What’s YOUR Gut Reaction?
Implications of Leaky Gut

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Systems biology approach recognizes that all the systems of the body work together in a network, and if one is affected, the others are too.

Identifies the *why* in the disease process – root causes

Looks at the *whole* person

Concept of “unique biochemical individuality”

Individualized medicine

Genetic uniqueness

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Patient Center Approach Identifies:

ANTECEDENTS (Predisposing factors) - Vulnerable

TRIGGERS (Precipitating factors) – Initiate illness

MEDIATORS (Perpetuating factors) – Maintain maladaptive behaviors

ANTECEDENTS, TRIGGERS, MEDIATORS

ANTECEDENTS
- Genetic
- Congenital
- Demographic
- Dietary
- Environmental
- Occupational
- Learned
- Traumatic
- Disease-induced
- Drug-induced

TRIGGERS
- Trauma
- Microbes
- Antigens
- Environmental Toxins
- Radiation
- Social Interactions
- Memories
- Diverse Sensory Stimuli

MEDIATORS
- Hormones,
- Cytokines, etc.
- Ions
- Reactive Oxygen Species
- Metabolites
- Thoughts
- Beliefs
- Social
- Reinforcement
- Classical
- Conditioning
Organizing the Patients Clinical Imbalances

**Assimilation:**
Digestion, Absorption, Microbiota/GI, Respiration

**Structural/Integrity:**
Subcellular membranes to Musculoskeletal Structure

**Communication:**
Endocrine, Neurotransmitters, Immune messengers

**Transport:**
Cardiovascular, Lymphatic System

**Biotransformation and Elimination:**
Toxicity, Detoxification

**Energy:**
Energy regulation, Mitochondrial Function

**Defense and Repair:**
Immune, Inflammation, Infection/Microbiota
Identifying the **WHAT** and the **WHY** and then Educating on the **HOW**

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Retelling the Patient’s Story

1st Meeting – 1-2 hours

Identifying what is causing problems, root origins, what contributes to their progression
Analyze where to intervene to begin reversing the process

• **Antecedents**
  - Predisposing factors such as Genetics and Environmental
  - Family Hx: Depression, CV, Type II DM,

• **Triggering Events**
  - Stress, Poor diet – SAD, Mold exposure, Mercury exposure, Sedentary

• **Mediators/Perpetuators (Contributors)**
  - Stress, Poor sleep hygiene, lack of social contact

• **Personalizing Lifestyle Factors (MODIFIABLE)**
  - Sleep and Relaxation
  - Exercise & Movement
  - Nutrition & Hydration
  - Stress & Resilience
  - Relationships & Networks
Further Investigation

- Inflammatory markers testing (hsCRP, IL levels, homocysteine)
- Nutritional status
  - Essential fatty acids, methylation pathways (MTHFR)
  - Organic acid metabolites
  - Micronutrient Deficiency panel
- Markers of detoxification (functional capacity for biotransformation)
- Neurotransmitters and hormone cascades
- GI microbiome testing (parasites, bacteria balance, fungi)

Specialized testing is an important tool in the field of Functional Medicine
Institute for Functional Medicine New Paradigm

Don’t Treat the Disease- Treat the Imbalances

One Condition → MANY Imbalances

One Imbalance → MANY Conditions

Systems Biology Approach to Assessment
It ALL begins in the GUT!

“If your gut isn’t healthy, YOU are not healthy!”
~ 25% of American adults have functional GI complaints that affect their quality of life.

~50% have experienced 1 or more upper GI symptoms in the past 3 months.

Over 95 million Americans have some sort of digestive issue.

*American College of Gastroenterology
Digestive wellness entails DIGESTION, ABSORPTION & ELIMINATION

- **Breaking down** food into tiny nutrients
- **Absorbing** food through the intestinal lining and into the bloodstream
- **Assimilating** the nutrients – ie, bringing them into the cells
- Healthy **elimination of waste** products through the kidneys or bowel
Digestive wellness also involves:

**BARRIER & IMMUNE FUNCTION**

- Protection against non-self particles, toxins and pathogens
- Monitoring and controlling movement of particles and pathogens into and out of our physiology
- Healthy communication with our Immune System
From beginning to end, the digestive tract runs 25-35 feet long.

If you spread that tissue flat, it would cover a tennis court!

Liz Lipski, PhD
STRUCTURE AND FUNCTION of the GI Tract

GALT – GUT ASSOCIATED LYMPHOID TISSUE

Underneath the EPITHELIAL LINING is rich IMMUNE tissue called GALT and MALT.

EPITHELIAL LINING

- Lining of the GI tract is the “mucosa”, or the epithelial lining
- This layer is only one cell thick!
- Healthy tissue will regenerate every 3-5 days!
- Fluid and enzymes are sloughed off and recycled to help with digestion.

• 2/3 of our lymphocytes reside in the small intestine
• 70-80% of our immune tissue is in the GUT

The small intestine is the largest immune organ in the body!

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Absorption of antigens and toxins through the mucosa of the GI tract is tightly controlled by the TIGHT JUNCTIONS between the individual cells.

A healthy digestive tract will allow only small amounts of antigens to be absorbed through the single cell epithelial junctions. The immune system has mechanisms so that we don’t react to most of them.
GALT TISSUE CONSISTS OF:

- **Lymphoid nodules** (Peyer’s patches)
  - Predominantly CD-4 lymphocytes (helper cells)
  - CD-4 lymphocytes trigger an increase in IgA to the antigen

- **Intraepithelial lymphocytes** (IEL) IEL’s are mostly CD-8 (cytotoxic/suppressor phenotype) (tolerance)
  - IEL’s trigger inflammatory cytokines (to fight off the antigens) and inflammation (IBD)
  - Presence of elevated IEL’s indicates ongoing inflammation or neoplasm (marker of celiac)

- **Other lymphocytes** scattered throughout the lamina propria (connective tissue of the mucosa)

- **Epithelial villi**

**Impaired immunity allows pathogens to establish themselves and SIBO.**
Villi

• Mucus and bacteria protect the villi tissue.
• The mucus contains an antibody called secretory IgA.
• SecIgA neutralizes bacteria, fungus, parasites, viruses and food residue by preventing them from attaching to the lining of the intestine.

Deficiency of secretory IgA is the most common immunodeficiency and leads to susceptibility to: asthma, autoimmune disease, candidiasis, celiac disease, food allergies and more.
STRUCTURE AND FUNCTION of the GI Tract

NEUROENDOCRINE CONTROL

Digestive anatomy

Nutrients pass through the EPITHELIAL LINING into the bloodstream in the capillaries of the Villi.
There is a continuous interplay between the gut and the brain...
GUT- BRAIN Connection

The Gut Nervous System has been called “the Second Brain”

- The GUT produces ¾ of the body’s neurotransmitters
- It has greater metabolic activity than the liver.

The enteric nervous system (GUT nervous system) works with all the CNS neurotransmitters to control gut motility.
- All of these complex relationships work together for proper gut function


Nature Reviews Neuroscience 13, 701-712 (October 2012) | doi:10.1038/nrn3346

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Many Steps are involved in Efficient Assimilation of Nutrients

**Digestion**
- Chewing
- Peristalsis
- Digestive enzymes
- Other secretions that support the enzyme function.

**Absorption**
- Movement between the intestinal lumen and the bloodstream (circulation) through the single cell layered intestinal epithelium.
- Absorption is supported by the immense surface area of the small intestine and its villi and microvilli surface area.
- Accomplished by either active transport or passive diffusion (intercellular, or paracellular) all along the length of the small and large intestine.
Healthy BARRIER FUNCTION of the GUT

The GUT controls movement from ENVIRONMENT TO SELF

- The GI tract acts as the first line of defense against bacteria, parasites, and toxins from the food we eat.
- The GUT is the “Interface” between the environment and our physiology.
- Controls the “Exchange” of information from the outside world to our self.

Over a lifetime you consume between 7 and 9 tons of food!
Health or Disease?
GUT HEALTH and GENETICS

= Combination of our GENES and our ENVIRONMENT

ENVIRONMENT

GENOTYPE

Diet

GMO’s, processed foods, high fat, high sugar
Lifestyle
Exercise
Stress
Toxins
Pollutants
Chemicals
Medications

PHENOTYPIC
EXPRESSION

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Health or Disease?

NEW WINDOW of INFORMATION:

The GUT is the point of entry between our GENES and the ENVIRONMENT!

What information gets in → is controlled by our GUT PERMEABILITY!

SO....

GUT PERMEABILITY determines whether we move in the direction of health or disease!

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Normal Gut Permeability = Tight Junctions

- Initial digestion of food from mouth and stomach
- Partially digested food enters small intestine
- Enzymes from pancreas and villi surface continue to break food down to the tiniest particles
- Indigestible food and larger particles are excreted in stool
- **Nutrients pass into the bloodstream**
- Fuels the body

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TRANSPORT FUNCTION
(Nutrients, Antigens, Microbes, etc.)

ROUTES for TRANSPORT

• Transcellular
  • Passive (water + Mg)
  • Active (glucose, most Vitamins + Minerals)

• Paracellular
  • Passive only

• Endocytosis – Macromolecules
  Antigens, Micelles, Microbes and particulate matter

Molecular Structure of Tight Junctions and Their Role in Epithelial Transport
James Melvin Anderson. Physiology Published 1 June 2001 Vol. 16 no. 126-130
(c) 2016 Optimal Health Solutions LLC
Transcellular and Paracellular Transport work in concert with each other.

**Transcellular** transport is directional, **energy dependent** and controlled by “transporters and channels on the cell membranes”

**Paracellular** transport is **passive**, and results from diffusion or osmosis down the gradient created by the transcellular mechanisms.

The TIGHT JUNCTION is the main component of Paracellular barrier.
Altered Transcellular Permeability

Factors that Can Affect Transcellular Permeability

• Hypoxia or starvation can damage the mucosa which leads to bacterial overgrowth in the gut.

• Genetics (gene mutations)
  Hemochromatosis and Idiopathic Hypercalciuria
  ➔ Excessive absorption of Fe and Calcium due to upregulated enzyme driven transport
Nutritional Deficiencies and ACTIVE TRANSPORT

Complex Effects on Transcellular Mucosal Permeability

- Minerals like Calcium, Fe and Zinc require specific protein carriers (transport proteins) for absorption.
  - Deficiencies upregulate the carrier protein for those minerals

- Certain nutrients affect energy metabolism of the cell. These nutritional deficiencies may limit the active transport over the mucosa → resulting in malabsorption of the nutrient.

ACTIVE TRANSPORT is dependent on B3 Cofactors. B3 Deficiency impairs small intestine function even though the villi’s architecture is normal and not damaged.
## Ability to Absorb and Utilize Nutrients is a Key to Health

Table 21.5, Integrative Medicine, A Practitioner’s Guide

<table>
<thead>
<tr>
<th>Nutrients Absorbed by Passive Diffusion</th>
<th>Nutrients Absorbed by Active Transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Free fatty acids</td>
<td>- Amino acids, peptides</td>
</tr>
<tr>
<td>- Magnesium</td>
<td>- Monosaccharides</td>
</tr>
<tr>
<td>- Monoglycerides</td>
<td>- Sodium</td>
</tr>
<tr>
<td>- Lysolecithin</td>
<td>- Zinc</td>
</tr>
</tbody>
</table>

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Most Permeability happens within Paracellular Transport

- ALWAYS passive
- Tight Junctions and **adhesion molecules** that make up those junctions control passive transport.

**Stress and high glucose concentrations** in the gut stimulate the epithelial cells to contract which opens the junctions


**Prostaglandin E** maintains normal paracellular permeability (inflammation control)


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Oral Tolerance
Normal Antigenic Sampling

• With “normal” intestinal permeability, there is a minor amount of antigenic material that crosses the barrier
  • Usually smaller particles
  • Active sampling of intestinal antigen challenges the immune system to begin normal immune responses and intestinal homeostasis.


• The immune system monitors these particles and develops “oral tolerance” to them in several ways:
  • The immune system is unresponsive to the trigger (anergy)
  • The immune system triggers apoptosis (death) of the particle(cell)
  • Regulatory T cells (TREGS) suppress the reaction to the trigger particle

Integrative Medicine, Principles for Practice, McGraw-Hill Medical Publishing Division. Kleiger and Lee

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Oral Tolerance

Merriam Webster Dictionary

“the capacity of the immune system to recognize substances taken in through the digestive system and to weaken or suppress the immune response to them”

“…evolved to prevent hypersensitivity reactions to food proteins and bacterial antigens present in the mucosal flora.”


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Loss of Oral Tolerance occurs with immune system dysfunction

KEY TAKEAWAY:
An increase in Intestinal Permeability leads to immune system dysregulation and defective oral tolerance.
Oral tolerance, an active immunologic process mediated by multiple mechanisms

Table 1
Mechanisms of immune tolerance and their relationship to oral tolerance

<table>
<thead>
<tr>
<th>Mechanism of tolerance</th>
<th>Dose administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deletion</td>
<td>High dose</td>
</tr>
<tr>
<td>Anergy</td>
<td>High dose</td>
</tr>
<tr>
<td>Receptor downregulation</td>
<td>High dose</td>
</tr>
<tr>
<td>Cellular regulation</td>
<td></td>
</tr>
<tr>
<td>Th2 cells (IL-4)</td>
<td>Low dose</td>
</tr>
<tr>
<td>Th3 cells (TGF-β)</td>
<td>Low dose</td>
</tr>
<tr>
<td>Tr1 cells (IL-10)</td>
<td>Low dose</td>
</tr>
<tr>
<td>CD25⁺CD4⁺ cells</td>
<td>High/low dose</td>
</tr>
</tbody>
</table>

The dose relationships may be modified by adjuvants, antigen structure, and dosing frequency.
Loss of Oral Tolerance to Antigens

Dr. Alessio FASANO Researcher on Celiac and NCGS suggests that Loss of Oral Tolerance is related to

• A change in the gut flora (microbiome)
• Triggers new genes and expression of mixed genes

Fasano suggests that once those genes are turned on it is a permanent condition that then leads to loss of oral tolerance and autoimmunity

GUT FLORA affect not only our IMMUNE FUNCTION, but our GENETICS as well!

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EPIGENETIC CONTROL of OUR PHENOTYPE

Health or Disease?
= Combination of our GENES and our ENVIRONMENT

ENVIRONMENT

GENOTYPE

Diet
GMO’s, processed foods, high fat, high sugar
Lifestyle
Exercise
Stress
Toxins
Pollutants
Chemicals
Medications

PHENOTYPIC EXPRESSION

GUT FLORA COMPOSITION

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Leaky gut syndrome
(intestinal permeability)

The tight junctions between the cells of the intestinal lining become compromised and loosen.

Larger particles (food, bacteria, parasites, toxins) are able to “leak” through the lining (and into the bloodstream) resulting in an immune response.

This immune response can put out inflammatory cytokines which alert the WBCs to fight off the “foreign” objects that have “leaked” into the bloodstream.

This inflammation travels to ANY part of the body through the bloodstream causing systemic damage.

INFLAMMATION IS THE PRECURSOR TO CHRONIC DISEASE

These changes can then trigger the turning on of genes and can be the precursor to many conditions and chronic disease!
Control of Tight Junctions

- **Occludin** is an integral membrane protein localizing at tight junctions
  - Involved in paracellular permeability and cellular adhesion.
  - The first to be identified.
- **Claudins** are another membrane protein in the tight junctions.
  - Regulated by extracellular stimuli.

**ZONULIN Upregulation**

- Zonulin was discovered in 2000 by Dr. Alessio Fasano
- It is a modulator of intercellular Tight Junction and helps regulate the paracellular pathway of absorption in the intestinal epithelium


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ZONULIN Upregulation

- Small intestinal exposure to bacteria
- Exposure to gluten (the gliadin particle)

trigger ZONULIN release and increase in intestinal permeability

Infections triggered a response *only on the part of the mucosa exposed to the bacteria.*

Followed by an immediate increase in intestinal permeability.

The level of virulence didn’t matter.

- May be a defense mechanism to flush out microorganisms
- Protects against bacterial colonization of the small intestine
- Part of the host’s innate immune system response
- May play a role in the development of autoimmune process in Celiac and Type I diabetes

**First the intestinal permeability ➔ then the autoimmunity**

AUTOIMMUNITY requires 3 elements:

- Genetic Makeup
- Environmental Trigger
- Intestinal Permeability

INFLAMMATION opens TIGHT JUNCTIONS

- Insults to the GI tract trigger NFkB upregulation
- NFkB is a potent inflammatory cytokine
- NFkB triggers the release of MLCK (Myosin Light Chain Kinase) which opens tight junctions
Leaky gut syndrome

(intestinal permeability)

- Triggers: *endogenous* toxins from resident microflora, resistant or overgrowth microflora as a result of antibiotic usage
- Triggers: *exogenous* toxins such as NSAIDS, undigested food, alcohol, drugs and foreign microbes

Commonly seen in intestinal inflammation, food intolerances, gluten sensitivity, and celiac sprue, and chemotherapy patients.
INNATE AND ADAPTIVE IMMUNE SYSTEM

One Trigger (gluten) → Two Mechanisms: NCGS vs. Celiac

**NCGS is innate immune reaction--Celiac is adaptive immune reaction**

- **Innate Immunity** – *present from birth*. First phase of the immune response.
  - Creates inflammation with cytokine response of innate immune system
  - No destruction of the intestines
  - NCGS is an innate immune system mechanism

- **Adaptive Immunity** – *develops over time*. The genes and the exposure to the trigger/antigen must meet for it to begin.
  - Celiac is an adaptive immune response mechanism
  - Autoimmunity process begins in the first year of life, whether they express the disease soon after or much later in life.
  - Damages the villi over time.

The additional “switch” seems to be GUT MICROBIOTA composition!
Progression of Immune Response to Antigens in the GUT

• When the body is exposed to an antigen via the digestive tract lymphocyte’s respond
• The body produces IgA antibodies first, before IgG or IgM.
• Some of the antibodies from the salivary glands are secreted into the blood, so IgA can be detected first in saliva and then in blood.
• If the patient consumes more and more of the same antigen, an inflammatory reaction may occur in the gut, causing the tight junctions to open.
• Antigens flood into the submucosa
• Then they migrate into the regional lymph nodes
• Then into the circulation.
• At this point the body will begin producing IgM or IgG antibodies against those food antigens.
Intestinal Immune Function Strongly Affected by Diet and Nutritional Status

- **Pro-Cal Malnutrition**
  - impairs cell-mediated immunity
  - secretion of Sec IgA and
  - induces SIBO (Small Intestinal Bacterial Overgrowth)

- **Nutrient Deficiencies**
  - affect “systemic” immune function
  - predispose to GI disease

- **Low Zinc, Fe, Vit A and Se**
  - Associated with increased susceptibility to mucosal yeast infection
  - *These are common deficiencies with GI disorder pts.*

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### FATS

**Dietary Fats** are **Immune Modulating** in the Intestinal Tract

**Omega -3 Fatty Acids** are anti-inflammatory and are part of the standard protocol for Gut Healing!

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Integrative Medicine, A Practitioner’s Guide, p462

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Elements/Mechanisms that Affect the Tight Junction

- Inflammation
- High sugar high fat diet
- Intense exercise – NO production
- Adhesion cells – Occludin and claudin
- Zonulin activation
- Gluten exposure
- High stress levels
- Medications
Junction Control

If the movement between the environment and self stays tightly controlled, we have HEALTH.

If the junctions are compromised, we move towards IMBALANCE and DISEASE.

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Gut barrier dysfunction may lead to inflammation, toxicity and chronic conditions

GI inflammation and leaky gut initiate a cascade of signaling events that can increase inflammation.

The Role of the Liver

Dysbiosis leads to “overload” of the liver’s detoxification pathways

- Dysbiosis in the gut occurs when the balance of good and bad bacteria is upset.
- Extra toxins and inflammatory irritants from undigested food must pass through the liver, putting added stress on the system and making it harder for the liver to neutralize the substances.
- This process is very nutrient dependent.
- Nutrient deficiencies will temper the detoxification process.

**Phase I Detoxification – Cyt P450 enzymatic pathway**
- Fat soluble toxins broken down into intermediary product for elimination

**Phase II Detoxification**
- Intermediary products converted to water soluble product for excretion in urine or stool.

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Nutritional Status and Detoxification

Figure 9.3  Liver detoxification pathways and supportive nutrients

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Nutritional Interplay: Complex Interaction Affects This Process

- Phase I and Phase II detox pathways are very nutrient dependent
  - Utilize large amounts of nutrients
  - Detoxification process gets tempered when there is nutrient deficiency
- Inflammatory cascade “burns” up anti-oxidant nutrients to fight off the damage and can result in other nutrient deficiencies
- Poor absorption may lower nutrient status affecting ability to detoxify
- Dysbiosis – poor gut flora results in poor production of several vitamins, including the B-Vit’s and Vit K
The GUT MICROBIOME
Symbiosis: “Living Together”

- More than a trillion microbes live in our gut
- There are 10X more bugs in your gut than cells in your entire body!
- Healthy balance is beneficial (eu-symbiosis) or neutral (commensalism)
- In healthy individuals, gut flora is quite stable.

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Symbiosis vs. Dysbiosis
Many Functions of the Microbiota

**METABOLIC**
- Vitamin production
- IEC differentiation
- Protection against cancer (digests dietary carcinogens)
- Ferments non-digestible compounds
- Produces SCFAs (energy)

**STRUCTURAL**
- Produces Sec IgA
- Maintains intestinal villi
- Tight Junctions
- Mucous Layer

**IMMUNE SYSTEM & BARRIER FUNCTION**
- Protective
  - Against colonization of “bad” bacteria
  - Innate and Adaptive immunity
  - Mediates Inflammatory cytokine

**PROTECTIVE**

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Dysbiosis  “Dys-Symbiosis”

Imbalance of good and bad bacteria - Injurious to our health

- Normally occurring flora protect against pathogens
- Dysbiosis compromises immune function
- Increases risk of infection

NEW WINDOW:
GUT MICROBIOME not only affects GUT HEALTH and IMMUNE FUNCTION, but it also makes up part of the HUMAN GENOME......
GUT MICROBIOME: and the GUT Associated Lymph Tissue

The development of the intestinal immune system is largely dependent upon exposure to microorganisms.


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Human: Gut Interplay

Humans have 2 genomes:
the Human Genome + the GUT MICROBIOME

• The human species has only 25,000 genes.
• The Gut Microbiome is 100x more complex genetically than the human genome.
• There is an interplay between the Gut and our Genetics.
• The “health” of our Gut Microbiome is critical to maintaining our health.

Fasano. Gluten Summit. P.56-57

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The GUT MICROBIOME

• Stool cultures only cultivate approximately 1% of the bacterial mix in the gut. The other 99% we cannot culture.
• There are approximately 1000-1200 different live microorganisms in the gut at any one time.
• No two people have the same mix in their MICROBIOME.
• The Gut Microbiome is greatly affected by our environment.
• Natural childbirth transfers a wealth of bacteria from the mother to the baby.
• C-section babies don’t get the same mix and can get more of the “bad” bugs and less of the “good” bugs.
• C-section babies have an increased risk of autoimmune disease by 3-4x!

Imbalanced GUT = Inflammation!

Normal Gut Flora

Protect against potential pathogens establishing infection in several ways:

• Production of SCFA and bacteriocin (an endogenous antibiotic)
• Lower free radical damage (affect oxidation reduction potential)
• Good flora compete for nutrients that pathogens need to survive
• Changes the structure of bile acids so they become bacteriostatic, i.e., stops bacterial growth (deconjugates bile acids)
• Block receptor sites for pathogens by binding with them
• Breakdown bacterial toxins

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Normal Gut Flora

• Ferments soluble fiber to SCFA
  • 5-10% of human energy requirements
  • Feeds the epithelial cells
  • Lowers the pH of the stool (slightly acidic and cancer protective)

• Synthesize at least 7 essential nutrients:
  • Folic acid
  • Biotin
  • Pantothenic acid
  • Riboflavin
  • Pyridoxine
  • Cobalamin
  • Vitamin K
How Dietary CHO and Fiber Regulate GI Flora

Carbohydrates (& fiber) support growth and fermentation of bacteria and fungi.

- **SIMPLE CHO’s** – increase bacterial growth and fermentation by microbes in the mouth, stomach and upper small intestine (SIBO)
  - Fermented bacteria in the small bowel may act as an irritant.
  - Lactic acid may trigger lactose intolerance.

- **COMPLEX CHO’s** - increase microbes growth and fermentation in the ileum

- **SOLUBLE FIBER** – increases growth and fermentation in the cecum and colon

- **INSOLUBLE FIBER** (many vegetables and wheat bran) – lowers colon enzyme concentrations and activity

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Integrative Medicine A Practitioners Guide, p. 460
HOW PROTEIN AFFECTS GI FLORA

• Protein causes the intestinal bacteria to produce enzymes for protein catabolism.
• Produces the odor of stool and increases ammonia production.
• Studies show too high of protein intake linked to colon cancer.

EXCEPTION
Glutamine (diamino acid)

• Feeds the intestinal epithelium and the LYMPHOCYTES of the GALT tissue.
• It is a critical nutrient for the gut healing process
• Conditionally essential amino acid

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DIETARY FAT and GI FLORA

• Free fatty acids are bacteriostatic
• Increased bile flow from increased fat is also bacteriostatic
• BUT, certain protozoans (Giardia lamblia) thrive on elevated amounts of bile
• High amounts of bile increase bile acids and stool pH (alkaline), and both are associated with increased risk of colon cancer.
MICRONUTRIENTS and GUT FLORA

• Iron appears to have the greatest effect on gut flora
• ALL microbes, EXCEPT lactobacilli and bifidobacteria, DEPEND UPON IRON FOR GROWTH
• Feeding iron to patients with bowel disease can INDUCE overgrowth of the pathogenic microbes!

LACTOFERRINS (iron binding proteins in COLOSTRUM and LEUKOCYTES) help to absorb iron in the intestine and to INHIBIT bacterial, fungal and protozoan overgrowth
Causes of Dysbiosis and Hyperpermeability

- NSAID use
- Proton pump inhibitors
- Cytotoxic medications
- Infectious agents (viral, bacterial and protozoan)
- Antibiotics
- Alcohol
- Poor diet- high fat, high sugar, SAD
- Stress
- Pathogenic organisms/infections
- Food sensitivities/allergens – mast cells release histamine and serotonin which increase permeability

Andre C, Andre F, Colin L. Effect of allergen 7-51 ingestion challenge with and without cromoglycate cover on intestinal permeability in atopic dermatitis, urticarial and other symptoms of food allergy. Allergy. 1989;9

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NSAIDS cause ENTEROPATHY

- **107,000** hospitalizations
- **16,500** NSAID-related annual deaths
- **15th** most common cause of death in the United States
- **80%** of patients have no reliable warning signs
- **Intestinal injury can begin within 72 hours of use**


Long-term NSAIDs and COX-2–selective agents cause comparable small-bowel damage.
- This suggests an important role for COX-2 in the maintenance of small-bowel integrity.


(c) 2016 Optimal Health Solutions LLC
The effect of H2-receptor antagonist and proton pump inhibitor on microbial proliferation in the stomach.

Wang K, Lin HJ, Perng CL, Tseng GY, Yu KW, Chang FY, Lee SD.
Division of Gastroenterology, Department of Medicine, Cardinal Tien Hospital and School of Medicine Fu-Jen Catholic University, Taipei, Taiwan, ROC.

BACKGROUND/AIMS: Intra-gastric bacterial proliferation is frequent in patients with hypochlorhydria. However, status of gastric bacterial infection in patients receiving proton pump inhibitor or H2-receptor antagonist remains controversial. The purpose of this study was to investigate the microbial condition of the stomach in patients who received H2-receptor antagonist or proton pump inhibitor.

METHODOLOGY: Between November 2000 and January 2002, 102 patients were enrolled in this study. Of these, 52 did not receive any treatment (group I), 26 received H2-receptor antagonist (group II), and 24 received proton pump inhibitor (group III). Ten mL of gastric juice were aspirated for culture during endoscopic examination. The aerobic and anaerobic bacterial and fungal cultures were performed immediately. A glass pH meter measured the pH of the gastric juice.

RESULTS: The intra-gastric pH was 2.91±2.06 (mean ±SD), 4.12±2.83, and 5.11±2.47 for groups I, II, and III, respectively (p=0.001 between groups I and III, p>0.05 between groups I and II, and groups II and III). The positive bacterial culture rates were 66.7% (16/24) in group III, 46.2% (12/26) in group II, and 28.8% (15/52) in group I (p=0.007 between groups III and I, p>0.05 between groups I and II, and groups II and III). The positive candidal culture rates were 12.5% (3/24) in group III, 11.5% (3/26) in group II, and 17.3% (9/52) in group I (p>0.05). CONCLUSIONS: Patients who received proton pump inhibitor had more... intra-gastric bacterial infection than those of the control group.

“Conclusion: Patients who received proton pump inhibitor had more... intra-gastric bacterial infection than those of the control group.”
Antibiotic Use

Latest research shows it can take up to 1 year to restore gut flora balance after only 1 bout of antibiotics.

**Clinical pearl:**
Take probiotics 2 hours after antibiotic dosing to replenish good bacteria in the gut!
Leaky Gut is Associated with Many Diseases and Systemic Conditions

Obesity

Alcoholic Liver Disease

Inflammatory Bowel Disease

Atherosclerosis

Systemic and localized Inflammation

Chronic Fatigue

Diabetes Type 1 and 2
• *Chen F, BBRC* Vol 332 p1, 2005

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**Dysglycemic Intestinal Permeability**

**Metabolic diseases and pro- and prebiotics: Mechanistic insights.**

“Specific intestinal bacteria seem to serve as lipopolysaccharide (LPS) sources through LPS and/or bacterial translocation into the circulation due to a vulnerable microbial barrier and increased intestinal permeability and to play a role in systemic inflammation and progression of metabolic diseases.”

*That is.....LPS translocate into the circulation due to LEAKY GUT and increase inflammation and progression of metabolic diseases including dysglycemia.*

Nutr Metab (Lond). 2012 Jun 19;9(1):60

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Leaky gut and diabetes mellitus: what is the link?

“Recent studies investigating the underlying mechanisms involved in disease development in diabetes point to the role of the dys-regulation of the intestinal barrier.”

Vicious Circle

Intestinal Permeability

Dysglycemia

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Clell Erridge, Teresa Attina, Corinne M Spickett, and David J Webb

ABSTRACT

Background: Bacterial endotoxin is a gram-negative endotoxin that is abundant in the human gut. Concentrations in the blood of all healthy individuals are associated with splanchnic endotoxemia.

Objective: We sought to determine whether smoking increases plasma endotoxin concentrations and whether such concentrations are of physiologic importance.

Design: Plasma endotoxin and endotoxin-neutralizing antibodies were measured for 4 h in 12 healthy men after a high-fat meal, or a high-fat meal with nicotine exposure.

Results: Baseline endotoxin concentrations (quartile range: 3.4–13.5 pg/ml) increased significantly within 0.5 h (p < 0.05) by ~50% after a high-fat meal or after smoking. Plasma endotoxin concentrations did not increase after smoking in the absence of meal exposure. Neutralizing antibodies, detected by measuring the titer of endotoxin-neutralizing antibodies by an antibody-neutralization assay, were present in 11 of 12 men; levels did not change significantly after smoking and meal exposure.

Conclusions: Low-grade endotoxemia may contribute to the postprandial inflammatory state and could represent a novel potential contributor to atherosclerosis.


Clinical Pearl: Atherosclerosis beginnings are now considered an autoimmune process.
Gluten sensitivity may be an underlying factor to developing leaky gut

10,000 years ago in the Middle East, people noticed plants grew from seeds that dropped on the ground and agriculture began.

Before that, humans didn’t eat grasses or grains.

“A leaky gut has been recently proposed to be a universal initiating trigger for autoimmune diseases”

Fasano A. Surprises from celiac disease. Sci Am. 2009 Aug;301(2):54-61
Prevalence of gluten sensitivity in various patient populations

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>% Positive Stool Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Volunteers</td>
<td>65</td>
<td>29%</td>
</tr>
<tr>
<td>Autoimmune Disease</td>
<td>2747</td>
<td>62%</td>
</tr>
<tr>
<td>Family history of gluten sensitivity</td>
<td>1217</td>
<td>68%</td>
</tr>
<tr>
<td>Microscopic Colitis</td>
<td>419</td>
<td>69%</td>
</tr>
<tr>
<td>Chronic fatigue</td>
<td>141</td>
<td>61%</td>
</tr>
<tr>
<td>Celiac Sprue</td>
<td>45</td>
<td>100%</td>
</tr>
</tbody>
</table>

Research from Dr. Kenneth Fine

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**NCGS**
- Negative for IgA against transglutaminase
- Positive for IgG or IgA against gliadin.
- Symptoms are triggered by gluten ingestion
- No villous atrophy
- No evidence of tissue transglutaminase antibodies
- Usually HLA DQ2/DQ8 negative
- **Greater production of IgA and/or IgG antibodies** and other autoantibodies
- **Cross-reaction with different tissue antigens;** many types of complications; various autoimmune conditions. (Hashimoto’s; autoimmune gastritis)

**CELIAC DISEASE**
- Diagnostic workup requires positive IgA antibodies against both transglutaminase 2 and gliadin
- Villous atrophy
- Positive for genotype HLA DQ2/DQ8
- Various autoimmunities and cancer (Hashimoto’s; Type I Diabetes)

Townsend Letter, Jan. 2013. (c) 2016 Optimal Health Solutions LLC
NCGS
Extra-Gut Symptoms

- Fatigue
- Headache
- Arthralgia/myalgia
- Brain fog
- Skin rashes
- Fe Deficiency Anemia
- Aphthous stomatitis (mouth ulcers)
- Osteopenia
- Malabsorption
- Abnormal: Ferritin, Folic Acid, Vit D, Vit B12, Ca+, Lactose, Nickel Allergy**, Fructose Intolerance (40%)
- FODMAP diet may play a role for NCGS patients

**Consuming large amounts of corn can increase sensitivity to nickel. Mechanism unknown**

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Symptoms/Conditions Suspicious of “Leaky Gut Syndrome”

- Previous surgery or trauma to the intestines
- Dysbiosis that is resistant to treatment
- Food allergies/sensitivities
- Chemical sensitivities
- Multiple, diffuse symptoms
- Fatigue issues, pain syndromes, recurrent infections, sinus issues
- Arthritis/asthma
- Autoimmunity
- Depression
- Multiple nutritional deficiencies
- Family history of autoimmunity or neurodegeneration

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ASSESSING LEAKY GUT

GENETICS

• Individuality plays a role here. Look at family history.
• HLA-DQ2 and HLA-DQ8 are the two genes needed to develop Celiac Disease.
• Gluten Intolerance/ Celiac are potent triggers to Leaky Gut.
• Up to 70% of 1st degree relatives of Celiac Disease patients who are ASYMPTOMATIC have intestinal permeability.

ENVIRONMENT

• Dysbiosis - Bacteria, yeast, viruses, parasites. STOOL TESTING available to analyze Gut Microbiota
• Trauma – injury and surgeries
• Stress – disease, malnutrition, excessive strenuous exercise, radiation (inflammatory)
• Medications
• Allergenic foods – FOOD SENSITIVITY TESTING (look at multiple immune mechanisms – IgA, IgG and IgM)

FAMILY and MEDICAL HISTORY

• Use of medications: antibiotics, NSAIDS, steroids, PPI’s
• Chemotherapy or radiation treatment
• History of chronic yeast infections
• Digestive enzyme insufficiencies
ASSESSMENT:
Leaky Gut Questionnaire

Indirect Assessment using Patient History, Complaints, Functional Intracellular Analysis of Nutrients and Leaky Gut Questionnaire
ASSESSMENT: DIET HISTORY

- Malnutrition/ Poor nutrient intake/absorption/nutritional deficiencies
  (Intake; History; Lab Testing Intracellular analysis)
- SAD – Standard American Diet
  - High Fat, High Sugar Diet
  - Low fiber diet
- Excessive alcohol or caffeine consumption
- Food allergens in cosmetics, medications, supplements
- Food sensitivities (Gluten/Dairy/Others)

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ASSESSMENT: LAB TESTING

Current technology
• Lactulose/mannitol testing
  • Lactulose absorption suggests intestinal permeability
  • Limitation: Sugar molecule is actually much smaller than food antigen particles

New technology
• LMIPI – Large Molecule Intestinal Permeability Identification
  • Looks at larger molecules closer to the size of food particles for better identification of Intestinal Permeability that allows antigens to leak through the lining.
  • Measures:
    • Bacterial Endotoxin LPS – Lipopolysaccharides
      • (Assesses Permeability/Dysbiosis)
    • Zonulin/Occludin antibodies
      • (Assesses tight junction damage)
    • Actomyacin Network
      • (Assesses Epithelial Cell Damage)
ASSESSMENT: LAB TESTING

Measuring Intracellular Function of Nutrients

• Functional intracellular analysis - 33 different nutrients
• Intracellular function therefore takes into account absorption issues
• Extremely helpful in identifying core contributions to multiple symptomatology
• Indirect “confirmation” of suspicion of leaky gut
• Identifies strategies for nutritional intervention for healing

Multiple deficiencies red flag for:

• Leaky gut – poor absorption
• Poor diet – poor intake
• Genetic snps – for ex. MTHFR Polymorphism – Poor conversion of nutrients from inactive to active form
• Lack of supportive nutrients – Nutrients work in concert with each other. Function of one may be limited by deficiency of another
• Inflammatory cascade – eats up antioxidant nutrients as body tries to neutralize the inflammation

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INFLAMMATORY MARKERS in the GUT

**CALPROTECTIN**
- Non-invasive biomarker of intestinal inflammation
- *Level of CALPROTECTIN correlated with the degree of mucosal inflammation*
- Involved in the regulation of intestinal inflammation
- Significantly increased in organic disorders: Crohn’s, colitis and neoplasms
- Lower levels (but still increased) in functional disorders such as IBS

Costa et al. Digestive and Liver Disease 35; (2005), 643-647.

**INTRA-EPITHELIAL LYMPHOCYTES – IEL’s**
- *Produced in the mucosa of the small intestine as an innate immune response to inflammatory cytokines.*
- IEL’s are produced to protect us against the food/toxins coming in.
- Elevated levels mean the body is trying to protect itself and *indicates increased inflammation in the small intestine.*

Volta, Umberto. Gluten Summit, 2103.

**LIPOPOLYSACCHARIDES – LPS**
- Virulent ENDOTOXIN
- Bacterial lipopolysaccharides (LPS) are in the outer surface membrane components in almost all Gram-negative bacteria
- Act as extremely strong stimulators of innate or natural immunity.
- Triggers the IL-1 pathway and *inflammation*


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Inflammatory markers play a role in chronic inflammatory diseases

- prostaglandin (PG) E$_2$
- nitric oxide (NO)
- tumor necrosis factor-α (TNF-α)
- interleukins (ILs)

**Occurrence of IEL’s in Different Populations**

<table>
<thead>
<tr>
<th>Population</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>NCGS</td>
<td>25-40%</td>
</tr>
<tr>
<td>Celiac</td>
<td>&gt;40%</td>
</tr>
</tbody>
</table>

## ASSESSMENT: FOOD SENSITIVITY TESTING

### IgG Food Antibody Results

<table>
<thead>
<tr>
<th>Dairy</th>
<th>Vegetables</th>
<th>Fish/Shelfish</th>
<th>Nuts and Grains</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein</td>
<td>Alfa</td>
<td>Clam</td>
<td>Almond</td>
<td>CoQ10</td>
</tr>
<tr>
<td>Cheddar cheese</td>
<td>Asparagus</td>
<td>Cod</td>
<td>Buckwheat</td>
<td>Cane sugar</td>
</tr>
<tr>
<td>Cottage cheese</td>
<td>Avocado</td>
<td>Lobster</td>
<td>Corn</td>
<td>Casein</td>
</tr>
<tr>
<td>Cows' milk</td>
<td>Broccoli</td>
<td>Oyster</td>
<td>Corn gluten</td>
<td>Cow's milk</td>
</tr>
<tr>
<td>Goat's milk</td>
<td>Carrot</td>
<td>Red snapper</td>
<td>Glutens</td>
<td>Cilantro</td>
</tr>
<tr>
<td>Lactalbumin</td>
<td>Collage</td>
<td>Salmon</td>
<td>Kidney bean</td>
<td>Cumin</td>
</tr>
<tr>
<td>Yogurt</td>
<td>Curley</td>
<td>Sardine</td>
<td>Lentil</td>
<td>Cumin sugar</td>
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<tr>
<td>Fruits</td>
<td>Fruits</td>
<td>Strips</td>
<td>Lima bean</td>
<td>Cumin spice</td>
</tr>
<tr>
<td>Apple</td>
<td>Garlic</td>
<td>Trout</td>
<td>Oat</td>
<td>Cumin seed</td>
</tr>
<tr>
<td>Apricot</td>
<td>Green Pepper</td>
<td>Tuna</td>
<td>Pangolin</td>
<td>Cumin seed</td>
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<td>Banana</td>
<td>Grape</td>
<td>Trout</td>
<td>Peanut</td>
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<td>Blueberry</td>
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<tr>
<td>Date</td>
<td>Green Apple</td>
<td>Trout</td>
<td>Pinto bean</td>
<td>Cumin seed</td>
</tr>
<tr>
<td>Fig</td>
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<tr>
<td>Strawberries</td>
<td>Green Apple</td>
<td>Trout</td>
<td>Pinto bean</td>
<td>Cumin seed</td>
</tr>
</tbody>
</table>

### Total IgE

<table>
<thead>
<tr>
<th>Inside</th>
<th>Outside</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>55.4</td>
<td></td>
<td>&lt;=7.0 kU/L/LM</td>
</tr>
</tbody>
</table>

- **0**: None Detected
- **VL**: Very Low
- **1+**: Low
- **2+**: Moderate
- **3+**: High

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ASSESSMENT: GI ECOLOGY
Stool Test for Bacteria Balance/ Parasites/ Fungi

Functions of Prominent Bacteria
- Resistance to colonization of bad bacteria, pathogens.
- Aid in digestion and absorption
- Produce Vitamins and SCFA
- Stimulate GI immune system

Opportunistic Bacteria
- Cause symptoms
- Produce endotoxins and inflammation
- Associated with disease

Testing helps to fine tune treatment protocol and identify possible causes of gut symptoms which also may be contributing to Intestinal Permeability.
There are up to 500 other parasites people are exposed to commonly from food choices.

- Herbal remedies include formulas that contain oregano and berberine.
- Rotate herbs every other day.
- Take for 4-6 weeks maximum dosing.
- Appropriate probiotics.

- Whey with immunoglobulins
- Lactoferrin
- Lactoperoxidase
- Proteins that support GI health, microbial balance and immune function
- Prebiotics that feed the probiotics
TREATMENT:
Address GI Issues With The 4R Program

**Remove**
What does this patient need to have *Removed* for healthy GI function?

**Replace**
What does this patient need to have *Replaced* to support normal GI function?

**Re-inoculate**
What does this patient need to support or re-establish a healthy balance of microflora?

**Regenerate**
What does this patient need to support the healing of the mucosal barrier?

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GI Restoration Program

REMOVE

- Allergenic food(s)
- Elimination Diet – Gluten
- Food Sensitivity Testing
  - IgE and IgG testing
  - IgA occur first and then IgG and IgM occur later
- Stool testing: Fecal Anti-gliadin IgA antibodies
  - Small bowel overgrowth
  - Pathogen(s)
  - *H. pylori*
  - Candida
  - Parasitic microbes
  - *Saccharomyces boulardii*
- Acid Inhibitors
- NSAIDs

“Removing the underlying issue of the imbalance is the first step in addressing the core issue of gastrointestinal complaints.”
Use Nutritional Tools /Herbal Blends

- BERBERINE supports secretion of bile and aids in the elimination of pathogenic microbes

  “Currently, the predominant clinical uses of berberine include bacterial diarrhea, intestinal parasite infections”

- Essential oils from RED THYME and OREGANO support the health of the GI tract
  - THYME historically used as a “vermifuge” in ancient Egypt
  - OREGANO – 30 biologically active ingredients; 12 have antibiotic, antiviral, antiparasitic or antifungal effects

- Dry leaf extracts of SAGE and LEMON BALM – strong antioxidants; kills candida and other bacteria

- GARLIC and GRAPEFRUIT SEED EXTRACT – anti-microbials


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• CINNAMON is an antifungal
• TUMERIC (Curcumin) reduces the concentration of fermented bacteria
• ONION (allium) – antimicrobial
  o Decreases flatulence (gas and bloating)
• GINGER - 400 biologically active components
  o Anti-inflammatory, antiulcer, antiparasitic
  o Helps digestion
• SPICES protect against enteric infections
• FERMENTED/CULTURED FOODS - probiotics
GI Restoration Program
REPLACE: Digestive Aids

- **Betaine HCl**
  - Production of hydrochloric acid decreases with age
  - Needed for protein digestion
  - Produces indigestion, gas and bloating within the *first half hour after eating*.

- **Broad spectrum vegetarian digestive enzymes**
- **Lipotropic factors**
  - Lipases and proteases and enzymes that split proteins, peptides, carbohydrates, fats, cellulose, maltose, lactose, and sucrose.

Replacing and augmenting vital digestive chemistry allows the patient to improve digestion/absorption—the primary role of the gastrointestinal tract.
Pancreatic Digestive Enzymes

- Gas and bloating 2 hours after a meal
- Decrease with age
- Lower with alcohol consumption
- Decreased with inflammation
- Affected by pancreatitis, cystic fibrosis, diabetes, gallstones
- Take 2 tablets 20 minutes prior to a meal
- Lack of Digestive enzymes increases antigen activity (undigested larger food particles)
GI Restoration Program: REINOCULATE

Re-inoculate with probiotics

• Optimize gut microbiome composition
• Limit proliferation of pathogenic bacteria, Candida and microbes
• Maintain a desirable balance of GI microflora

Add beneficial bacteria

Lactobacilli
Bifidobacteria
LACTOBACILLUS ACIDOPHILUS

**Antimicrobial activity** – Very strong in vitro data showing antimicrobial activity against *foodborne pathogens* such as *Staphylococcus aureus*, *Salmonella typhimurium*, *Escherichia coli* and *Clostridium perfringens*.

**Intestinal Cell Adherence** – Strong in vitro data suggests LA sticks to specific intestinal cells and implants well in the intestinal tract.

**Small Bowel Bacterial Overgrowth – SIBO**
Chronic kidney disease patients on dialysis showed a reduction in toxic metabolites produced in the small bowel by bacterial overgrowth and improved nutritional status.

**Decreased risk of colon cancer** – Human studies show a 2 to 4-fold reduction in microbial fecal enzymes such as *B*-glucuronidase, nitroreductase and azoreductase which are thought to play a role in risk to colon cancer.
GI Restoration Program: **REGENERATE**

Regenerating utilizes specific macro- and micronutrients to nourish the cells of the colonic mucosa and support gastrointestinal integrity

- Glutamine, licorice, aloe
- Fiber/prebiotic
- Arabinogalactins, plantain fruit
- Tumeric, quercetin, rosemary, ginger
- Low-allergy-potential rice protein
- EPA/DHA

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GI Restoration Program: REGENERATE PREBIOTICS

Prebiotics nourish and balance healthy GI microflora

Arabinogalactans selectively feed Lactobacillus and Bifidobacteria
- good source of fiber
- increases production of SCFA (butyrate and propionate)
  (colonic epithelial cells use for energy)
- decreases production of and absorption of ammonia
- increases natural killer (NK) cell activity
- enhances additional immune system function

Rice bran fiber supports growth of beneficial microflora

REGENERATE : PREBIOTICS (FOS) Fructooligosaccharides

- FOS are dietary fiber (oligosaccharides) that occur naturally in plants such as onion, chicory, garlic, asparagus, banana, artichoke, among many others.
- Made of linear chains of fructose units- (2 to 60 units long)
- Often terminate in a glucose unit
- Not hydrolyzed by small intestinal enzymes \(\rightarrow\) reach the cecum structurally unchanged
- Metabolized by the gut microflora

**HEALTH BENEFITS of FOS:**

- Low carcinogenicity
- **Prebiotic effect** – stimulate the growth of “good” bacteria
- Improve mineral absorption
- Decrease levels of serum cholesterol, triacylglycerols and phospholipids
- Dose of 4-15 g/day given to healthy subjects will reduce constipation, increase the bulk and frequency of stool

REGENERATE

Medical food to reduce inflammation and heal the gut

- RIAA – reduced iso-alpha acids (HOPS)
- Curcumin
- Vit D3
- Selenium
- Zinc
- Zinc-Carnosine

Inflammation is mediated by several transcription factors which activate multiple signaling pathways such as:

- NF-κB
- MAPK ERK1/2
- p38
- PI3K

in the presence of a stimulus such as LPS (lipopolysaccharides).

RIAA inhibited NF-κB and other signaling pathways triggered by LPS.

REGENERATE : CURCUMIN

- **CURCUMIN** is an anti-inflammatory phenol
- Effective in ulcerative colitis and inflammatory IBD patients
- Targets preferentially intestinal epithelial cells.
  - Intestinal epithelium is part of the gut innate immune system
- **Interferon-γ** profoundly affects the epithelium structure and function and limits healing of the gut
- **CURCUMIN inhibits IFN-γ**
  - TUMERIC – strongest anti-inflammatory – tempers NF-κB


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OTHER NUTRIENTS

- GLUTAMINE - essentially conditional aa in times of stress/need
- CINNAMON inhibits growth of *h. pylori* bacteria
- ANTIOXIDANTS to lower inflammation
- GINGER - “gingerols” in ginger are an anti-oxidant, are anti-inflammatory, and gastroprotective
- COLOSTRUM – immune support and GI healing
Study: Colostrum helps treat leaky gut syndrome

London School of Medicine and Dentistry.

Heavy athletic training can lead to Leaky Gut!

• Athletes ran for 20 minutes at 80% VO2max (aerobic capacity)
• Afterwards, gut permeability increased by 250% and body T increased by 2°
• Increased gut permeability can dramatically temper athlete’s performance

• Colostrum (first milk) loaded with immunoglobulins, antibodies, immune-boosting nutrients.
• Breast fed humans have a healthier gut microbiome and stronger immune function.
• Studies are looking at using bovine colostrum supplements for healing leaky gut.

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GI Restoration Program: RETAIN

Retain patients’ lifestyle for lasting relief of gastrointestinal complaints. Determining the triggers or lifestyle habits that may have lead to the core issue.

- Diet
  - Fiber, probiotics
- Stress reduction
- Movement

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Hippocrates
“Bad digestion is the root of all evil”

Elie Metchnikoff
Nobel Prize in Medicine for work on the intestinal milieu

“Death begins in the colon”
“If your gut isn’t healthy, YOU are not healthy!”

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Outstanding resource for educating yourself about using Functional Medicine in your practice

The Dietitians in Integrative and Functional Medicine is a specialty practice group of over 3000 nutrition practitioners whose core philosophy centers around a holistic, personalized approach to health and healing. Our members integrate a variety of nutrition therapies including whole foods, tailored supplements and mind body modalities in clinical practice.

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