Welcome!

THE SCHOOL OF
Applied Functional Medicine™

An Introduction to Functional Gut Impact!

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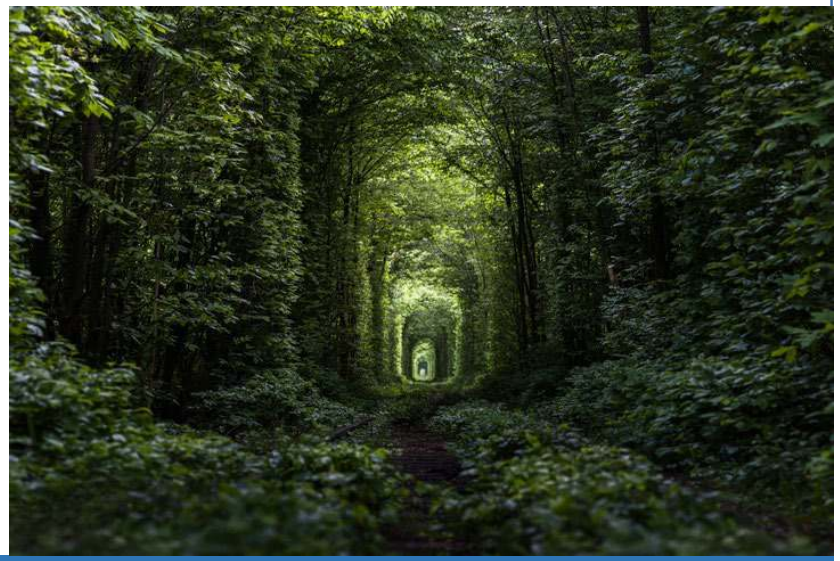
- A weird, weird world.
- Essentially a 25-30 ft. tunnel that is a well-guarded and regulated **exchange corridor** which is ultimately *outside of the systemic body*.
- The entryway for essential **nutrition to fuel every cell** in the body.
- The exit path for most **toxins and waste** – of exogenous *and* endogenous origin.
- Guarded by a planetary level population and **diversity of microbes.** Our biochemistry is regulated by their behavior and DNA (which transfers genes across species and to humans).*
- Home to **2/3+ of the immune system,** surveilling our intake, outflow, and microbial balance.
- Exchange controlled by a very complex, one-cell thick **semi-permeable interface.**
- Housing **its own nervous system** which generates neurotransmitters used throughout the body. **
- The gut and brain work as an integrated axis, connected via the **vagus nerve** with 90% of the nerve fibers going from the gut *to the brain* (afferent).***



* https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-017-3649-y
https://www.the-scientist.com/?articles.view/articleNo/47125/title/Bacteria-and-Humans-Have-Been-Swapping-DNA-for-Millennia/
** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5772764/ , https://link.springer.com/article/10.1007%2Fs11481-019-09851-4
*** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5808284/ , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5859128/

Digestion/Absorption Gone Wrong? Dis-ease Begins!

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- In the **Brain**: Stress, anxiety, ruminating, depression. All these suppress parasympathetic response and downstream vagal stimulation of All digestive functions!
- In the **Mouth:** Impaired by poor chewing (especially due to rushed, distracted eating), low saliva production (e.g. dehydration, some drugs (antihistamines, beta blockers, anticholinergics), very low estrogen, Sjogren's).
- In the **Stomach:** Impaired by what does (or doesn't) happen upstream in the mouth *and also impaired by* eating in a stressed or rushed state*, drinking copious liquid during meals, bariatric surgery, hypochlorhydria e.g. medications (e.g. proton pump inhibitors, H2 receptor blockers, NSAIDs), *Helicobacter pylori* overgrowth, age, allergy/asthma, hypothyroid function, hypoadrenal function.
- In the **Small Intestines:** Impaired by what does (or doesn't) happen upstream *and also impaired by* stress or lack of sleep, low digestive enzyme secretion (e.g. insulin resistance, hypochlorhydria), microbial imbalance or overgrowth, poor bile consistency or flow (e.g. NAFLD, taurine, B6, missing GB, high estrogen states), microbial imbalance (e.g. SIBO, pathogens), food allergy or sensitivity, medications (e.g. birth control pills, corticosteroids, NSAIDs, statins?**), thinning of or damage to mucosal lining /villi (e.g. celiac, dysbiosis), hypothyroid / hypoadrenal.
- In the **Large Intestines** (Colon): Impaired by what does (or doesn't) happen upstream *and also impaired* by food grazing (in sensitive folks), low-fiber diets, high dietary sugar or chemicals, toxin transport, neuropathy, diarrhea, antibiotic use (bacteria make enzymes too!), diverticulosis, constipation.

* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC26223/
** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5550934/

Stomach Acid: Digestive Hero!

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- Hydrochloric acid (HCl) is produced by parietal cells in the lining of the stomach (and pepsin from goblet cells). Required to denature proteins & isolate/prepare nutrients for absorption.
- **Suboptimal HCl may be caused by many factors*** e.g. poor eating hygiene, sympathetic nervous system state, hypothyroid and/or hypoadrenal state, SIBO or other dysbiosis (antibiotics), chronic use of NSAIDs, *H. pylori* infection, autoimmune antibodies, age, chronically low estrogen***, and/or – of course – acid-suppressing drugs.
- What else are they consuming? **Acid-suppressing medication use** is very common in some populations e.g. PPIs, H2 receptor blockers/antihistamines, NSAIDs. Taking too many mineral supplements with a meal can create an overly alkaline environment, insufficient for optimal digestion. Excessive bicarbonate intake (e.g. baking soda) can also naturally restrain HCl production.
- Suboptimal HCl (hypochlorhydria) may create an opportunity for **microbial overgrowth/pathogens****, immune hyper-reactivity to maldigested foods (e.g. allergy/sensitivity), or nutrient/drug malabsorption.
- Internal production decays with age, most often because of simmering *H. pylori* overgrowth. **Study shows up to half of adults in their 60s and 80% of people over age 85 have hypochlorhydria**. Pepsin production decays with age regardless of *H. pylori* status.*
- Maldigestion creates downstream dis-ease and dysfunction! Hypochlorhydria may cause:
  - **Delayed gastric emptying** which can then promote GERD, bloating, and impaired first-pass insulin response. Note that delayed gastric emptying may also be caused by other dynamics such as poor vagal tone, low estrogen, hypothyroid, and/or hypoadrenal states.#
  - Inhibited pancreatic enzyme and bile release, and thus **impaired downstream digestion**.
  - **Poor denaturation of protein** digestion and absorption (and thus, potentially, sensitivities/allergies).
  - **Nutrient deficiencies**, especially amino acids, vitamin B12, Minerals (e.g. Ca, Fe, Zn, Mg), and Folate.
  - **Many other disease dynamics**! Ulcers, Osteoporosis, Low energy, Indigestion, Depression, Anemia, Weak immune function, Dysbiosis, Food Sensitivity, Allergy, Autoimmunity, Cardiovascular disease, Arthritis, Cognitive impairment.

* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6502205/
** https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2761273 *** https://www.spandidos-publications.com/10.3892/etm.2018.6406
# https://journals.physiology.org/doi/full/10.1152/ajpgi.00144.2019 , https://pubmed.ncbi.nlm.nih.gov/32124195/ , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6850045/

Disease from Seemingly Humble Beginnings?

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Dysfunction	Affects	Resulting In (e.g.)
Low stomach acid	Low Vitamin B12	Low energy, Neuropathy, Arterial inflammation
Low stomach acid	Low magnesium	Osteopenia, Chronic Headaches, Constipation, Muscle spasm, Atrial fibrillation, Hypertension, GERD
Low stomach acid	Low iron	Anemia (low RBC), Fatigue, Poor tissue oxygenation (cold, numb), Hypothyroidism
Bacterial imbalance or overgrowth	Poor essential fat absorption	Depression, Anxiety, Dry skin, Elevated triglycerides
Bacterial imbalance or overgrowth	Poor serotonin creation	Insomnia, Depression, Constipation
Low pancreatic enzymes	High diet residue in intestines	Bloating, Flatulence, Fatigue, IBS, Bacterial overgrowths, Constipation
Low pancreatic enzymes (coincident insulin resistance?)	Inadequate tyrosine	Hypothyroidism, ADHD/ADD, Depression, Restless Leg Syndrome

Cues and Clues of Hypochlorhydria/Maldigestion

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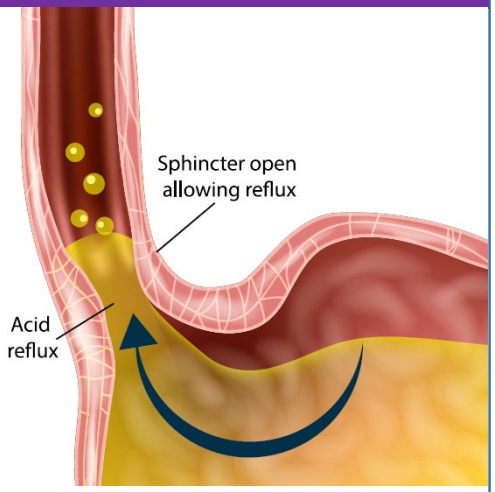
- Frequent daily belching, especially during or soon after eating
- Upper GI bloating, belching, an early sense of satiety/heaviness during or right after meals
- Feeling nauseated after taking supplements with food (except zinc which may promote nausea on its own or except when limited to excessive calcium/magnesium at once)
- Feeling particularly fatigued after meals (especially if meal was otherwise consumed slowly)
- Chronic indigestion or GERD
- Clearly seeing undigested food in stools
- Irritable bowel syndrome (IBS) or SIBO/IMO or frequent gut infection (e.g. parasite) or microbial imbalance (e.g. *Candida* overgrowth)
- Insufficient levels of Vitamin B12 despite eating a carnivorous diet
- Multiple mineral (e.g. iron, zinc, magnesium, calcium, copper) and/or protein insufficiencies despite an ample, whole foods diet
- Rosacea
- Multiple food allergies or sensitivities
- Chronic allergy or urticaria
- Chronic asthma, especially if wheezing is also involved
- Hair or nails that break frequently or are thin
- Osteoporosis or advanced osteopenia

Stomach Acid Gone Wrong: GERD

It's seldom the case that there is too much stomach acid; instead, acid reflux is often caused by Stomach Acid being in the wrong place!



- **Insufficient stomach acid (hypochlorhydria)** is often an acid reflux driver in part because it promotes delayed gastric emptying.
- PPI drug use increases risk of GERD (and death, with ongoing use) significantly. In some populations, they are highly-prescribed, available OTC, and overused.*
- **Weak lower esophageal sphincter (LES)** caused by stress, medications, insufficient magnesium, high sugar diet, refined carbohydrate (chips, fries), & chemicals.
- **Common LES irritants:** citrus, cooked tomatoes, peppery/spicy foods, fried foods, peppermint, chocolate/tea/coffee, alcohol.
- Stomach juices bubble up into the esophagus where there is insufficient mucus protection from acidic juices (it hurts!). Pepsin can erode this tissue but also directly causes an inflammatory response.
- GERD may just be an issue of eating in a rushed and/or stressed state or drinking too much liquid during a meal, especially a rushed one. The combination of hypochlorhydria paired with insufficient magnesium, poor eating hygiene, and food sensitivity is often the perfect storm of factors in chronic GERD. Other factors negatively affecting motility or digestive secretions may also be involved e.g. hypothyroid, anxiety.
- **Bacterial overgrowth** is often involved in chronic acid reflux. GERD is often coincident with IBS/SIBO/IMO. **Hiatal hernia** may be involved, and if so, complementary therapy may help e.g. chiropractic, visceral manipulation. **Schatzki rings** often involve GERD and a sliding hiatal hernia.
- Soothe inflamed tissue with **mucilaginous herbs (esp. lozenges) and/or zinc carnosine**, but you must address the root causes of GERD in a unique individual in order for there to be sustained relief!

* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5642790/ , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707629/ , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8171048/ , https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2755847, and http://onlinelibrary.wiley.com/doi/10.1002/pds.4135/pdf. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5095572/ on overuse of PPIs for infant reflux.

Disease Begins In the Gut?

- **Maldigestion/Malabsorption of key nutrients** (e.g. iron affecting T4 to T3 thyroid function, magnesium affecting GABA/glutamate balance, Vitamin B12 affecting nervous tissue health, Vitamin A affecting immune strength and eye health e.g. night blindness).
- **Oxalates*** (aka oxalic acid) from foods and microbes (e.g. *Candida albicans)* may be overly absorbed into systemic circulation and contribute to kidney stones and pain syndromes (e.g. vulvodynia), especially in people with (1) poor gallbladder function or post-cholecystectomy, and/or (2) Vitamin B6 insufficiency (required for oxalate degradation), and/or (3) microbiome with low *Oxalobacteria* presence paired with overall low bacterial diversity.
- **Histamines*** from foods, many different microbes, and our own immune system (e.g. eosinophils, mast cells) are broken down by (1) diamine oxidase (DAO) which is an enzyme produced in a healthy intestinal brush border in the gut and also intracellularly by (2) the methylation-dependent enzyme HNMT (Histamine N-methyltransferase). Histamine intolerance Often begins in the gut!**
- **Enhanced intestinal permeability (EIP)** creates systemic inflammation from dynamics such as food sensitivities (e.g. joint pain, brain fog, fatigue, elevated cortisol) from excessive immune exposure to partially digested foods and systemic exposure to endotoxins (e.g. LPS)*** from our microbiome. Localized immune response to these perceived threats increases immune reactivity (oxidative stress) including higher histamine levels in the gut which can worsen mucosal damage and further increase intestinal permeability.
- **Lipopolysaccharides (LPS)** and other endotoxins/wastes from gut microbes can gain access to systemic circulation via enhanced intestinal permeability, promote increased systemic inflammation, and increase permeability of the blood-brain barrier (BBB), which can contribute to **neurological challenges, neurotoxicity, and mood imbalances** (e.g. NMDA receptor upregulation may increase glutamate activation and downstream hypervigilance, anxiety, wakefulness).****
- **Stress** impairs motility, digestive secretions, mucosal integrity, barrier function, and immune function in the gut, all of which can strongly trigger or exacerbate nearly Any systemic disease dynamic in the body, especially when chronic.

* These food components are addressed in more detail in the *Nutrition and Supplements 101* course.
** Overview of histamine intolerance: https://schoolafm.com/ws_clinical_know/can-you-spot-histamine-intolerance/ or a deeper dive here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7463562/. For patients, https://healinghistamine.com . A deep dive into how/why it often begins in the gut: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8069563/ . *** For a deep dive on LPS, see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6091223/.
**** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4660627/ , SAFM students see course Document "How the Microbiome Influences the Brain", and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8278099/

A Perspective Shift on Gut Priorities?

What FM Today Gets Right

- Eat real food
- Don't eat chemicals
- Digestion is not a given
- Arrest overgrowths (e.g. SIBO)
- Leaky gut is real (but not universal)
- NSAIDs are toxic
- Optimize bowel movements
- The gut is Immune Central

Where we Need to Focus More!

- **Mouth** (e.g. microbes, mercury (Hg), root canals, secretory IgA)
- **Eating Hygiene**, especially Chewing
- **Motility** (e.g. microbial regulation, GB motility, Migrating Motor Complex (MMC), peristalsis, gastric emptying effect on Insulin regulation)
- **pH** (e.g. HCl, bicarbonate, bile, yes! But also Enzyme activation, acid-producing microbes)
- **Barrier Integrity** (e.g. LPS, IL-6, histamine, alcohol, SCFAs, BBB permeability, hydrogen sulfide)
- **Epithelial Function** (e.g. brush border enzymes, metformin, MALT, detoxification)
- **Microbial Diversity** (e.g. maximize it, avoid antimicrobials, opportunistic species wake-up call vs. a "kill everything questionable" approach)
- **Parasympathetic activation** (e.g. vagal function/tone, breathing, immune brake, sleep)
- **Systemic Regulation** (gut-microbe-brain axis)

A broader focus on optimizing the environment (terrain!) in which the gut can thrive!

Thank You for Joining Us!

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