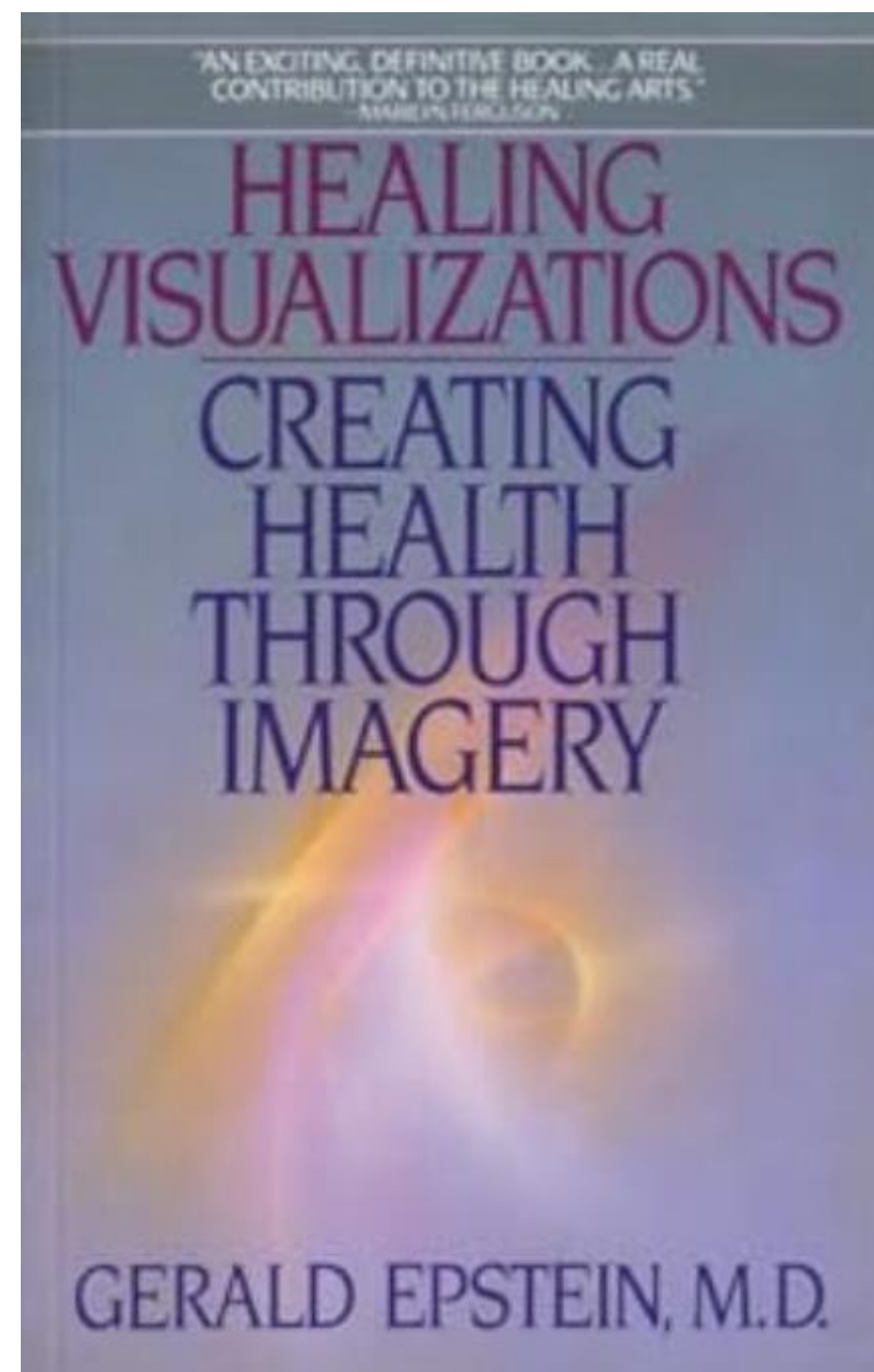
Stressed State

- The False Emergency State by Gerald Epstein, MD
- Parasympathetic vs Sympathetic balance - the vacation effect, vagal tone
- Pay Attention - add to your food journal your stress reactions.
- How to cultivate the parasympathetic nervous system
 - Deep and Slow Breathing
 - Splashing face with Cold Water
 - Regular Exercise
 - Yoga, meditation, qigong, prayer
 - Laughter and social engagement

Mental State

Using Imagination as a tool for growth

- Using Mental imagery for healing and growth.
- Assessing physical, mental, emotional, spiritual and moral aspects of our lives.



Advanced or additional Lab Testing

If time allows

- Micronutrient profiles
- Leaky Gut Tests
- Methylation Tests if homocysteine is high
- Fasting Insulin and HBA1c
- Gut Zoomer test from Vibrant Labs

We all become teachers

See one, do one, teach one

The Talmud quotes Rabbi Chanina who declared that, “I have learned much from my teachers, more from my colleagues and most from students.”