INTESTINAL PERMEABILITY: SYMPTOMS, CONTROVERSY, AND TREATMENT APPROACHES

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Medicines from the Earth Symposium 2025

DISCLOSURES

NONE

OBJECTIVES

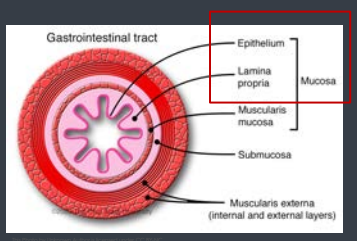
- Understand meaning and historical context of intestinal permeability
- Review common symptoms and associated conditions
- Understand approaches to testing
- Review why this concept can be controversial
- Understand botanical, dietary, and natural approaches to treatment

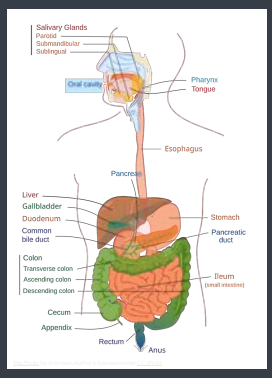
INTESTINAL PERMEABILITY

"LEAKY GUT"

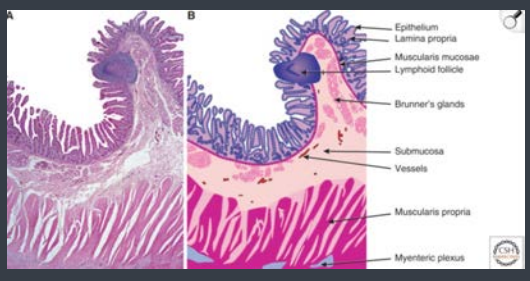
- "Unmediated passage through intestinal epithelium.... that may allow entry of harmful microorganisms, toxins, or undigested food particles through the junctions of the intestinal epithelium, reaching the bloodstream and being able to affect the hormonal, immune, nervous, respiratory or reproductive systems" (Aleman et al, 2023)
- Compromised barriers in GI mucosa allow passage of items into circulation, which can trigger local and systemic symptoms

"GUT" MEANS AREAS OF ABSORPTION & ASSIMILATION [BUT ALSO... SUPPORT ORGANS]

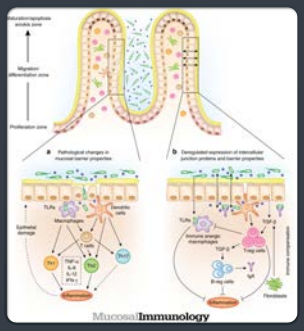




ANOTHER PERSPECTIVE



Buckley A, Turner JR. Cell Biology of Tight Junction Barrier Regulation and Mucosal Disease. Cold Spring Harb Perspect Biol. 2018;10(1):a029314. Published 2018 Jan 2. doi:10.1101/cshperspect.a029314



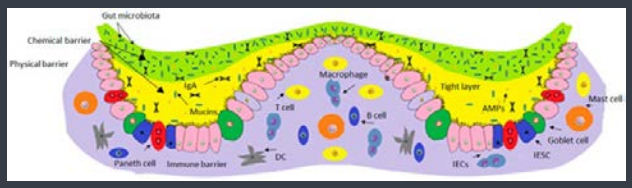
MUCOSAL EPITHELIUM

- Single layer of epithelial cells, highly folded to increase surface area (Ogobuiro et al, 2023)
- The largest interface with the external environment
- Must be able to permit absorption of nutrients and water
- Must also limit access to toxins and antigens (Ahmad bet al, 2017)
- Function is supported by immune cels, mucous, bacteria/commensal microbiota

Mucosal Immunology (2017) **10**, 307-317; doi:10.1038/mi.2016.128

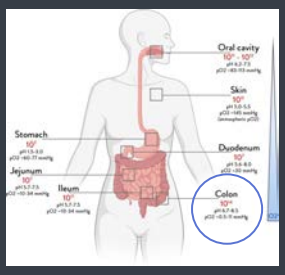
COMPOSITION AND ANATOMICAL STRUCTURE OF THE GUT BARRIER

Epithelium protected by microbiota, chemical barriers, mucous layer, immune cells



Aleman RS, Moncada M, Aryana KJ. Leaky Gut and the Ingredients That Help Treat It: A Review. Molecules. 2023;28(2):619. Published 2023 Jan 7. doi:10.3390/molecules28020619

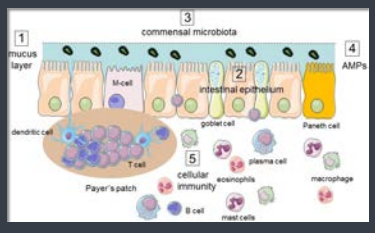
GUT BARRIER – MICROBIOTA



- Microbiota vary at different areas of the GI system – influenced by pH, bile, oxygen availability, nutrients/substrate, and host immune cells/function
- Not *just* a barrier, but do support a barrier function
- Metabolites include short chain fatty acids, vitamin K and folate, and signaling molecules
- Modulates immune function, endocrine balance, and whole-body homeostasis
- 60% of fecal mass is due to microbiota (Farré et al, 2023, de Vos et al,2022)

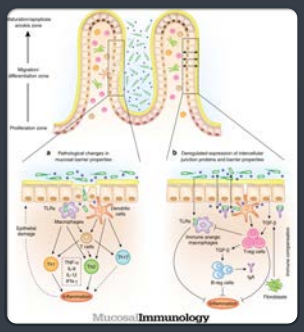
de Vos WM, Tilg H, Van Hul M, Cani PD. Gut microbiome and health: mechanistic insights. Gut. 2022;71(5):1020-1032. doi:10.1136/gutjnl-2021-326789

GUT BARRIER – MUCOUS LAYER



- Mucins secreted by goblet cells
- Allows passage of small materials but prevents large bacteria from passing to the epithelium
- Protects epithelium from acid, bile, and other potentially damaging substance (Farré et al, 2023)
- Supports proper immune function
- Mice without the mucus layer developed spontaneous colitis (Park et al, 2021)
- Decreased goblet cells in those with UC (Park et al, 2021)

Farré R, Fiorani M, Abdu Rahiman S, Matteoli G. Intestinal Permeability, Inflammation and the Role of Nutrients. *Nutrients*. 2020;12(4):1185. Published 2020 Apr 23. doi:10.3390/nu12041185



MUCOSAL EPITHELIUM TRANSPORT

- Epithelial cells can move substances *though* the cells or *between* them (Ahmad et al, 2017)
- Paracellular transport regulated by tight junction complex (Buckley & Turner, 2018)

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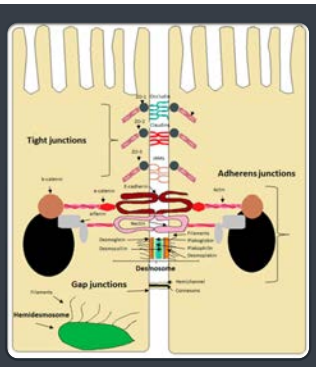

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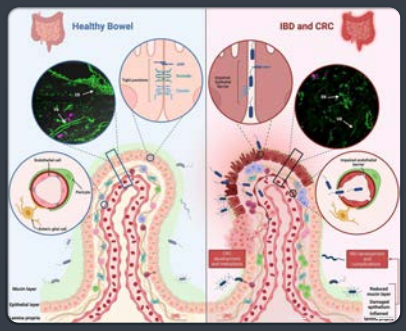
EPITHELIAL JUNCTIONS

- Apical junction complex
  - Tight junctions
    - Zonula occludins (ZO) stitch cells together to prevent passage
  - Adherent junctions (zonula adherens)
    - Cadherins connect to actin filaments of neighboring cells
  - Desmosome (macula adherens)
    - Anchor / support for mechanical stress (Buckley & Turner, 2018)
- Gap junctions
  - Connexins / protein channels that allow communication between cells (Aleman et al, 2023)

MUICOSA: LAMINA PROPRIA

- Layer of connective tissue beneath the epithelial cells
- Contains innate and adaptive immune cells which can remove waste products, toxins, pathogens
- Low Paneth cells seen in people with IBD (Park et al, 2021)
- In susceptible people, gluten causes a reaction that increases release of zonulin, which causes the tight junction to disassemble (Park et al, 2021)



CAUSES OF GI PERMEABILITY

- Pathogens (food poisoning, parasites)
- Diet: lacking nutrients, inflammatory
- Toxins or irritants - chemo, iron, alcohol, NSAIDs
- Frequent antibiotic use without microbiota support
- Immune reaction (Celiac, allergies/atopy)
- Acute or chronic stress
- Genetic susceptibility (Park et al, 2021)

Altered microbiome

Inflammation & immune response

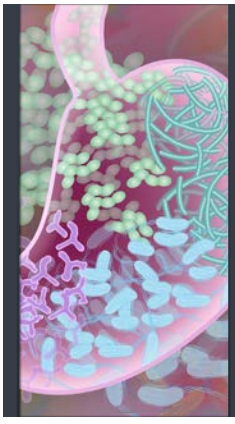
Damage due to toxins or irritants

Nutrient deficiency & poor repair

Stress

HISTORICAL CONTEXT

- Ayurvedic medicine: ama (undigested/unripe)
  - When not adequately removed, ama accumulate, clogs channels, and disturbs normal body processes → fatigue, indigestion, stagnation, altered taste, heartburn, diarrhea, loss of sexual vitality, mental confusion (Pandey et al, 2023)
  - Amaya: disease or "that which is born out of ama"
- Chinese medicine: disruption of spleen/stomach which can generate damp/stagnation (Park et al, 2021)
- Naturopathic Medicine:
  - Poor digestion damages the body's terrain which creates an environment where disease can flourish
  - Maldigestion causes an accumulation of normally excreted substances (toxemia) (Newman Turner et al, 2025)

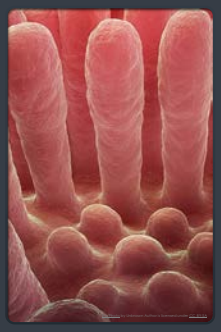


SYMPTOMS OF INTESTINAL PERMEABILITY

- Gas, bloating, abdominal distention
- Indigestion
- Diarrhea or constipation
- Sensitivity to many foods, "reactive"
- Fatigue, exercise intolerance
- Nutrient deficiency without other cause
- Pain
- Forgetfulness, brain fog
- Rashes

ASSOCIATED CONDITIONS AND SEQUALAE

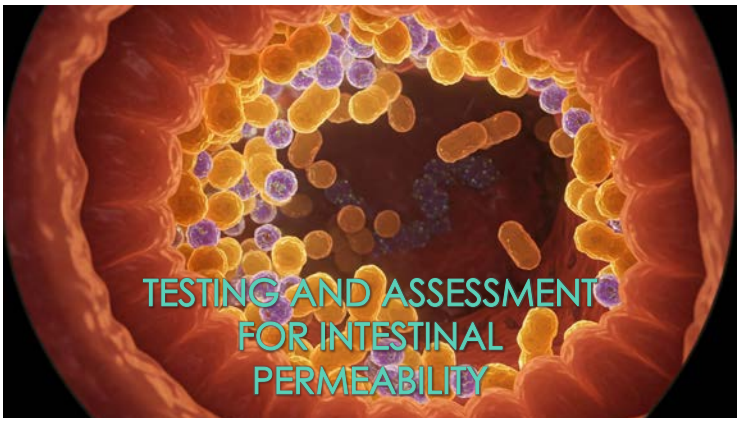
- Inflammatory bowel disease (IBD): Crohn's disease and ulcerative colitis
  - Disrupted tight junctions (Aleman et al, 2023)
- Irritable bowel syndrome (IBS)
  - Have less zonula occludin protein (Aleman et al, 2023)
- Celiac disease
  - Reaction to gluten triggers inflammatory response and alters tight junction function (Aleman et al, 2023)



Rashes, eczema	Allergies	Acne	Autism	Asthma	Migraines	CVD / CHF
Obesity	Type I Diabetes	Alzheimer's dementia	Cancer	Autoimmune conditions	Type II Diabetes	MAFLD / fatty liver
H. pylori infection	Chronic fatigue	Psoriasis	IBD, Celiac disease	Fibromyalgia	SIBO / IMO	Dysbiosis

ASSOCIATED CONDITIONS AND SEQUALAE

(Aleman et al, 2023)



TESTING AND ASSESSMENT FOR INTESTINAL PERMEABILITY

TESTING CONSIDERATIONS

- Most tests are *indirect* markers
- Tests run will depend on symptoms, finances, collection ability, & accessibility
- Results indicating permeability/"leaky gut" do not necessarily provide treatment direction
- Testing can be helpful. Many treatments are safe to start based on clinical suspicion

URINE TESTS

Lactulose-mannitol test

Lactulose is not absorbed but mannitol is; both solutions are ingested, and levels are measured in urine. High lactulose – more permeability. Low mannitol suggests malabsorption.

Takes 5-6 hours

Results not easily comparable between labs

Connot be done in people with high glucose in urine (diabetes)

Must stop some medications 3 days prior

Organic acids test (OAT) / Microbial organic acid test (MOAT)

Metabolites suggest yeast and bacterial overgrowth, nutrient absorption, toxin exposure, methylation status, and antioxidants

First morning urine; some foods, supplements, and antibiotics must be avoided for 2-4 days before collection

Easier collection than stool and blood for many kids

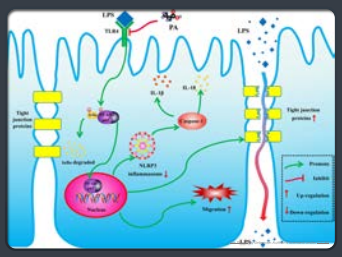
BREATH TEST FOR SIBO / IMO

- Small Intestinal Bacterial Overgrowth & Intestinal Methanogen Overgrowth (IMO)
  - Excessive hydrogen (H2) or hydrogen sulfide (H2S) bacteria in small intestine
  - Excessive methane (CH4) in small or large intestine
- Most common symptoms: diarrhea/ constipation, bloating/gas/distention, heartburn, abdominal pain, malabsorption, many food sensitivities
- Must be diagnosed with a breath (not stool) test
- SIBO/IMO is a motility problem
  - Food poisoning – cytolethal distending toxin B (CdtB) in pathogens triggers production of antibodies that attack vinculin. Vinculin plays a role in cell adhesion and is found in the interstitial cells of Cajal which drive slow wave contractions in the migrating motor complex (Kim et al, 2020)

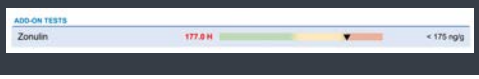
IBS SMART TEST

- Blood test: measures cytolethal distending toxin B (anti-CdtB) and anti-vinculin [antibodies]
- Can support IBS-D (rarely IBS-C) diagnosis - although these are clinical diagnoses
- Can help understand If past food poisoning has caused a reaction
- Not used to diagnose SIBO

ZONULIN TEST



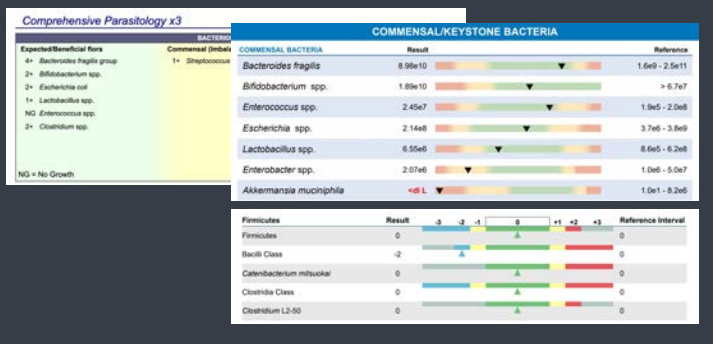
- Zonulin protein regulates tight junctions between cells by triggering assembly/disassembly of zonulin occluden-1 complexes (ZO-1)
  - Breakdown of tight junctions associated with increased permeability (Riviere et al, 2022)
- Fecal zonulin
  - If elevated, suggests GI permeability
  - Much more common than serum testing in availability and research



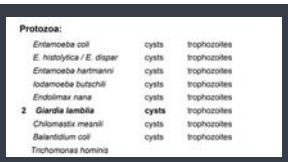
MICROBIOME TESTS

- Many options!
- Quantitative assessment of beneficial flora, commensal flora, dysbiotic flora, and yeast
  - Can add on parasitology, protozoa, helminths, virus testing
- Collection: smear up to 3 stool samples (different days) depending on the lab
  - Best practice when whole stool not required: catch whole stool and sample from 10-15 locations or collect from several stools on different days and pool them
  - Typical diet for at least a week prior to collection
  - No probiotics or antibiotics/antimicrobials for at least 2 weeks prior
- Analysis types: culture and microscopy, PCR, next gen sequencing (16S rRNA, whole genome sequencing or WGS)
  - Stool tests microbiota in lumen of colon; there is an inner layer by mucosa that can only be sampled with biopsy
  - Microbiome fluctuates!

EXAMPLE RESULTS; CULTURE, PCR



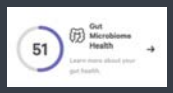
EXAMPLE RESULTS PARASITES, PROTOZOA, HELMINTHS

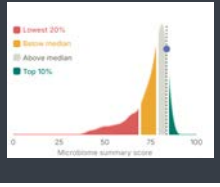


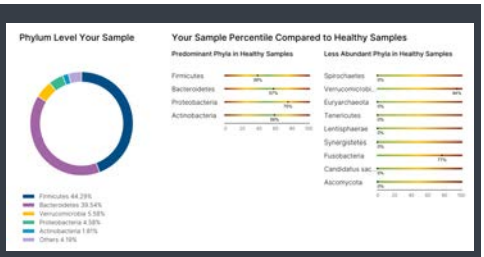
Parasites	Result
Cryptosporidium (*C. parvum* and *C. hominis*)	Negative
Entamoeba histolytica	Negative
Giardia duodenalis (AKA *intestinalis* & *lamblia*)	Negative

Yersinia enterocolitica	4.46e3	< 1.00e5
PARASITIC PATHOGENS		
Cryptosporidium	< dl	< 1.00e6
Entamoeba histolytica	< dl	< 1.00e4
Giardia	< dl	< 5.00e3

EXAMPLE RESULTS WGS







OTHER INFORMATION FROM STOOL

- Occult blood: colorectal cancer, IBD
- Short chain fatty acids butyrate, acetate, propionate, produced by microbiota
  - Butyrate increases concentration of tight junctions (claudin-1, ZO-1, and occludin)
  - Butyrate strengthens mucous layer through increased expression of Mucin 2
  - Butyrate supports glutathione, can induce differentiation and apoptosis of colon cells, support metabolism (Fusco et al, 2023)
- Fecal calprotectin: inflammation
  - Fecal lactoferrin: inflammation (less common)
- Pancreatic elastase 1: exocrine pancreatic insufficiency
- Fecal fat, steatocrit: fat malabsorption
- sIgA: immune function
- Color, undigested food, etc

TESTS	RESULT	FLAG	UNITS	REFERENCE
Calprotectin, Fecal	42		ug/g	
Concentration	Interpretation	Follow-Up		
< 5 - 50 ug/g	Normal	None		
>50 -120 ug/g	Borderline	Re-evaluate in 4-6 weeks		
>120 ug/g	Abnormal	Repeat as clinically indicated		

FOOD SENSITIVITY PANEL

- Not an allergy panel! IgG and IgA testing show delayed response
  - Blood test – serum vs spot test
  - These foods are not "forever allergies" but are causing an immune response
  - Controversial
  - I find it helpful. If many food sensitives are present, presume GI permeability
- Consider evaluation for IgE allergies in those with asthma, allergies, atopy
  - Scratch test, blood test

TEST	SCORE	CLASS
MEAT, POULTRY & FISH		
Beef	0.165	0
Buffalo	0.150	0
Chicken	0.178	0
Duck	0.173	0
Egg, White	0.158	0
Egg, Yolk	0.198	0
Lamb	0.166	0
Pork	0.145	0
Turkey	0.163	0
Venison	0.152	0
FISH & SHELLFISH		
Anchovy	0.168	0
Bass	0.154	0
Cod	0.144	0
Crayfish	0.167	1
Crab	0.151	0
Flounder	0.156	0
Haddock	0.153	0
Halibut	0.150	0
Herring	0.148	0
Lobster	0.148	0
Mackerel	0.168	0
Mussel	0.215	1
Oyster	0.229	1
Perch	0.158	0
Red Snapper	0.140	0
Salmon	0.167	0
Scallop	0.177	0
Shrimp	0.155	0
Sole	0.149	0
Squid	0.196	0
Swordfish	0.186	0
Trout	0.163	0
Tuna	0.252	1
Walleye Pike	0.157	0
GRAINS & STARCHES		
Amaranth	0.244	1
Arrowroot	0.158	0
Barley	0.148	0
Bran	0.229	1
Buckwheat	0.185	0
Corn	0.152	0
Gluten	0.173	0
Kaya	0.211	1
Malt	0.180	1
Millet	0.227	1
Oats	0.193	0
Quinoa	0.232	1
Rice	0.211	1
Rye	0.227	1
Sorghum	0.184	0
Tapioca	0.175	0
Teff	0.254	1
Wheat	0.181	0

TEST	SCORE	CLASS
VEGETABLES		
Artichoke	0.186	0
Arugula	0.274	1
Asparagus	0.187	0
Beets	0.161	0
Bell Pepper	0.161	0
Bok Choy	0.184	0
Broccoli	0.154	0
Brussel Sprouts	0.169	0
Cabbage	0.182	0
Carrot	0.179	0
Cauliflower	0.251	1
Celery	0.181	0
Cucumber	0.173	0
Eggplant	0.150	0
Garlic	0.181	0
Green Bean	0.218	1
Kale	0.166	0
Kelp	0.192	0
Lettuce	0.180	0
Mushroom	0.249	1
Okra	0.167	0
Olive, Green	0.146	0
Onion	0.161	0
Parsley	0.181	0
Parsnip	0.219	1
Potato, Sweet	0.178	0
Pumpkin	0.166	0
Radish	0.224	1
Spinach	0.170	0
Squash	0.158	0
Tomato	0.170	0
Turnip	0.198	0
Zucchini	0.195	0
LEGUMES & PULSES		
Black Bean	0.250	1
Black-eyed Pea	0.276	1
Chickpea	0.158	0
Fava Bean	0.162	0
Green Pea	0.178	0
Kidney Bean	0.286	1
Lentil	0.168	0
Lima Bean	0.196	0
Navy Bean	0.245	1
Peanut	0.185	0
Pinto Bean	0.272	1
Soybean	0.188	0

TEST	SCORE	CLASS
DAIRY		
Casein	0.198	0
Cheddar Cheese	0.156	0
Milk, A1 Cow's	0.187	0
Milk, A2 Organic Cow's	0.195	0
Milk, Goat's	0.194	0
Milk, Sheep's	0.174	0
Whey	0.188	0
Yogurt	0.188	0
FRUITS		
Apple	0.148	0
Apricot	0.149	0
Avocado	0.151	0
Banana	0.151	0
Blackberry	0.149	0
Blueberry	0.148	0
Cantaloupe	0.145	0
Cherry	0.181	0
Coconut	0.233	1
Cranberry	0.182	0
Date	0.156	0
Fig	0.224	1
Grape	0.160	0
Grapefruit	0.153	0
Honeydew	0.150	0
Kiwi	0.152	0
Lemon	0.153	0
Lime	0.252	1
Mango	0.168	0
Orange	0.150	0
Papaya	0.181	0
Peach	0.143	0
Pear	0.152	0
Pineapple	0.171	0
Plum	0.158	0
Raspberry	0.167	0
Rhubarb	0.190	0
Strawberry	0.147	0
Tangerine	0.150	0
Watermelon	0.198	0
BEVERAGES & MISC		
Black Tea	0.175	0
Carob	0.166	0
Cocoa	0.215	1
Coffee	0.150	0
Green Tea	0.231	1
Honey	0.231	1
Meat Glue (transglutaminase)	0.216	1
Yeast, Baker's	0.212	2
Yeast, Brewer's	0.279	1

TEST	SCORE	CLASS
NUTS, SEEDS & OILS		
Almond	0.174	0
Brazil Nut	0.185	0
Canola	0.147	0
Cashew	0.188	0
Chia Seed	0.193	0
Flaxseed	0.175	0
Hazelnut	0.174	0
Hemp	0.190	0
Macadamia Nut	0.212	1
Pecan	0.160	0
Pine Nut	0.178	0
Pistachio	0.175	0
Poppy Seed	0.157	0
Safflower	0.245	1
Sesame	0.239	1
Sunflower Seed	0.171	0
Walnut	0.181	0
HERBS, SPICES & FLAVORINGS		
Basil	0.158	0
Black Pepper	0.247	1
Cilantro/Coriander	0.154	0
Cinnamon	0.189	0
Cloves	0.187	0
Dill	0.182	0
Fennel Seed	0.187	0
Ginger	0.190	0
Ginseng	0.157	0
Horseradish	0.198	0
Licorice	0.195	0
Mustard	0.295	1
Nutmeg	0.185	0
Oregano	0.197	0
Paprika	0.196	0
Parsley	0.196	0
Peppermint	0.217	1
Rosemary	0.187	0
Sage	0.216	1
Tarragon	0.198	0
Thyme	0.194	0
Turmeric	0.170	0
Vanilla Bean	0.231	1

- Example IgG test
- Typically, tests ~100 foods or ~200 foods
  - Specialized diet tests available
- Testing available for
  - IgG – sensitivity
  - IgA- sensitivity
  - IgE – allergy
- Temporary elimination, support integrity, challenge foods

PERMEABILITY / LEAKY GUT CONTROVERSY

- Altered barriers have been demonstrated in stressed humans and animals
- Changes in microbiota do impact barriers – mucosa, tight junctions
- Long history of addressing GI healing to support many symptoms and whole person health
- Why controversy?
  - Barriers fluctuate
  - Altered barriers seen with symptoms, but *causation* is not clearly proven
  - Unclear if this is a "disease" or symptom - if altered barriers cause diseases, or treating heals underlying causes (Camilleri, 2019)
  - No [pharmaceutical] treatment

TREATMENTS FOR INTESTINAL PERMEABILITY

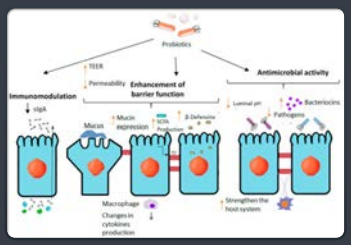
NATURAL SUPPORT FOR GI AND WHOLE PERSON HEALING

TREATMENT APPROACHES

- Support mucus layer
- Support healthy microbiota
- Support tight junction integrity
- Remove toxins/irritants
- Provide supports for epithelial healing
- Decrease inflammatory cascade and support immune function

SUPPORT OF MUCOUS LAYER

- Lactobacillus species (L. plantarum 299v, L. rhamnosus GG, and L. acidophilus DDS-1) enhance mucin production by goblet cells
- Demulcent herbs and foods stimulate goblet cells to produce mucous
  - Althaea officinalis (marshmallow), Ulmus rubra (slippery elm), Glycyrrhiza glabra (licorice), Zea mays (corn silk), Aloe vera gel
  - Slimy foods: nopales, okra, seaweed, sea vegetables, mushrooms, etc



Aleman RS, Moncada M, Aryana KJ. Leaky Gut and the Ingredients That Help Treat It: A Review. *Molecules*. 2023;28(2):619. Published 2023 Jan 7. doi:10.3390/molecules28020619

SUPPORT OF HEALTHY MICROBIOTA

- Also benefit inflammation, immune function, increase butyrate, and protect barrier
  - Lactobacillus rhamnosus GG
  - Lactobacillus acidophilus
  - Lactobacillus plantarum
  - Bifidobacterim infantis
  - E. coli Nissle 1917
  - Bifidobacterium animalis lactis BB-12 (Aleman et al, 2023)

MICROBIOTA SUPPORT: PREBIOTICS

- Taraxacum officinale (dandelion) root, Arctium lappa (burdock) root, Inula helenium (elecampane) root
- Jerusalem artichoke, chicory root, onion, garlic, asparagus, beet, banana, legumes, seaweed (Davani-Davari et al, 2019)
- Psyllium, flax, chia, pectin, FOS, inulin, β-glucans, guar gum, resistant starch
- Mucilaginous herbs: Althaea officinalis (marshmallow), Ulmus rubra (slippery elm), Glycyrrhiza glabra (licorice), Zea mays (corn silk), Aloe vera gel

NUTRIENTS FOR HEALING INTESTINAL PERMEABILITY

FAT SOLUBLE VITAMINS

- Improve diversity of healthy microbiota
- Enhance tight junctions (ZO-1, occludin, claudins)
- Modulate inflammation and immune response (Aleman et al, 2023)
- Vitamin A Dose
  - RDA Men 900 mcg RAE (3,000 IU) / women 750mcg RAE (2,333 IU) a day (retinol or beta-carotene)
  - Tolerable upper intake 3,000 mcg (10,000 IU) a day (NIH, Vitamin A and Carotenoids)
- Vitamin D Dose
  - 2,000 IU a day usually good maintenance dose; evaluate dose with serum levels
- Vitamin K (MK-7) (Chatterjee et al, 2023)
- Vitamin E

ZINC AND ZINC CARNOSINE

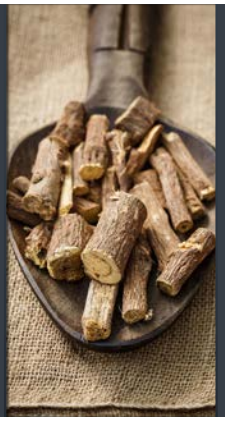
- Zinc
  - Zinc sulfate 110mg 3x.day (!) for 3 months decreased permeability I people with Crohn's disease using lactose mannitol test (Sturniolo et al, 2001)
  - Supports permeability, immune function, and gastric mucosa (Scarpellini et al, 2022)
  - Zinc picolinate 15-30mg once a day with food; for higher/longer term use combine with copper
- Zinc L-carnosine
  - Mucoprotective – ulcers
  - Slow dissociation rate in stomach, antioxidant and anti-inflammatory (Efthymakis and Neri, 2022)
  - 75mg 1-2x/day

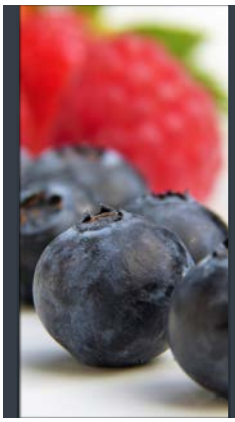
L-GLUTAMINE

- Most abundant amino acid in GI tract
- Regulates expression of tight junction proteins
- Decreases inflammation
- Synergistic with probiotics (Aleman et al, 2023)
- 5 grams in water 1-2x/day

ADDITIONAL BARRIER SUPPORT

- Glycyrrhiza glabra (licorice) or DGL
  - Protected gut barrier in vitro (Murugan et al, 2022)
  - Demulcent, inflammation modulating, vulnerary
- Colostrum (Dziewiecka et al, 2023)
  - Supports immune function, decreases inflammation
  - Derived from cows, not dairy free
  - Doses in studies varied, 5-9 grams a day typical in supplements
- Immunoglobulin (IgG) 1-5 grams a day



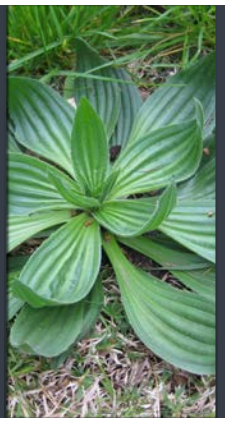


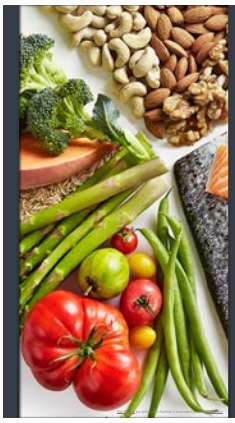
POLYPHENOLS

- Modulate inflammation at least in part due to inactivation of NF-κB. NF-κB and associated cytokines impair GI barrier by disrupting tight junction assembly.
- Antioxidant activity
- Increase mucous secretion
- Nourish microbiota
- Green tea, quercetin, blue/purple foods, turmeric
- Berberine-containing plants
  - Decreases inflammation, modulates microbiome
- Resveratrol (Aleman et al, 2023)

OTHER HERBAL SUPPORT

- Plantago lanceolata/ovale (plantain) leaf
- Camellia sinensis (green tea) leaf
- Quercus alba (oak) inner bark
- Hibiscus sabdariffa (roselle, hibiscus)calyx
- Zingiber officinalis (ginger) root
- Mentha piperita (peppermint) leaf (Aleman et al, 2023)
- Calendula officinalis flower
- Matricaria chamomilla (chamomile) flower
- Prunella vulgaris (heal all) areal



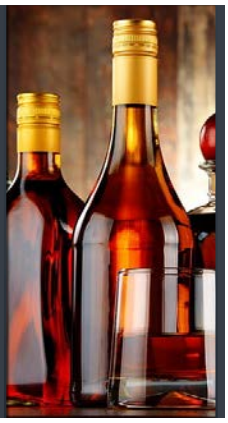


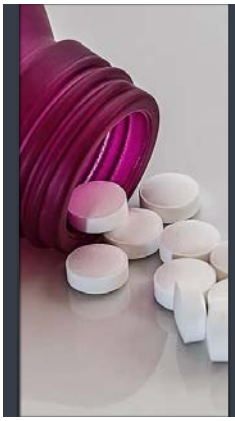
GI MUCOSA TOXINS AND IRRITANTS

- Enterotoxins: lipopolysaccharides from GM- bacteria
  - Food prep / hygiene
  - Support a healthy microbiome
  - Mediterranean diet vs standard American diet associated with lower LPS (Candelli et al, 2021)
- Chemotherapy, Radiation
  - Protect mucosa with L-glutamine and other demulcents [must comanage to avoid interactions]
- Iron
  - Bisglycinate form typically better tolerated than ferrous sulfate

ALCOHOL

- Single episode of binge drinking (> 4 drinks in a sitting) increased endotoxin and inflammatory cytokines TNFa and IL-6, most significantly in women (Bala et al, 2014)
- Excessive alcohol use negatively impacts microbiota – although challenging to understand if this is also due to diet, lifestyle, stress (Engen et al, 2015)
- Alcohol reduces ZO-1 and actin microfilaments suggesting barrier disruption (d'Angelo et al, 2023)
- Probiotics decrease alcohol-related GI symptoms (Engen et al, 2015)
- Support a decrease in alcohol intake
  - Nervines, acupuncture, therapy, drawing attention to use, support groups, etc





NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

- Ibuprofen (Advil, Motrin), naproxen (Aleve), aspirin
- NSAIDS inhibit cox enzymes – but some mucosal damage may be cox-independent
  - Cox 1 prostaglandins protect GI mucosa
  - Cox 2 prostaglandins mediate inflammation
- Use can cause heartburn, nausea, dyspepsia, and abdominal pain – but also perforations, erosions, ulcerations, and acute hemorrhage
  - Especially in the elderly and chronic users (d'Angelo et al, 2023)
- Alternatives: turmeric, ginger, white oak bark, Populus sp (birch, aspen, cottonwood)
  - Topical capsicum , castor oil, peppermint oil, Sr. John's wort oil, wintergreen
  - California poppy, skullcap, Baikal skullcap, corydalis

SAMPLE ASSESSMENT

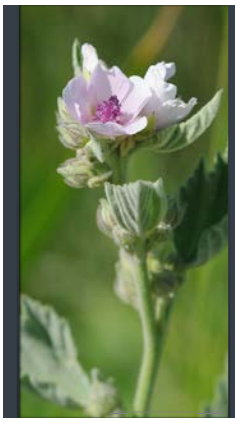
- Assess diet
  - Inflammatory foods
  - Nutrient-rich foods
  - Polyphenols, essential fatty acids
- Assess for alcohol use, meds/supplements including NSAIDs
- Review symptoms for red flags
  - Blood in stool
  - Unintentional weight loss
  - Fevers, chills
  - Severe abdominal pain
  - Fam Hx Celiac, IBS, cancer, autoimmune disorders, cardiometabolic conditions

TO TEST OR NOT TO TEST

- Decide if additional testing will be done
  - Do you need to adjust probiotics, supplements, diet before tests?
- Tests I tend to prefer, if there is a strong clinical suspicion
  - Celiac – blood test must be done WHILE eating gluten. Gold standard test is upper endoscopy with biopsy.
    - Genetic test HLA DQ2 and DQ8 genes can be done if gluten free, but often doesn't lead to diagnosis
  - SIBO/IMO breath test
  - Some type of microbiome assessment (stool) or at least Candida questionnaire
  - Food sensitivity panel per patient interest
- Consider sleep study

SAMPLE STARTING TREATMENT

- Diet
  - Mediterranean type diet: as many colors as possible - adequate fiber, protein [low FODMAP diet may be helpful]
  - Fish: low mercury, salmon is wild not farmer/Atlantic
  - Low in processed foods, fried foods, simple starches and added sugars
  - Adequate water
- Decrease alcohol
- Regular movement
  - Walks after meals
  - Regular cardio and weights/resistance
- Stress management activities and things that bring joy



SAMPLE TREATMENT
[NOT TEST DEPENDENT]

- L-glutamine 5 grams in water once a day (or combo with supportive herbs)
- Tea 1 cup 1-2x/day away from medications or supplements
  - Marshmallow cold infusion
  - Burdock root
  - Licorice
- Aloe juice (not heated)
- Carminatives: ginger, fennel, anise, peppermint, spearmint, lemon balm, cardamom, thyme, cinnamon added to tea, as tincture, or dietary spices
- Bitters/sours to support stomach acid & pancreatic secretions – before meals
  - Artichoke, turmeric, dandelion leaf/root, angelica, blessed thistle, burdock
  - Lemon/ACV in water, schisandra, hawthorne, shrubs/fire ciders

PROBIOTICS, PREBIOTICS, SYNBIOTICS, POST BIOTICS

- Ask about past response and tolerance
  - People with SIBO/IMO may aggravate
- Strains/types
  - Lactobacillus rhamnosus GG, Lactobacillus acidophilus, L. plantarum, Bifidobacterium infantis, B. animalis lactis BB-12
  - E. coli Nissle 1917
  - Bacillus caogulans and spore-based products
  - Saccharomyces boulardii
- Consider prebiotic in formula (combo sometimes called symbiotic)
- Postbiotic: metabolites from healthy donors

TREATMENT

- Replete nutrients needed for barrier support
  - Malabsorption is likely
- Always aim to have as varied a diet as possible
  - Variety supports nutrient sufficiency
  - We don't want to encourage restrictive or disordered eating
  - Fiber is essential – if intolerant, work on healing the root issues
- It may take years to develop intestinal permeability – so treatment can also take time
- Supporting a healthy microbiome also takes time
- Don't forget to consider stress/whole person

THANKS FOR LISTENING!

QUESTIONS?

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