



Addressing the Root Cause of Eczema: The Gut Microbiome

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Disclosures

- Biocidin Botanicals- Scientific Advisory Board
- Sponsors of Root Cause Dermatology Functional Dermatology Training Course: Diagnostic Solutions Laboratory, Precision Analytical Inc., Rupa Health, Biocidin Botanicals, Beyond Balance Inc., BLDG Active, Pendulum Therapeutics Inc, Integrative Therapeutics Inc., Ayush Herbs, Inc., Pure Encapsulations/Douglas Labs
- Mosaics Diagnostics (formerly Great Plains Laboratory)- speaker

Dr. Julie Greenberg, ND, RH(AHG), MBA



- ▶ **Licensed Naturopathic Doctor:** (CA, OR, WA)
- ▶ **Registered Herbalist (RH):** American Herbalist Guild
- ▶ Specializing in **Dermatology**
- ▶ **The Center for Integrative & Naturopathic Dermatology Inc**
- ▶ **Root Cause Dermatology**
- ▶ **ND, Bastyr University**
- ▶ **MBA, Stanford University**
- ▶ **BA, Northwestern University**





Eczema: Pathophysiology



What is Eczema/Atopic Dermatitis?



A disease of:

1. skin barrier dysfunction
2. inflammation



Immune Pathways & Inflammation

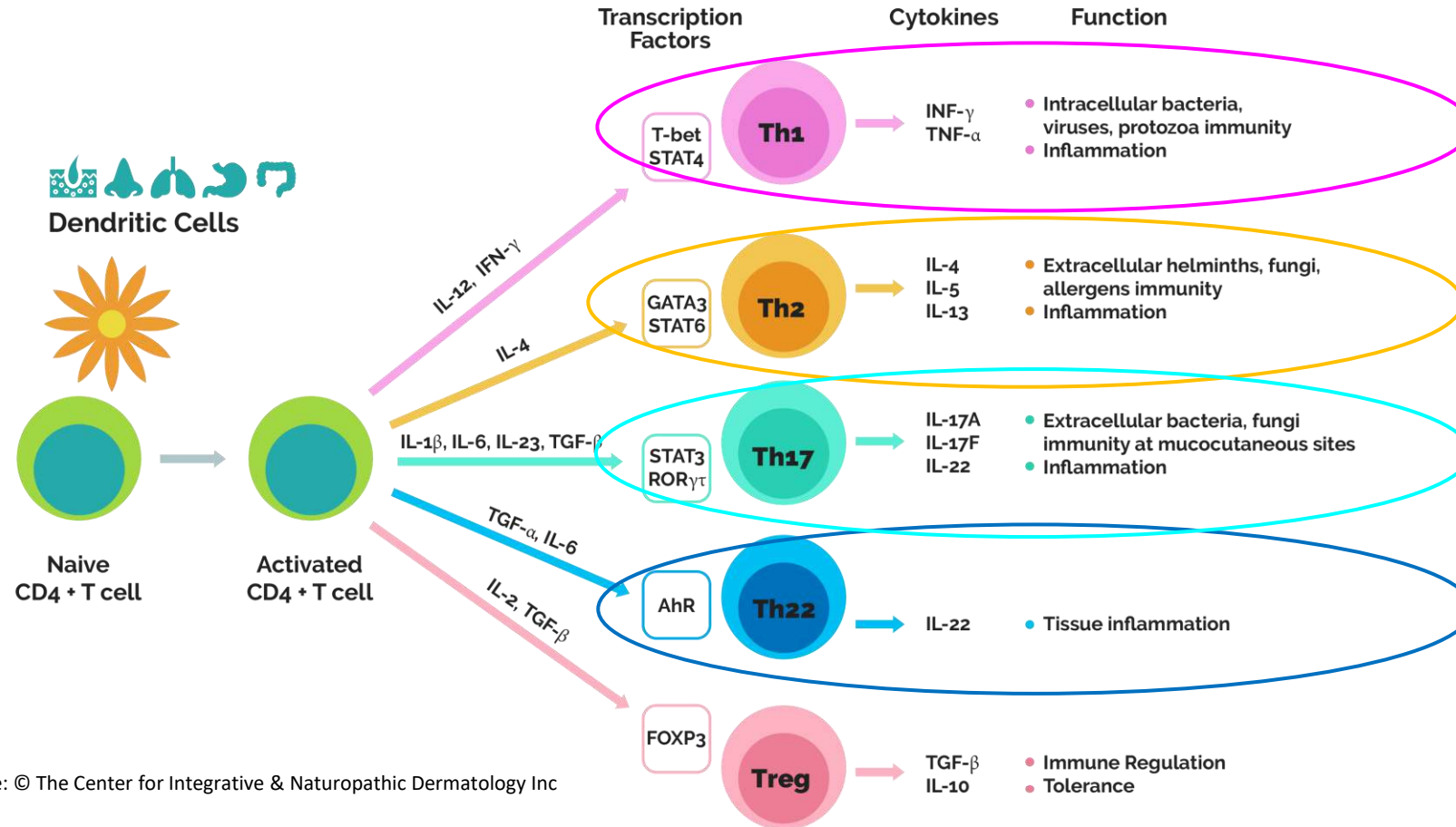
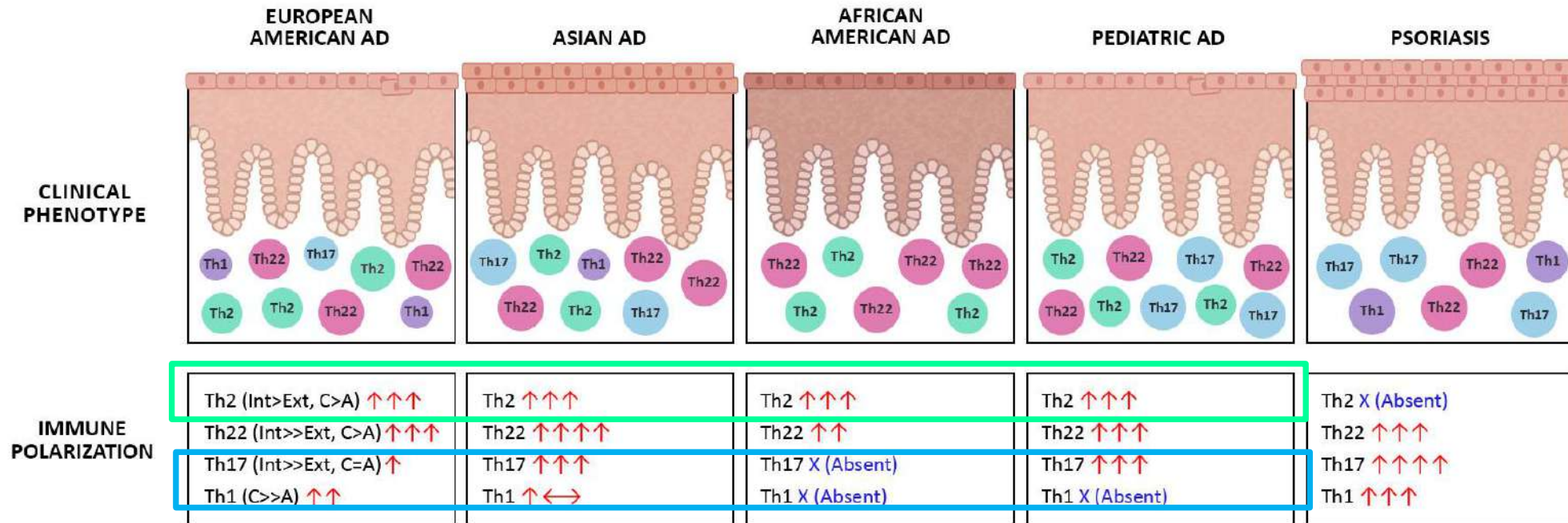


Image: © The Center for Integrative & Naturopathic Dermatology Inc

Zhu, X., & Zhu, J. (2020). CD4 T helper cell subsets and related human immunological disorders. *International Warrington, R., Watson, W., Kim, H. L., & Antonetti, F. R. (2011). An introduction to immunology and immunopathology. Allergy, Asthma & Clinical Immunology, 7(1), 1-8. journal of molecular sciences, 21(21), 8011. Schmidt-Weber, C. B., Akdis, M., & Akdis, C. A. (2007). TH17 cells in the big picture of immunology. Journal of Allergy and Clinical Immunology, 120(2), 247-254.*



Atopic Dermatitis Endotypes



Czarnowicki, T., et al. (2019). Atopic dermatitis endotypes and implications for targeted therapeutics. *Journal of Allergy and Clinical Immunology*, 143(1), 1-11.

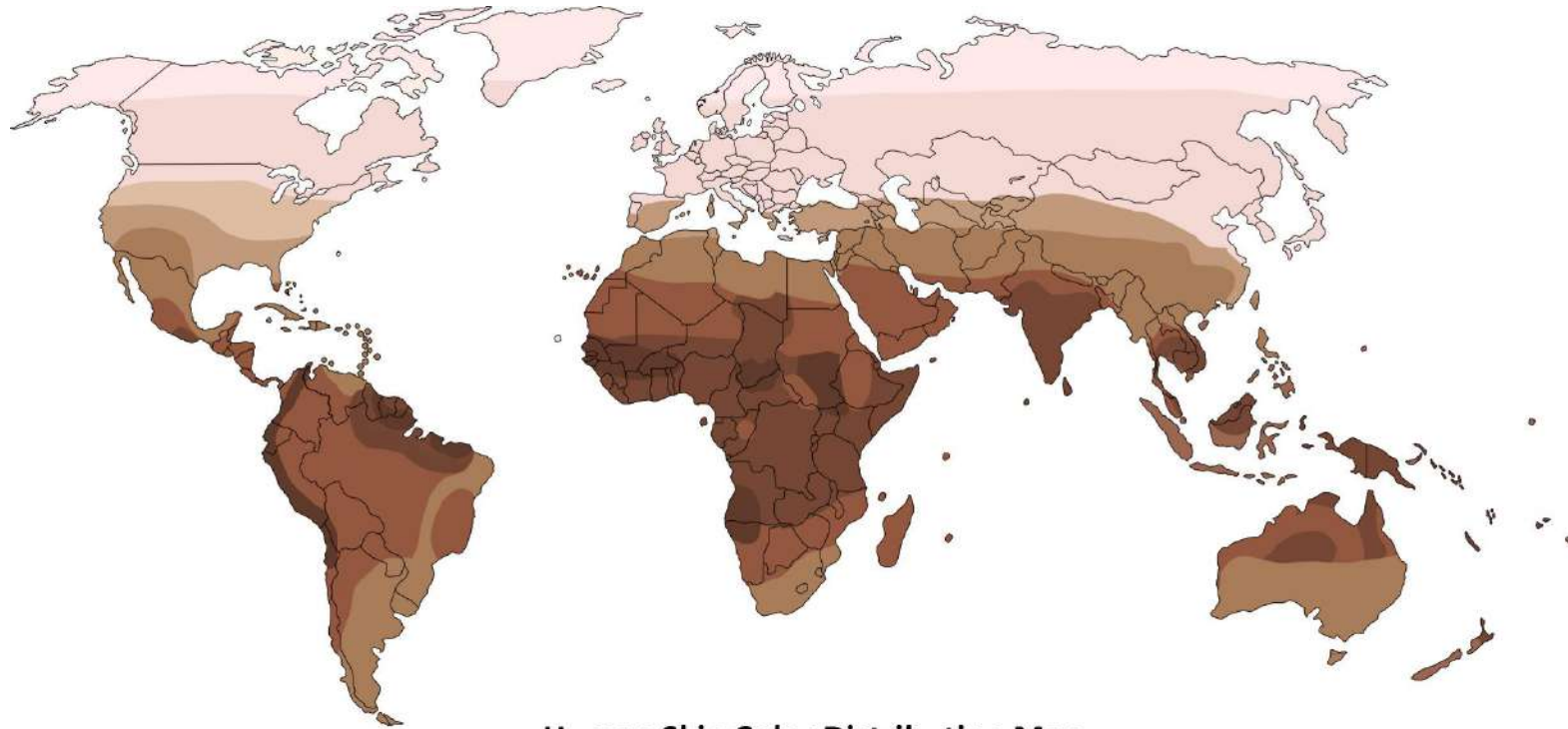


Eczema: skin of color

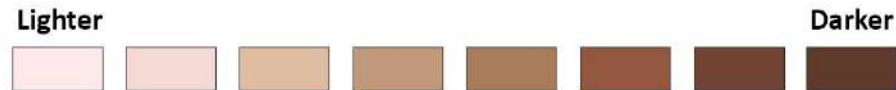




Skin of Color (SOC)



Human Skin Color Distribution Map



- ▶ Most of the world is people with skin of color
- ▶ By 2044, more than ½ the U.S. population will be skin of color

“Human Skin Color”, *Wikipedia*, Wikimedia Foundation Inc., 4 September 2023, https://en.wikipedia.org/wiki/Human_skin_color



Fitzpatrick Skin Type Scale



Developed in 1975 as a way to estimate the response of different types of skin to UV light

Problems in U.S. Dermatology



LACK OF EDUCATION REGARDING SKIN OF COLOR IN MEDICAL SCHOOL

Medical textbooks have predominantly pictures of Caucasian skin

This creates white normativity

This leads to misdiagnosis in patients with SOC



LACK OF CONTINUING EDUCATION REGARDING SKIN OF COLOR



LACK OF DIVERSITY AMONGST DERMATOLOGISTS IN CLINICAL PRACTICE AND IN TEACHING

Lack of mentors

Patients cannot see dermatologists who are from their own ethnic background

URM= underrepresented in medicine

Skin of Color: Diagnosis



- ▶ The same skin condition can look very different on different skin tones
- ▶ There may be no erythema at all
- ▶ Can appear more violaceous, hyperpigmented or/and hypopigmented

Redness Tougher to Detect in SOC



Image: © The Center for Integrative & Naturopathic Dermatology Inc

Can appear more **gray-purple (violaceous)** than **red-brown** in SOC

Andrew Alexis, MD, MPH, <https://nationaleczema.org/eczema-in-skin-of-color/>



Eczema: food allergies & leaky skin



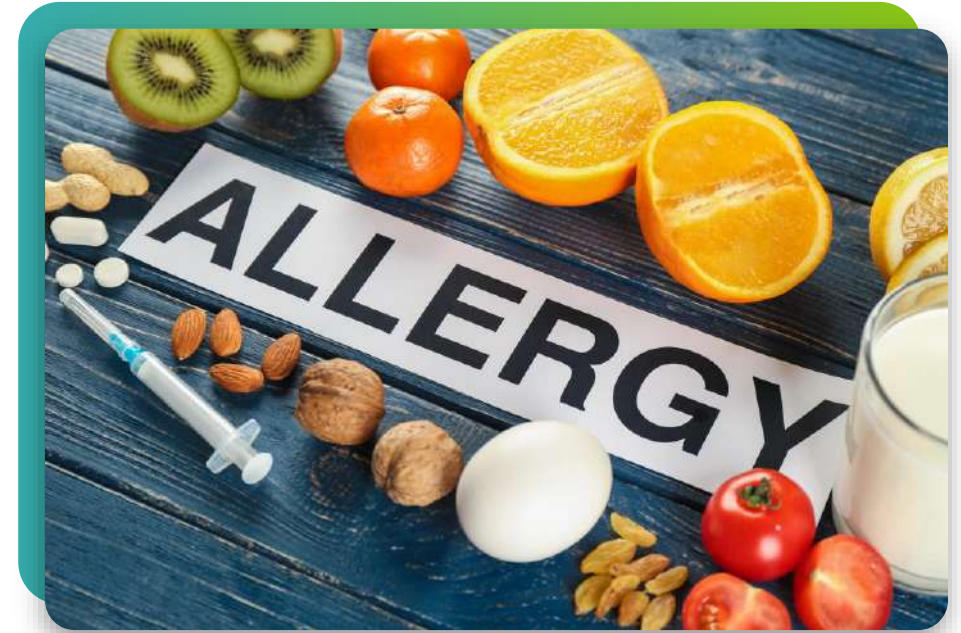
ROOT CAUSE
DERMATOLOGY

Food As a Trigger for AD



► Food allergy:

- most commonly a trigger in **infants and children with moderate to severe AD**
- **NOT** likely to be trigger for older children and adults





What Foods Trigger Eczema?

75% of the cases of food-induced AD flares are due to:

MILK



EGG



WHEAT



SOY



PEANUT



*These could be IgG, IgA, or IgE

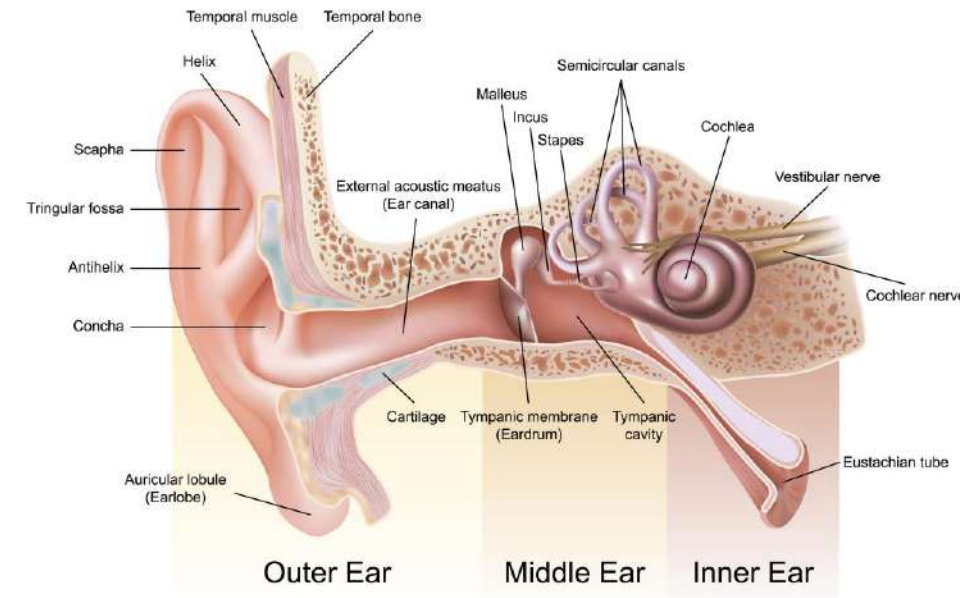
Werfel, T., & Breuer, K. (2004). Role of food allergy in atopic dermatitis. *Current opinion in allergy and clinical immunology*, 4(5), 379-385.

Ear Infections



- ▶ Many of your eczema patients will have ear infections or will have had them as kids.
- ▶ These can cause chronic issues that lead to overuse of antibiotics or even placement of tympanostomy tube insertion.
- ▶ Ear infections are caused by middle ear problems (the eustachian tube)
 - Embryology: derivative of first and third pharyngeal arches- **digestive system!**
- ▶ IgG food testing in 44 patients with tympanostomy tube insertions high results:
 - Cow's Milk 70%
 - Gluten 43%
 - Egg 27%
 - Yeast 7%
 - Soybean 7%

Anatomy of the Ear



“Prevalence of Food Sensitivities in Pediatric Patients Requiring Tympanostomy Tube Insertion”, Gregg S. Govett, MD, DABEM, AAEM Fall 2023 Conference
Environmental Influences on Gastrointestinal Health: Addressing the Foundations of Diet, Digestion, and Detoxification



Do Food Allergies Cause Eczema?

Yes
 No
 Maybe

But... up to **2/3** of patients with AD do not show sensitization to environmental allergens/foods.



- This is not to say that cutting out some foods (like dairy & wheat) won't help in some individuals – **it can!**



- But **don't** get stuck here if it's not working.

Tsakok, T., Marrs, et al. (2016). Does atopic dermatitis cause food allergy? A systematic review. *Journal of Allergy and Clinical Immunology*, 137(4), 1071-1078.

Does Eczema Cause Food Allergies?



Seems Likely!

Food sensitization is **6x more likely** to develop in children with AD than those without.

 GLUTEN	 CRUSTACEANS	 EGGS	 FISH	 PEANUTS	 MILK
 TREE NUTS	 CELERY	 MUSTARD	 SESAME	 SULPHITES	 MOLLUSCS



Don't even need AD, just **skin barrier disruption:**



- Neonatal skin barrier dysfunction at birth predicts food allergies at **age 2.**



- Children with skin barrier defects are more likely to develop **asthma.**

Strugar, Seité, Lin & Lio (2019). Connecting the Dots: From Skin Barrier Dysfunction to Allergic Sensitization, and the Role of Moisturizers in Repairing the Skin Barrier. *Journal of drugs in dermatology: JDD*, 18(6), 581-581.



Leaky skin

(Restoration via Skincare Products)

NORMAL SKIN

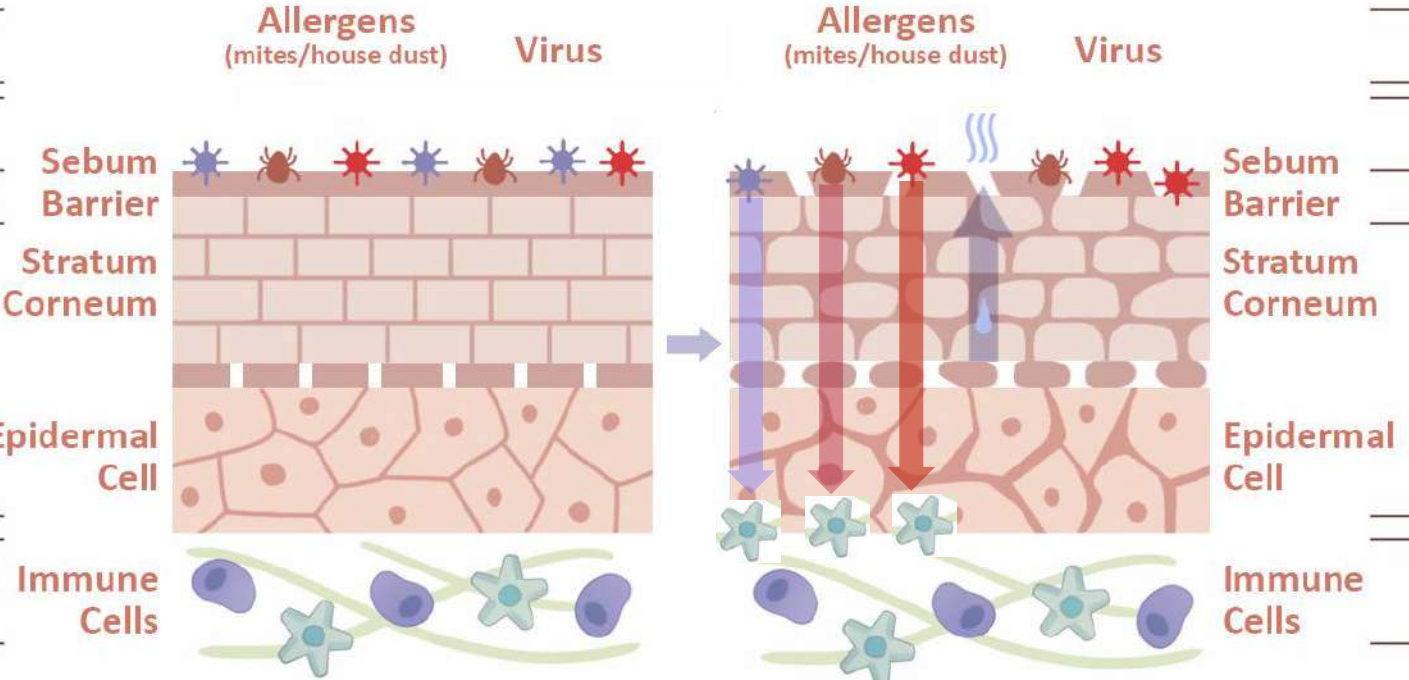
DAMAGED SKIN

A restored barrier prevents allergen entry

Enhanced bacterial diversity is achieved

Emollients provide moisture and lipids

Immune cells are separated from allergens by a functional skin barrier

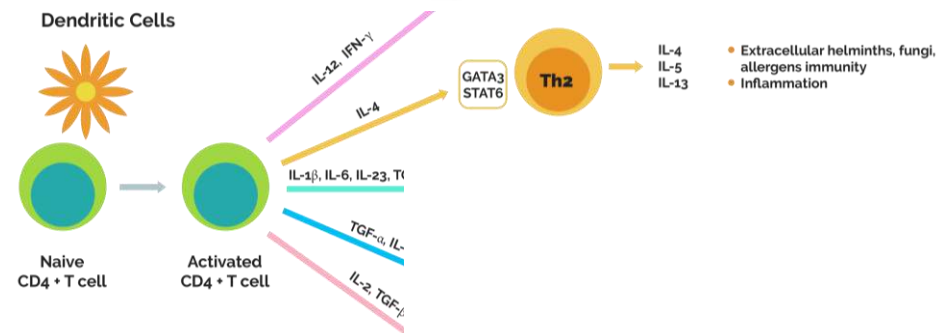


Allergens enter the impaired skin barrier

An imbalance of commensal/other microorganisms causes dysbiosis

Antimicrobial peptides and natural moisturizing factors are lost

Allergens are in contact w/immune cells, leading to sensitization and inflammation



Strugar, Seité, Lin & Lio (2019). Connecting the Dots: From Skin Barrier Dysfunction to Allergen Sensitization, and the Role of Moisturizers in Repairing the Skin Barrier. *Journal of drugs in dermatology: JDD*, 18(6), 581-581.



Food Allergy and Eczema Induced in Mice



- ▶ Mice were **shaved** and **tape-stripped 4x** to induce skin injury
- ▶ Gauze pad was soaked in **ovalbumin (OVA)** and **saline** and taped to skin for 1 week
- ▶ **3 one-week** exposures with **2 weeks** resting period in between each

- ▶ **Progressive and significant thickening** of the epidermis and dermis produced eczematous lesions
- ▶ **Significantly increased** dermal cell infiltration of eosinophils, mast cells and total **inflammatory** cells
- ▶ Total IgE, IgG2a and OVA-specific antibodies were **significantly increased** after the second and third exposure week
- ▶ **Gradual and/or significant increases** in mRNA expression of IL-1b, TNF-a, IL-4, IL-10, IL-13, IFN-g and IL-12p35 were found after each exposure week



Wang, G. et al. (2007). Repeated epicutaneous exposures to ovalbumin progressively induce atopic dermatitis-like skin lesions in mice. *Clinical & Experimental Allergy*, 37(1), 151-161.



Atopic Triad

- ▶ AD is often associated with **other atopic diseases**:
 - IgE-mediated food allergy
 - Asthma
- ▶ ~ **1/3 of all children** with early-onset AD progress through the atopic march
- ▶ **Stopping eczema could stop the march!**



Tsakok, T., Marrs, et al. (2016). Does atopic dermatitis cause food allergy? A systematic review. *Journal of Allergy and Clinical Immunology*, 137(4), 1071-1078.



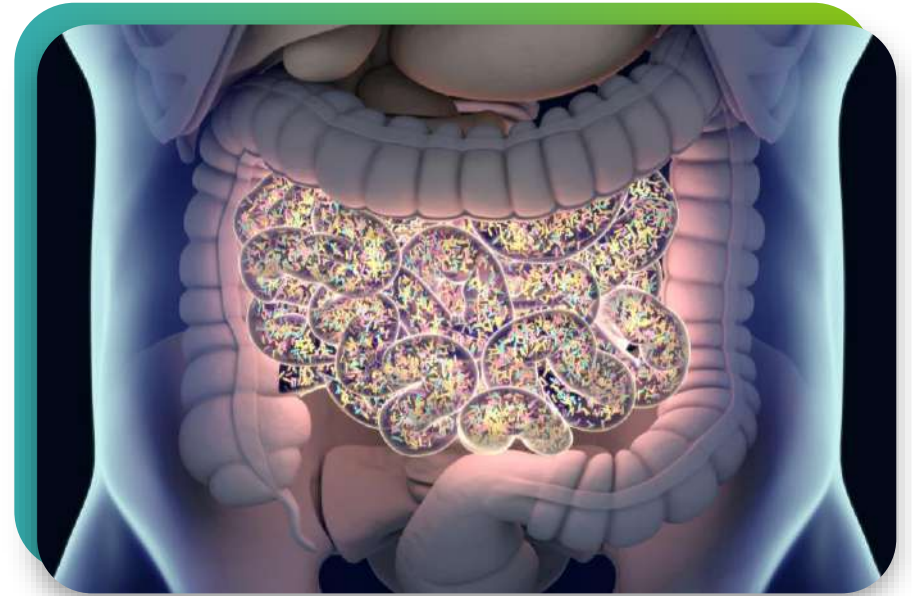
Eczema: dysbiosis & leaky gut





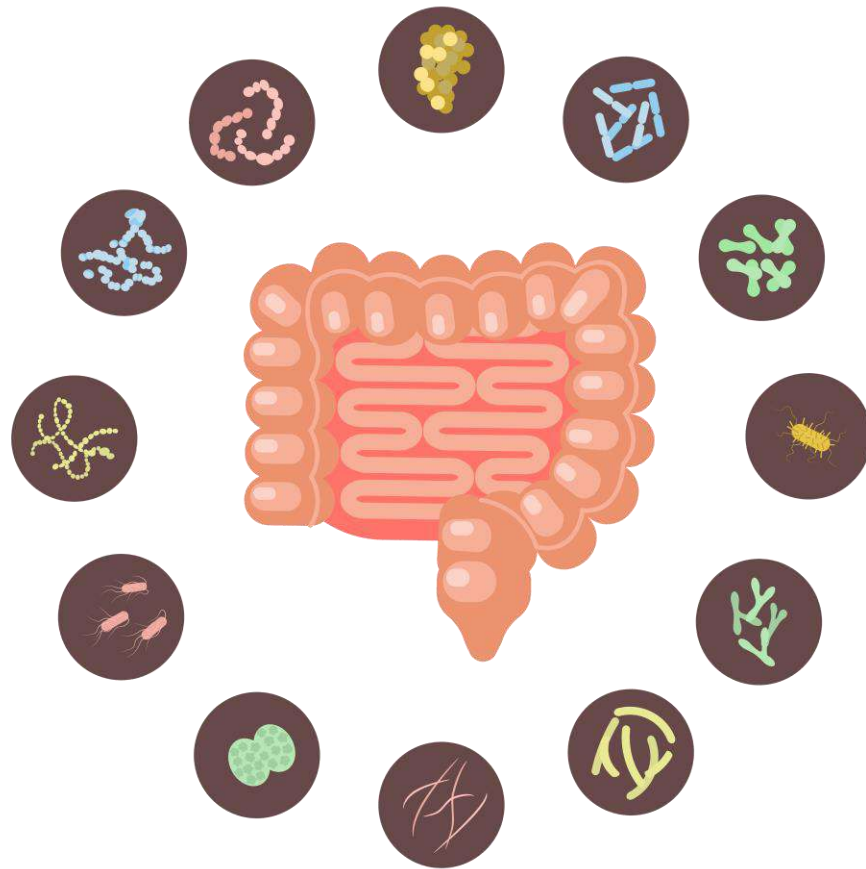
The Gut Microbiome

- The average human adult has **three to five pounds** of microbes in their gut!
- We house and feed them for free





Microbes in the Gut



Trillions of organisms live in the gut
(500-2,000) different species:

- Bacterial
- Fungal
- Viruses
- Archaea
- Bacteriophages
- Protozoa
- Worms

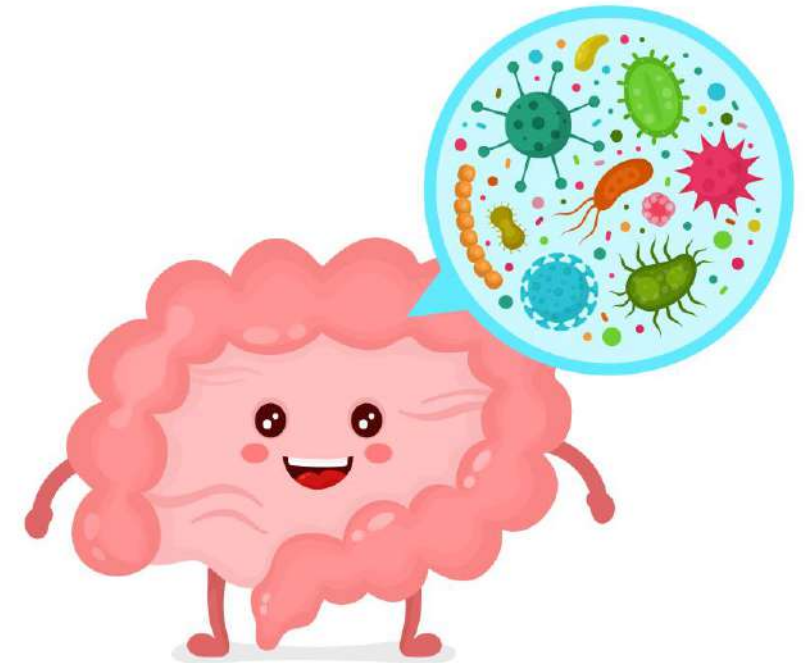
Why Do We Have Gut Microbes?



○ What do we get out of this deal?

○ **We can't survive without them!**

- They make things we need (such as Vitamin B12, butyrate)
- Crowd out pathogenic microbes
- Maintain a healthy ecosystem in the gut





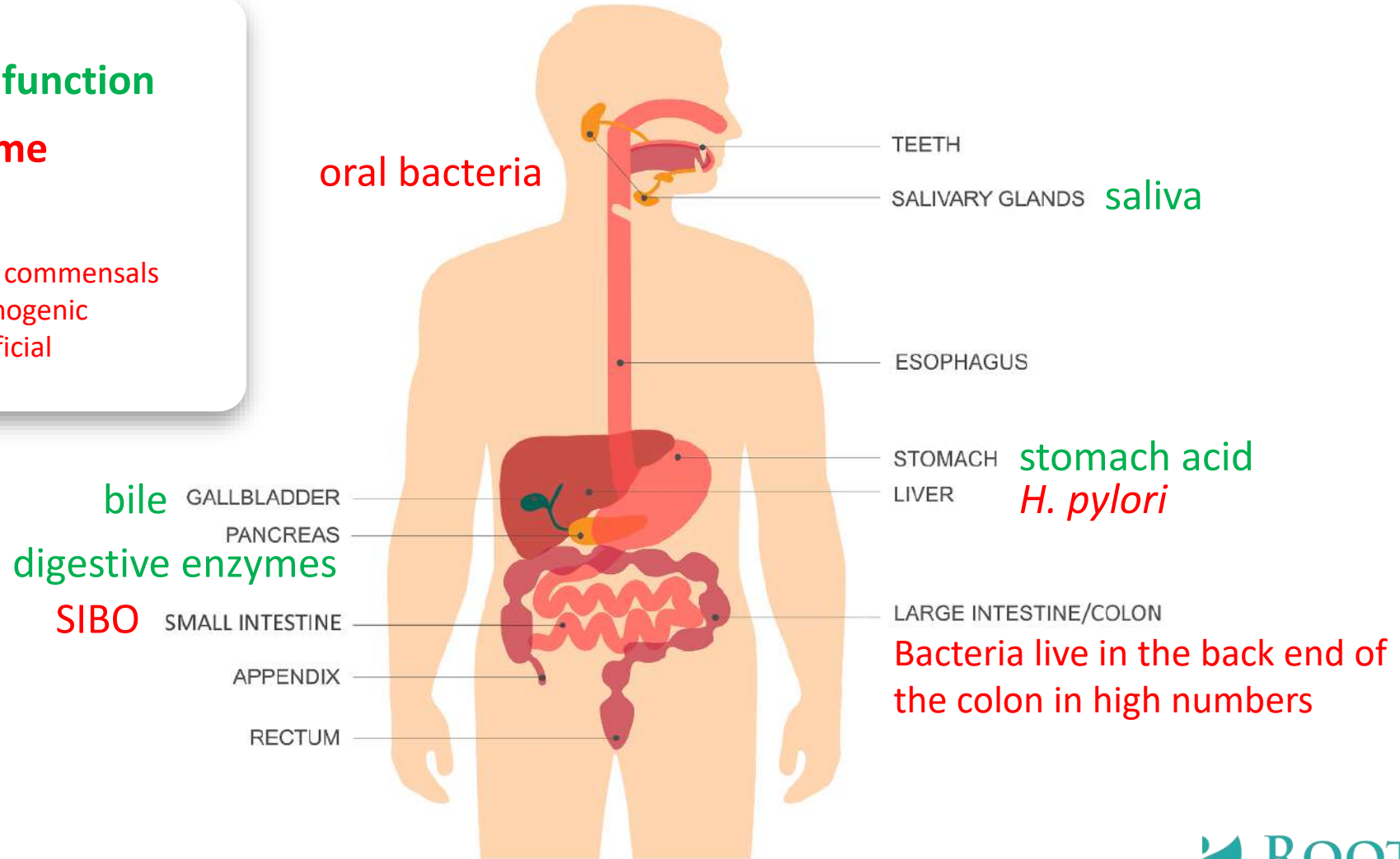
Test & Treat the Gut!

✓ Digestive function

✓ Microbiome

Dysbiosis:

- Overgrowth of commensals
- Growth of pathogenic
- Too little beneficial



Intestinal Dysbiosis- Atopic Derm



Skin disease	Lower levels of beneficial gut flora	Higher levels of pathogenic bacteria	Correlated GI diseases
Atopic Dermatitis	<i>Bifidobacteria</i> <i>Bacteroidetes</i> <i>Bacteroides</i>	<i>Clostridium difficile</i> <i>Escherichia coli</i> <i>Staphylococcus aureus</i>	IBS Constipation Dyspepsia

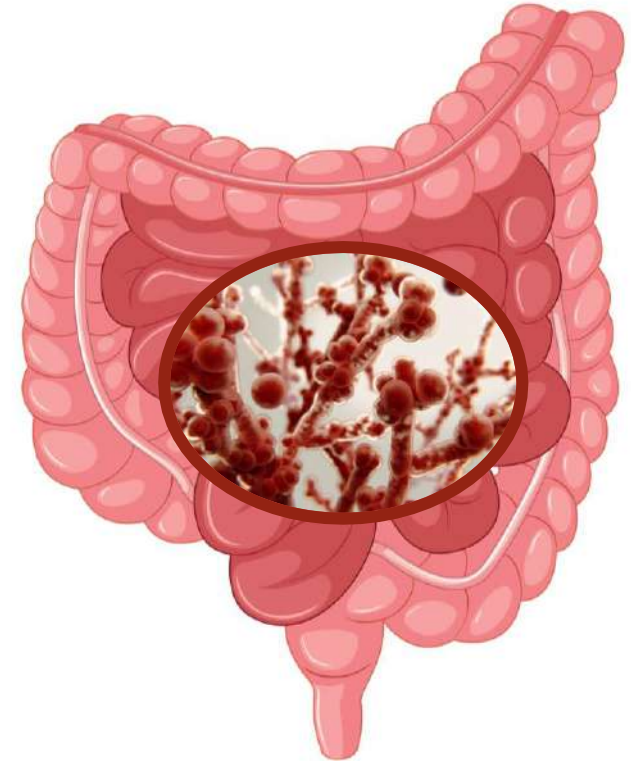
Jones MP, Walker MM, Ford AC, Talley NJ. The overlap of atopy and functional gastrointestinal disorders among 23 471 patients in primary care. *Aliment Pharmacol Ther.* 2014;40(4):382-391.
 Lee E, Lee S-Y, Kang M-J, et al. Clostridia in the gut and onset of atopic dermatitis via eosinophilic inflammation. *Ann Allergy Asthma Immunol.* 2016;117(1):91-92.e1.
 Kirjavainen PV, Arvola T, Salminen SJ, Isolauri E. Aberrant composition of gut microbiota of allergic infants: a target of bifidobacterial therapy at weaning? *Gut.* 2002;51(1):51-55.



Intestinal Dysbiosis- Fungal/Yeast



- ▶ AD patients with GI growth of candida have a **statistically significant** correlation with *C. albicans* IgE antibodies.
- ▶ Skin manifestations **improved** in AD patients treated with **antifungals** who had candida IgE antibodies.



What is Intestinal Hyperpermeability (“Leaky Gut”)

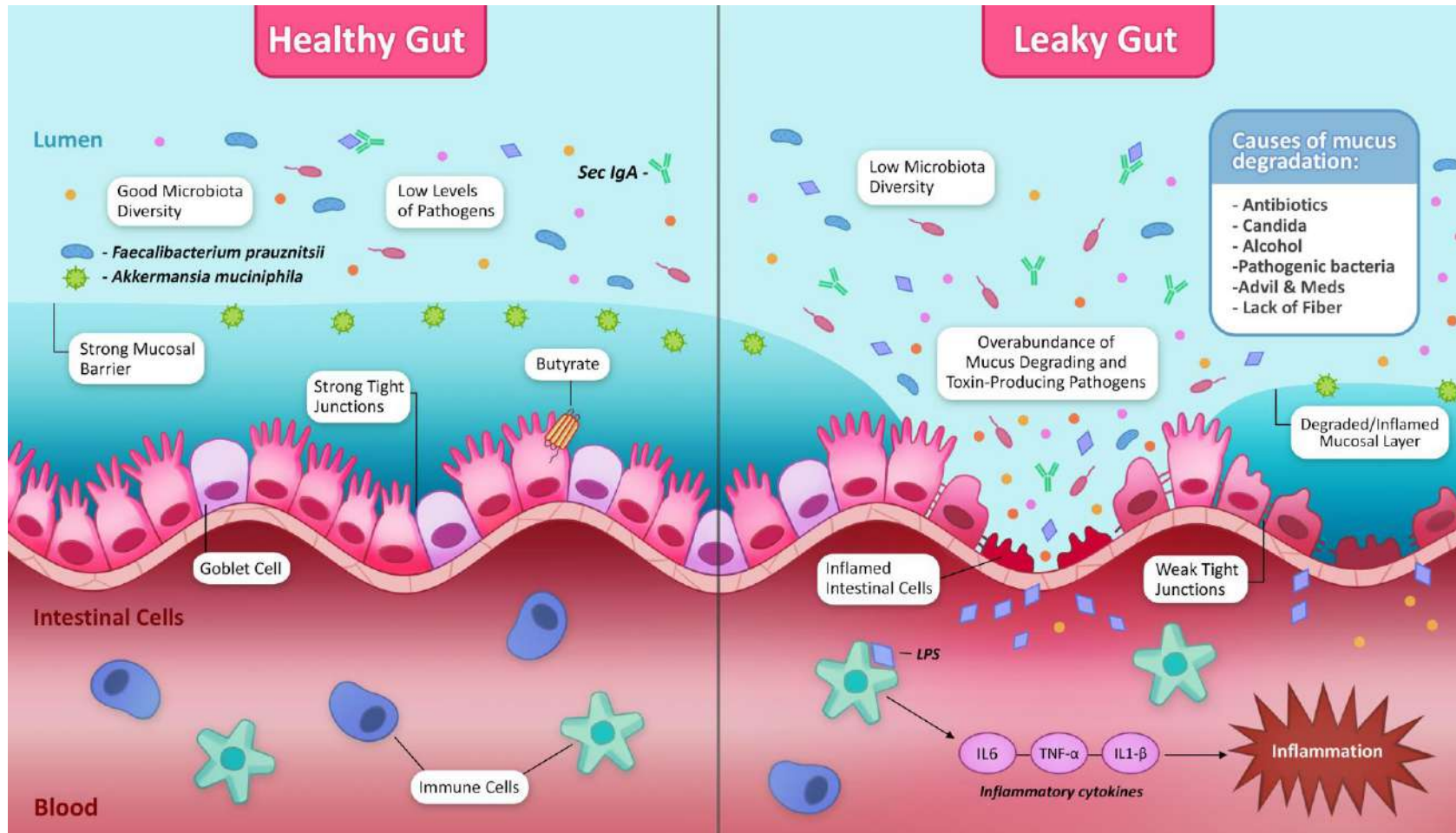


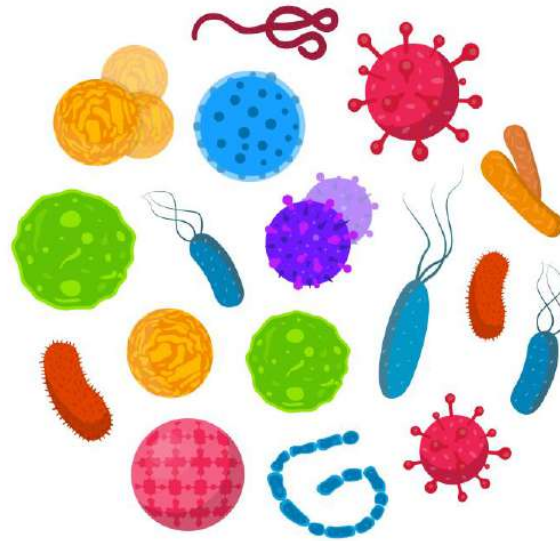
Image: © The Center for Integrative & Naturopathic Dermatology Inc

My Clinical Experience: Eczema Profile 1



HIGH

- ▶ *Staphylococcus aureus*
- ▶ *Streptococcus*
- ▶ *Candida*

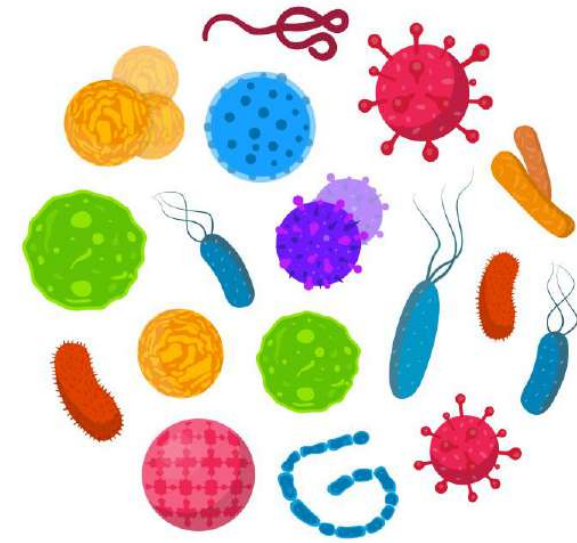


NO/LOW (leaky gut)

- ▶ *Akkermansia muciniphila*
- ▶ *Faecalibacterium prausnitzii*
- ▶ Sec IgA



My Clinical Experience: Eczema Profile 2

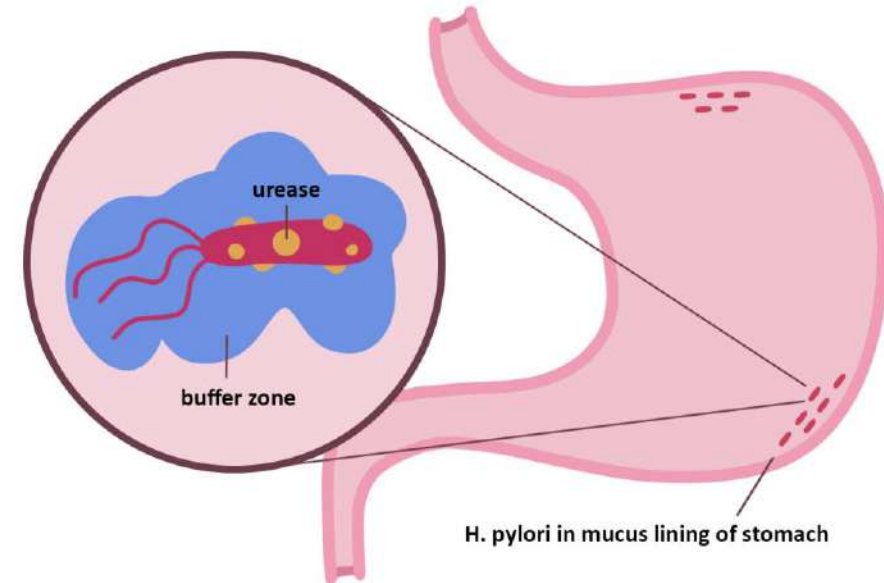


H. pylori- urease



Urease:

- **An enzyme** that combats the acidic environment of the stomach.
- **This neutralizes the strong acid of the stomach,** and creates a buffer zone around the *H. pylori* to protect it from the strong acids.



Result:

- Sub-optimal digestion
- Sub-optimal killing power

Kutlubay, Z., Zara, T., Engin, B., Serdaroglu, S., Tuzun, Y., Yilmaz, E., & Eren, B. (2014). Helicobacter pylori infection and skin disorders. Hong Kong Medical Journal, 20(4).



Protozoa



Giardia

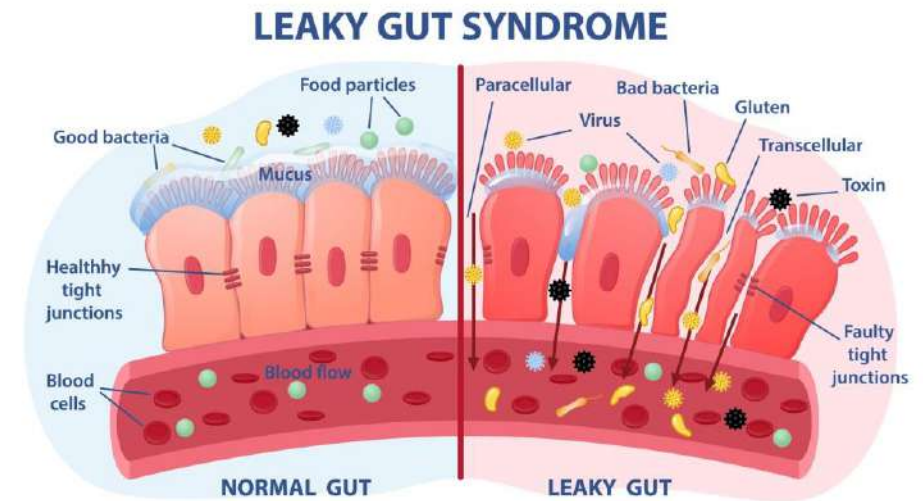
- **Single-cell eukaryotes**
- Protozoan means “**first animal**”
- There is **debate** as to whether protozoa in the gut are all pathogenic or if some are commensal.
- Can cause gas, bloating, GI issues
- **I treat ALL protozoa** (and usually see with *H. pylori*)

Chabé, M., Lokmer, A., & Ségurel, L. (2017). Gut protozoa: friends or foes of the human gut microbiota?. *Trends in Parasitology*, 33(12), 925-934.
Photo: By CDC / Janice Haney Carr - http://phil.cdc.gov/PHIL_images/8698/8698_lores.jpg, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=825607>



Leaky Gut & AD

- ▶ **Patients with AD appear to have an increased intestinal permeability**
 - positive association between level and AD severity



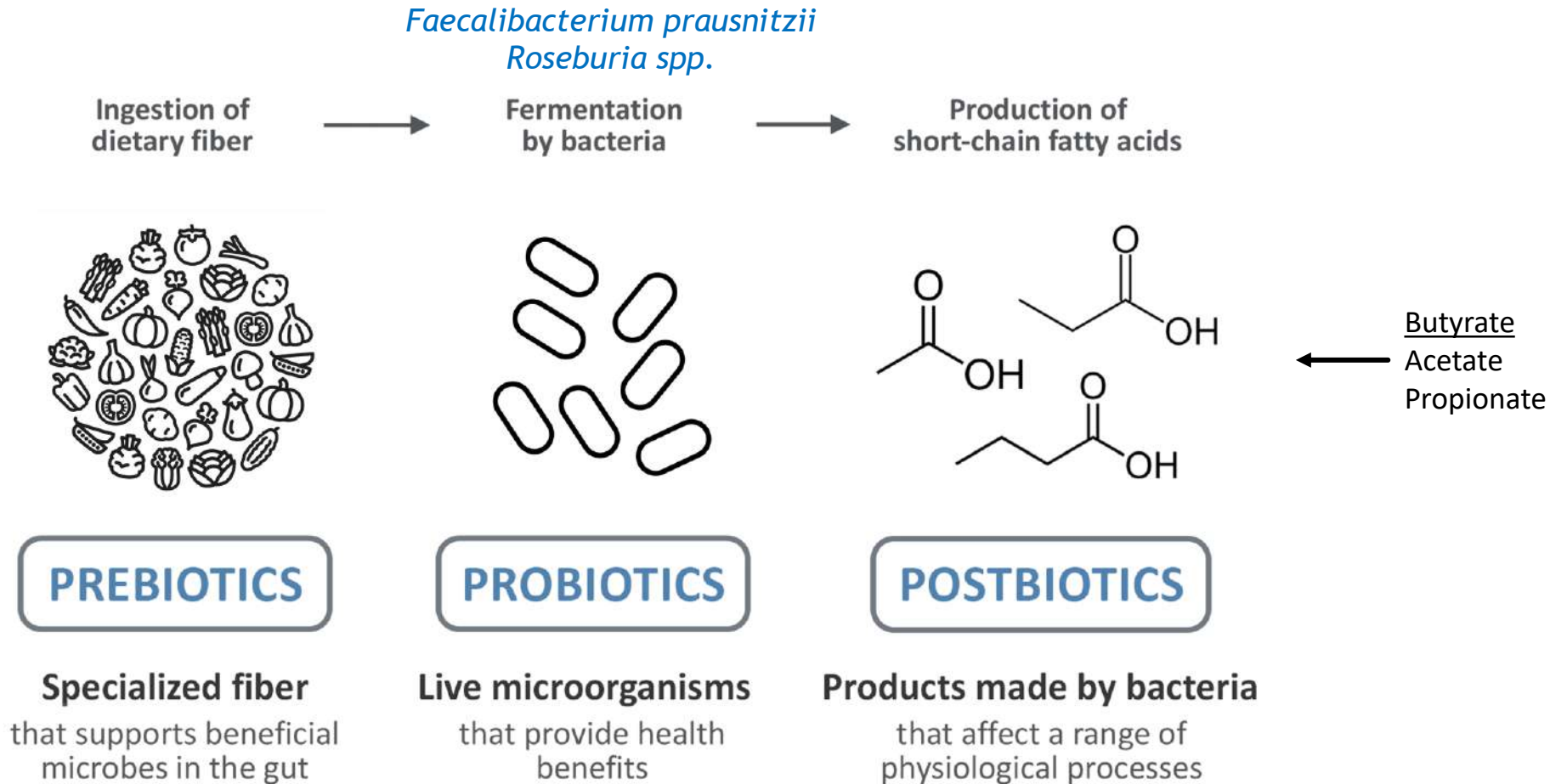
Rosenfeldt, V., et al. (2004). Effect of probiotics on gastrointestinal symptoms and small intestinal permeability in children with atopic dermatitis. *The Journal of pediatrics*, 145(5), 612-616.

Georas SN, Rezaee F. Epithelial barrier function: At the front line of asthma immunology and allergic airway inflammation. *J Allergy Clin Immunol*. 2014;134(3):509-520.

Pike MG, Heddle RJ, Boulton P, Turner MW, Atherton DJ. Increased intestinal permeability in atopic eczema. *J Invest Dermatol*. 1986;86(2):101-104. doi:10.1111/1523-1747.ep12284035



Short Chain Fatty Acids (SCFAs)



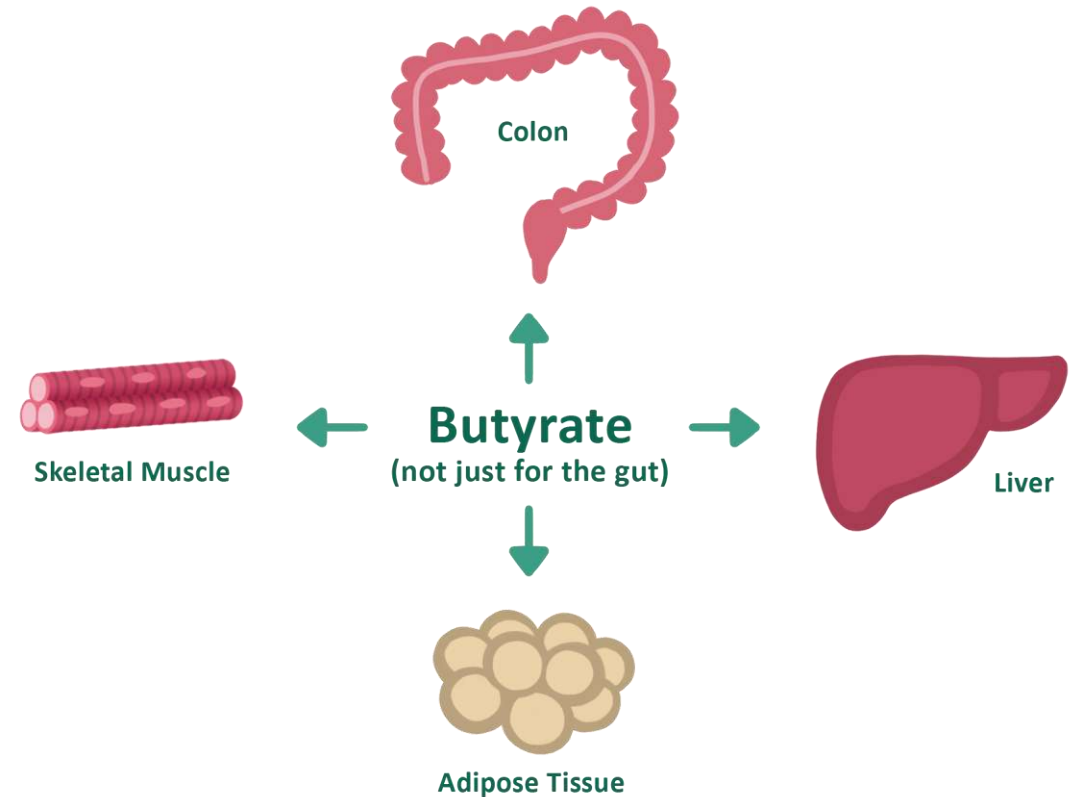
Cresci, G. A., & Bawden, E. (2015). Gut microbiome: what we do and don't know. *Nutrition in Clinical Practice*, 30(6), 734-746.
Guo, P., Zhang, K., Ma, X., & He, P. (2020). Clostridium species as probiotics: potentials and challenges. *Journal of animal science and biotechnology*, 11(1), 1-10.



SCFAs: Benefits

- Used as **preferred fuel** by enterocytes
- **Suppress immune responses** by inhibiting inflammatory cells such as cytokines
- **Protects** against inflammatory disorders and disease
- **Enforce tight junctions**

Faecalibacterium prausnitzii
Roseburia spp.



Salem I, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. *Front Microbiol* . 2018;9:1459.
 O'Neill CA, Monteleone G, McLaughlin JT, Paus R. The gut-skin axis in health and disease: A paradigm with therapeutic implications. *BioEssays* . 2016;38(11):1167-1176.
 Tan, J., McKenzie, et. al (2014). The role of short-chain fatty acids in health and disease. In *Advances in immunology* (Vol. 121, pp. 91-119). Academic Press.

SCFA & AD

“Severity of atopic disease inversely correlates with intestinal microbiota diversity and butyrate-producing bacteria”

- Healthy infants and infants with milder AD have higher levels of butyrate-producing bacteria compared to those with severe AD



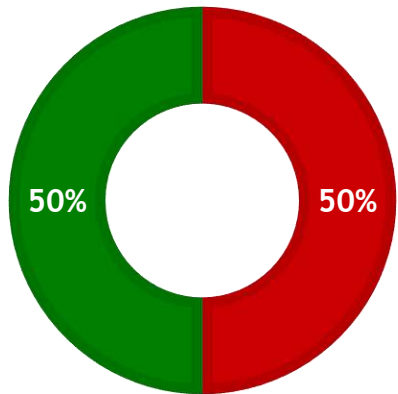


Supplement with oral probiotics?

Studies conflict with whether or not it helps

Why such conflicting results?

Systematic review of 44 studies showed:



- 50% showed a positive effect on severity of AD
- 50% showed no effect



May be related to:

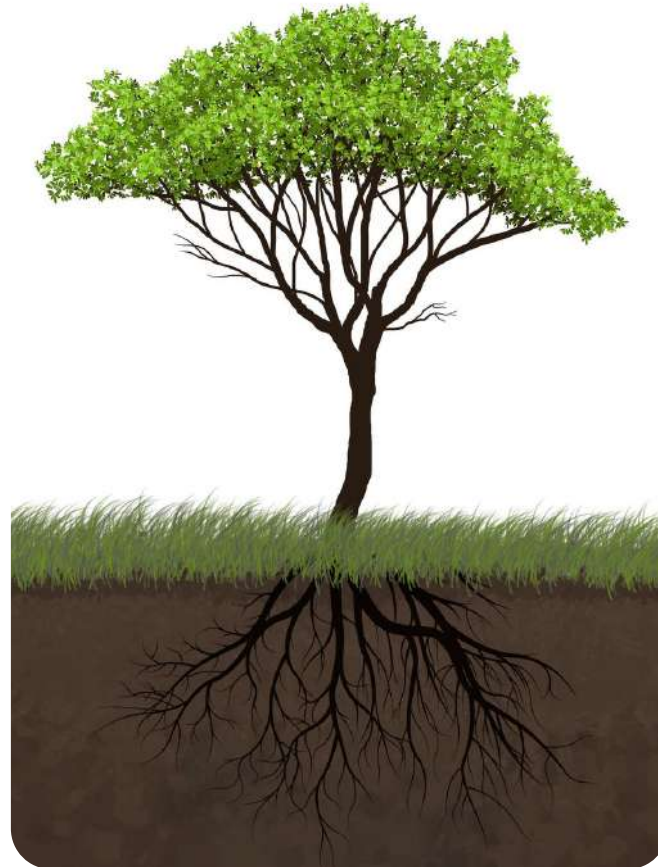
- **what strains, doses and courses of probiotics are used**

Petersen, E., Skov, L., Thyssen, J., & Jensen, P. (2019). Role of the gut microbiota in atopic dermatitis: a systematic review. *Acta dermato-venereologica*, 99(1-2), 5-11.

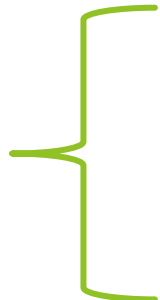
The Goal of Naturopathic/Functional Medicine



Symptoms



Root Causes



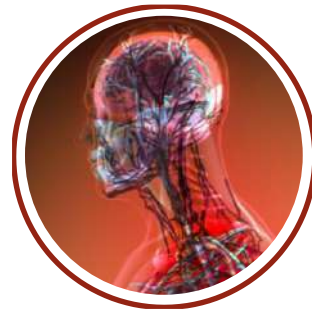
GOAL:
Treat the root
cause!



Gut-Skin Connection



**Gut
dysbiosis**



**Systemic
Inflammation**

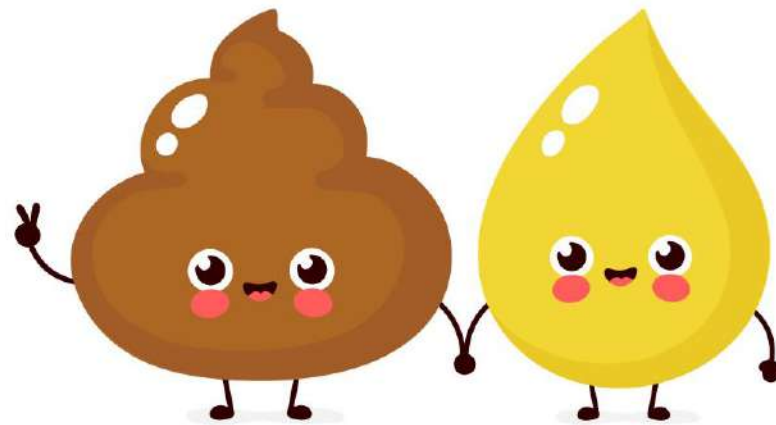


**Chronic
derm disease**

Test & Treat the Gut!



Eczema: testing the gut



What Are Functional Medicine Tests?



Urine Test



Stool Test



DNA Test

- Stool testing**
- Organic acid testing (OAT)**
- Adrenal testing
- Sex Hormone testing
- Mycotoxin testing
- Intestinal permeability testing
- SIBO
- Food sensitivity testing (IgG, IgA)

- Micronutrient testing
- Environmental toxin testing
- Heavy metal testing
- Lyme & co-infections testing
- DNA testing
- Thyroid panel testing
- and many, many more!



Blood Test



Saliva Test



Breath Test



Stool Testing



○ Pathogens & Commensals

○ Bacteria

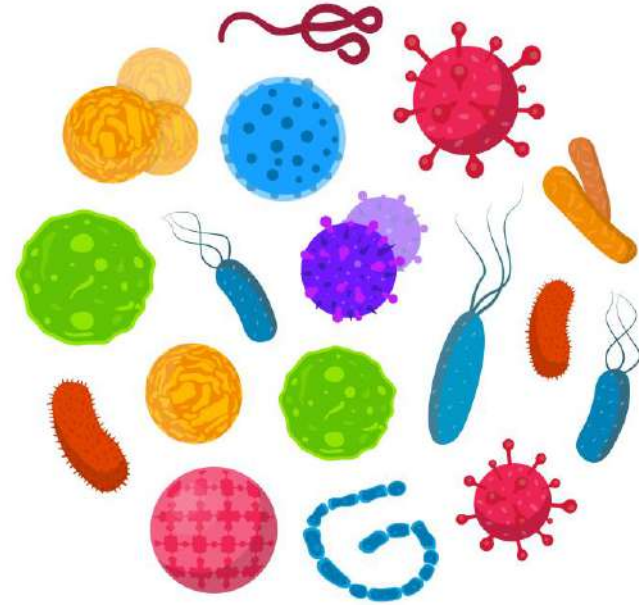
- H. pylori, normal, opportunistic, pathogens

○ Fungi/Yeast

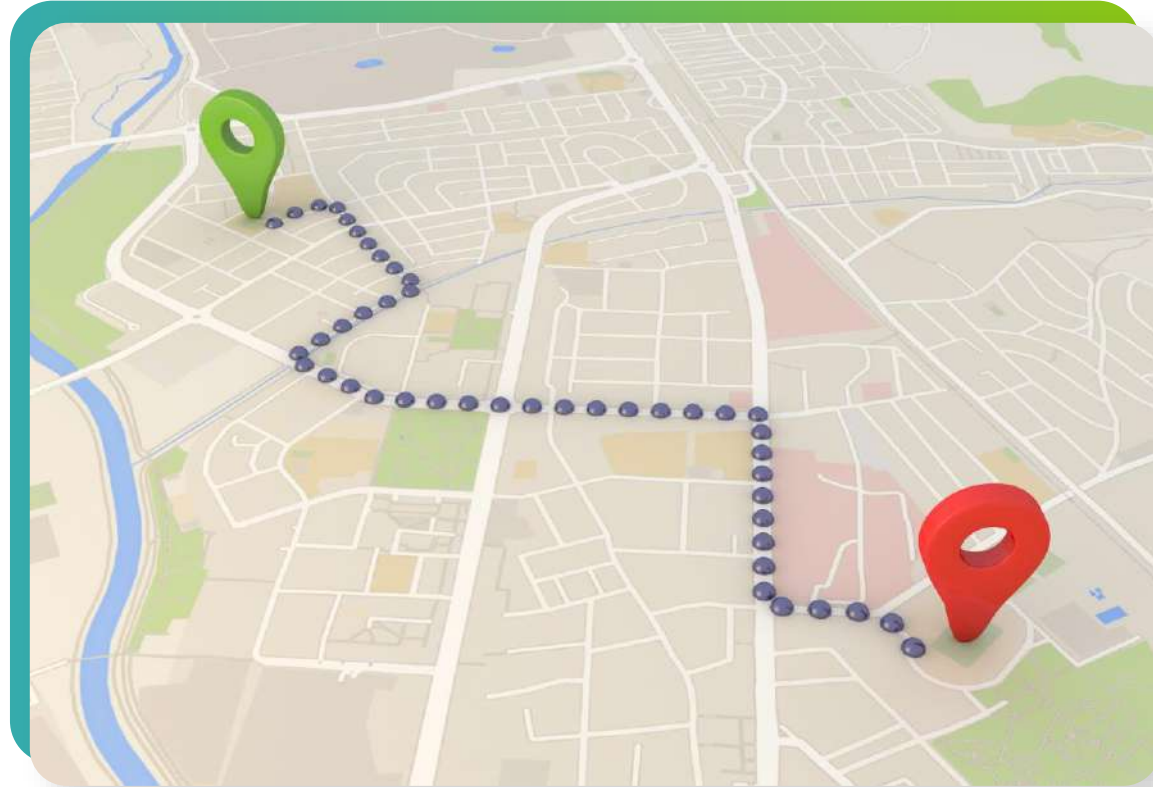
○ Parasites

- Protozoa, worms

○ Viruses

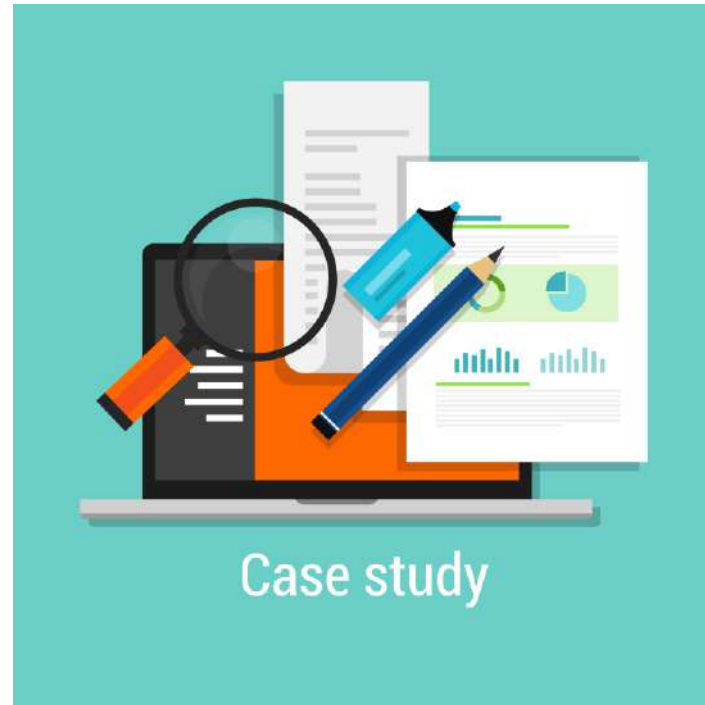


I Use the Labs as My Roadmap





Eczema: cases





Case Study: “Tina”

- ▶ 34 yo female
- ▶ Has had eczema since infancy
- ▶ For past 15 years has been using tacrolimus on eyes and face
- ▶ For past 6 months has been very bad. Has been Rx: hydrocortisone, triamcinolone, fluocinonide, betamethasone, clobetasol, montelukast
- ▶ Severe eczema all over her body
- ▶ Can't work, lost her job
- ▶ Next steps: stool test and OAT





Stool Test- Tina

H. pylori

	Result		Normal
<i>Helicobacter pylori</i>	1.0e3		<1.0e3

Normal Bacterial Flora

	Result		Normal
<i>Bacteroides fragilis</i>	7.56e11	High	1.60e9 - 2.50e11
<i>Bifidobacterium spp.</i>	2.14e10		>6.70e7
<i>Enterococcus spp.</i>	7.15e4	Low	1.9e5 - 2.00e8
<i>Escherichia spp.</i>	2.63e9		3.70e6 - 3.80e9
<i>Lactobacillus spp.</i>	4.53e7		8.6e5 - 6.20e8
<i>Clostridia (class)</i>	5.59e7	High	5.00e6 - 5.00e7
<i>Enterobacter spp.</i>	2.08e7		1.00e6 - 5.00e7
<i>Akkermansia muciniphila</i>	<dl		1.00e1 - 5.00e4
<i>Faecalibacterium prausnitzii</i>	6.13e5		1.00e3 - 5.00e8

Phyla Microbiota

	Result		Normal
<i>Bacteroidetes</i>	1.12e13	High	8.61e11 - 3.31e12
<i>Firmicutes</i>	6.59e11	High	5.70e10 - 3.04e11





Stool Test- Tina

Opportunistic Bacteria			
Additional Dysbiotic/Overgrowth Bacteria	Result		Normal
<i>Bacillus spp.</i>	1.16e6	High	<1.50e5
<i>Enterococcus faecalis</i>	3.33e3		<1.00e4
<i>Enterococcus faecium</i>	1.00e3		<1.00e4
<i>Morganella spp.</i>	8.53e7	High	<1.00e3
<i>Pseudomonas spp.</i>	<dl		<1.00e4
<i>Pseudomonas aeruginosa</i>	<dl		<5.00e2
<i>Staphylococcus spp.</i>	<dl		<1.00e4
<i>Staphylococcus aureus</i>	1.03e3	High	<5.00e2
<i>Streptococcus spp.</i>	4.50e4	High	<1.00e3
<i>Methanobacteriaceae</i> (family)	4.89e7		<5.00e9

Stool Test- Tina



Parasites

Protozoa	Result		Normal
<i>Blastocystis hominis</i>	5.65e3	High	<2.00e3

Intestinal Health

Anti-gliadin IgA	291	High	0 - 157 U/L
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OAT Test- Tina

Intestinal Microbial Overgrowth

Yeast and Fungal Markers

7 Arabinose

≤ 29 H 35



Oxalate Metabolites

21 Oxalic

6.8 - 101 H 235



Key Issues & Treatment- Tina



Issue	Treatment
H. pylori overgrowth	<input type="checkbox"/> H. Pylori herbs: mastic gum, DGL, black cumin seed
Bacterial overgrowth	<input type="checkbox"/> Anti-bacterial herbs: coptis, Oregon grape, olive leaf, garlic
Fungal overgrowth	<input type="checkbox"/> Anti-fungal herbs: rosemary, pau d'arco, uva ursi
Protozoal overgrowth	<input type="checkbox"/> Anti-protozoal herbs: artemisia, black walnut
No Akkermansia	<input type="checkbox"/> Akkermansia probiotic
General support	<input type="checkbox"/> Multivitamin, spore-based probiotics, 35g fiber, no gluten
Skin barrier support	<input type="checkbox"/> Botanical topicals; strong EO blends for infection



I couldn't imagine a life without eczema before. I didn't realize how much of my mental space and energy eczema took up . Now I feel free. You changed my life. Thank you!! -Tina



ROOT CAUSE
DERMATOLOGY



Does it work for other dermatologic conditions?





Contact Info

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