Integration of Functional Nutrition

Dr. Robert G. Silverman
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www.DrRobertSilverman.com

If an egg is broken by an outside force, life ends

If an egg is broken by an inside force, then life begins

Great things happen from the inside

— John F. Kennedy
What’s the Problem?

- Sugar consumption – 160 lbs per year
- Wheat consumption – 146 lbs per year
- Caloric sweeteners – 142 lbs per year
- NSAIDs/medications
- Toxins
- Stress

UNITED STATES OF DIABESITY
Obesity facts

Worldwide:
- 857 million in 1980
- 2.1 billion in 2013
- 145% growth
- 26% of children (U.S)
- 3.4 million people die each year

Deeper than obesity: A majority of people are now overfat

Chart shows the estimated percentages and numbers of overfat (in red) and underfat (in blue) adults and children worldwide (based on 2016 world population of 7.1 billion)
90% of American men and 50% of children are over-fat

Obesity in Women

- 4 in 10 American women now classified as obese
- 40% women are obese; 35% men are obese
- Rate of obesity higher across the world for women than men
- 15% of women, 11% of men worldwide are obese
- Obesity can trigger diabetes and lead to heart disease

Obesity as an Inflammatory Disorder

One of the more interesting discoveries of the past decade has been the recognition that the adipocyte produces inflammatory cytokines

Obesity, therefore, may be viewed as a low grade systemic inflammatory disease
Inflammation served with every meal

- Upon eating:
  - Body distributes glucose and fight bacteria ingested
  - Triggers inflammatory response activating immune system
- Healthy individuals – triggers immune system into action resulting in natural inflammatory response
- Overweight people – inflammatory effects fail and increased risk of diabetes

Nature Immunology Jan. 2017

Lipotoxicity: the result of unhealthy lifestyle choices

**Lipotoxicity**
- ectopic fat accumulation in various tissues and organs leading to pathologic changes and impaired function.

**Ectopic**
- occurring in an abnormal position or place; displaced.

Obesity = Postural Compensation
Limiting weight gain could help reduce risk of 13 various cancers

Preventable diseases shorten lifespan

- Heart disease, stroke, and type-2 diabetes may reduce lifespan by as much as 23 years
- Smoking reduces it by 10 years

Majority

- 52.3% of the entire US population in 2012 had either diabetes (14.3%) or prediabetes (38%)
Is SUGAR the world's most popular drug?

- Eases pain, addictive and show every sign of causing long-term health problems
- Induces same responses in region of the brain a.k.a. "reward center"—Nicotine, cocaine, heroin and alcohol

Sugar: What you didn’t know about

- Americans consume 160 lbs. per year
- Sugarcane was first domesticated about 10,000 years ago on the island of New Guinea
- Eating an excessive amount of added sugar can increase:
  - Triglyceride levels
  - Which increases risk of heart disease
  - It’s inflammatory
  - Contributes to obesity, diabetes

Sugar: What you didn’t know about (cont’d)

- 50 mins of running or 5 miles of walking—burns 250 calories and 16 tbsp. of sugar
- A 20-year study of 40,000 men revealed:
  - Consumption of 1 sugar beverage per day—increased H.A. by 20%
- Leave the cannoli, take the coffee
- A "sugar-free" food must contain less than 0.5 g of sugar per serving
Diet drinks not “diet” after all

- Diet are just as ineffective in preventing weight loss
- Diet drinks consumption in children doubled from 1999-2008
- Diet drinks cause stimulation of sweet taste receptors:
  - Increases appetite
  - Stimulates secretion of gut hormones

**PLOS Medicine, Jan. 3, 2010**

Diabetes risk doubles with more than 2 soft drinks daily

- This is true for regular and diet soda
- 2x more likely for LADA
- 2.4 more likely type-2

**European Journal of Endocrinology, Medical News Today, Oct. 21, 2016**

Top 5 sources of added sugar in U.S. diets

1) Sugar-sweetened beverages (soda, coffees, sports drinks) – 37.1%
2) Grain-based sweets (cakes, pies) – 13.7%
3) Fruit drinks (juice cocktails, fruit punch) – 8.9%
4) Dairy-based desserts (ice-cream, sweetened yogurt) – 6.1%
5) Candy (candy bars, jelly beans, lollipops) – 5.8%

**National Cancer Institute**
Sugar, Fat and CVD

- Large meta-analysis on sugar found significant link to CVD:
  - HR for CVD 1.3 lowest and 2.75 for highest sugar consumption. JAMA Intern Med. 2014;174(4):516-52
- Large meta-analysis found sugar CVD risk factor independent of weight gain. American Journal Clinical Nutrition 2014 May 7

New Dietary Guidelines

- Consumers should drastically cut back on sugar
- Limit to 10% of daily calories
- Limits on cholesterol removed
- W.H.O. also almost suggested removing sugar
- Men and boys should consume less protein

Reebok survey:

- 25,915 days in a person’s lifetime
- 9 country revealed:
  - Average human spend 0.69% of their life exercising
  - 41% spent engaging with technology
  - 29.75% of our lives sitting down
Sitting

- WHO ranks physical inactivity as:
  - 4th biggest preventable killer globally
  - Causes 3.2 million deaths annually
- CDC reports we're spending 75 cents of every healthcare dollar on chronic conditions linked to sedentary behavior

Health Topics: Physical Activity, WHO

Should a simple fitness check be part of your check-up?

- Aerobic fitness should be considered a vital sign according to the AHA
- AHA states that fitness can be an indicator of someone's risk for heart disease and early death
- If fitness is on the low side = exercise

NY Times. Nov 310, 2016

Why doesn't the old healthcare model work?

The primary driver of chronic disease is the interaction among genes, activities of daily living (lifestyle), and the environment

Failure of Current Treatment Models

• Calorie restriction – Failure of Model
• Why it fails: Compensatory mechanisms defend against weight loss by decreasing energy expenditure and increasing appetite
• Calorie hypothesis: Flaws
  • Multiple factors regulate metabolism:
    • Dietary composition, microbiome, toxins, infections, allergens, nutrient status, mitochondrial dysfunction, hormonal and neurotransmitters dysregulation, social

Are all calories equal?

1,300 calories
Shift focus from calorie counting to nutritional value for heart health

• It’s time to stop counting calories
• Start promoting nutritional value of foods:
  • Rapidly cut illness
  • Death from cardiovascular disease
  • Curb rising tide of obesity

Your DNA is not your destiny

• This means that genes may load the gun, but environmental factors pull the trigger

Translation:
Genes are your potential but require a certain environment in order to be expressed

What really determines health or disease for most of us?

Genetics
Physiology/Biochemistry
Environment
Lifestyle

70-90% of chronic disease
What is Functional Medicine?

Functional Medicine addresses underlying causes of chronic disease by examining all the systems contributing to the patient’s problem(s). These systems include:

- Digestion
- Immune / Inflammation
- Detoxification
- Genetics
- Oxidative Stress
- Nutrition
- Endocrine

Antecedents...  Triggers...  Mediators...
Section III: Functional Medicine

The Functional Medicine Orientation

Systems  Personalized  Etiology  Collaboration

From Stubborn Symptoms to Etiology

Stubborn Symptoms → Cause → SOLUTION

Treat the System, Not the Symptom

Disregarding the underlying causes and treating only risk factors is somewhat like mopping up the floor around an overflowing sink instead of turning the faucet off.
Functional medicine (wellness) model is a 4 P model

I partake in the medicine of etiology, not symptomatology

Nutrition is like shoes
no one-size-fits-all

Doctor Considerations

1) Is there anything special that this patient needs that (s)he is not getting enough of?
2) Is there anything special that this patient needs to avoid in order to optimize their health (food; gluten, dairy; stress, toxins...etc..)?
3) How complex is this patient?
4) How resilient is this patient?
5) Are there unresolved trauma or infections?
6) Are there other contributing factors?
HOW TO END CHRONIC DISEASE

Root cause resolution

Dr. Rob's Gut Matrix

Thyroid: Hypothyroidism, Hashimoto's disease
Musculoskeletal System: Arthritis, joint pain, soft-tissue injury
Body Composition: Obesity
Insulin: Blood sugar problems, insulin resistance, pre-diabetes, diabetes
Liver: Dysfunction, toxins/chemical overload
GI Tract: Food sensitivities, leaky gut syndrome, yeast/fungus, dysbiosis (good bacteria)
Brain: Satiety, inflammatory, neurodegeneration
Musculoskeletal System: Arthritis, joint pain, soft-tissue injury

All Disease Begins in the Gut
"The GI barrier adjacent to the GI microbiota appears to be the key to understanding the complex mechanisms that maintain gut health. Any impairment of the GI barrier can increase the risk of developing infectious, inflammatory and functional GI diseases, as well as extraintestinal diseases such as immune-mediated and metabolic disorders."

Gut health and microbiome are critical to gut, immune and systemic health

The gut and its key functions

Intact and functional gut

Food digestion for absorption of macro- and micronutrients

Immune functions, with 70% of the immune system in the gut

Leaky Gut vs. Healthy GI Tract

Gut-brain connection

- Microbiome has influence on psychology, including anxiety and depression
- This "gut-brain axis" – big piece of the puzzle
- "What happens in the gut does not stay in the gut"

Foster & Neufeld. Trends in Neurosciences, May 2013, 36(5)

"A high percentage of abnormal [Intestinal Permeability (leaky gut)] IPT values were found among patients with autism (36.7%) and their relatives (21.2%) compared with normal subjects (4.8%)."
Gut microbes linked to brain structure - IBS

• Research shows for first time, association between gut microbiota and brain regions involved in processing of sensory information from their bodies

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

Liver Stress/Kupffer Cell Activation

Digestion & Barrier Integrity Problems

Localized Inflammation

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

The Gut’s the Body’s Second Brain
**Human vs. gut microbiome**

**Human**
- 10 trillion cells
- 23,000 genes

**Gut**
- 100 trillion cells
- 3.3 million genes

- Over 1000 different bacterial species in the intestines
- Microbiota has 100 times greater metabolic capacity than humans

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**Dysbiosis is Associated with Compromised Gut Function**

<table>
<thead>
<tr>
<th>Eubiosis</th>
<th>Dysbiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain normal intestinal microbial diversity</td>
<td>Alteration of microbial diversity</td>
</tr>
<tr>
<td>Antagonistic effect on undesirable microorganisms</td>
<td>Enhanced growth of undesirable microorganisms</td>
</tr>
<tr>
<td>Stimulation to limit invasion, diffuse inflammation and stimulation of inflammatory systems</td>
<td>Detrimental to gut integrity, increased gas production</td>
</tr>
<tr>
<td>Nutrient digestion</td>
<td>Increased nutrient malabsorption</td>
</tr>
<tr>
<td>Vitamin synthesis</td>
<td>Inhibition of vitamin synthesis</td>
</tr>
<tr>
<td>Bacterial synthesis</td>
<td>Increased bacterial synthesis and increased need for energy</td>
</tr>
</tbody>
</table>

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**Diversity is important for a healthy microbiome**

- Increased diversity is associated with lower inflammation and healthy metabolic markers.
- Decreased diversity has been associated with obesity, insulin resistance, frailty in older people, and allergy in children.


Increased diversity is associated with lower inflammation and healthy metabolic markers.

Decreased diversity has been associated with obesity, insulin resistance, frailty in older people, and allergy in children.
Gut bacteria affect our metabolism

- Mice that received gut bacteria transplants from overweight humans known to gain more weight than mice transplanted with gut bacteria from normal weight subjects even when fed same diet

Reason – bacterial composition affects metabolism

Firmicutes to bacteroidetes

Firmicutes – more inflammation
- Adapt at extracting calories from food
- Increase caloric absorption
- More absorption of calories – greater likelihood of weight gain

Bacteroidetes – specialize in breaking down bulky plant starches and fibers into shorter fatty acid molecules

The ratio is “obesity biomarker”

Preventing obesity through gut bacteria

- Blocking on intestinal microbial pathway has potential to combat obesity and insulin resistance
- Can prompt fat tissue to more metabolically active
Gut microbes promote motor deficits in a mouse model of Parkinson’s disease

The research depicts the findings of Sampson, et al., who show that signals from gut microbes are required for the neuroinflammatory responses as well as hallmark gastrointestinal and α-synuclein-dependent motor deficits in a model of Parkinson’s disease.

Sampson et al. Cell 2016

Probiotics help spinal cord injury recovery

- Gut microbiota communicates with the CNS
- Researchers indicated that probiotics contained lactic acid producing bacteria, which activated a gut-associated immune cell that inhibits inflammation
- Cell – regulatory T cell
- Could prevent damage to the spinal cord after injury
- Probiotic promotes neuronal growth


Babies born by C-section

- Five-fold increased risk of allergies
- Triple the risk of ADHD
- Twice the risk of Autism
- 80% increased risk of celiac disease
- 50% increased risk of being obese as an adult
- 70% increased risk of type-1 diabetes

Dr. Perlmutter, Brain Maker, p.36
**Mode of Delivery**

- 33% of births in the U.S. are by Cesarean delivery
- Infants born by C-section:
  - Have lower gut flora diversity
  - Have altered microbial profiles
  - Are more likely to be colonized by pathogens

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**Cesarean Section and Chronic Immune Disorders**

**Conclusion:** Children delivered by cesarean delivery had significantly increased risk of asthma, systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, immune deficiencies, and leukemia

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**Mechanisms of Protection**

1. Enhancement of the epithelial barrier
2. Increased adhesion to intestinal mucosa
3. Inhibition of pathogen adhesion
4. Competitive exclusion of pathogenic microorganisms
5. Production of antimicrobial substances
6. Modulation of the immune system
Clinical Use of Probiotics

Where does the rubber meet the road?

Probiotics Protocol

<table>
<thead>
<tr>
<th>Clinical Focus</th>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily immune health and digestive health</td>
<td>Lactobacillus acidophilus NCFM, bifidobacterium lactis Bi-07, 15 billion live organisms</td>
<td>1 cap daily</td>
</tr>
<tr>
<td>Target relief for recurring intestinal distress (IBS)</td>
<td>Lactobacillus acidophilus NCFM, bifidobacterium lactis Bi-07, 60 billion live organisms</td>
<td>1 cap daily</td>
</tr>
<tr>
<td>Support for nasal, sinus, and respiratory health</td>
<td>Lactobacillus paracasei B700:2, lactobacillus plantarum HEAL9</td>
<td>1 cap daily</td>
</tr>
</tbody>
</table>

Probiotics Protocol (cont’d)

<table>
<thead>
<tr>
<th>Clinical Focus</th>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targeted relief for acute microbiota disruption</td>
<td>Bifidobacterium lactis Bi-07, lactobacillus acidophilus NCFM, lactobacillus para casei LPC-37, lactobacillus acidophilus Bi-04, lactobacillus lactis Bi-04, lactobacillus plantarum NCFM</td>
<td>1 cap 2 hrs after breakfast and antibiotic</td>
</tr>
<tr>
<td>Daily support for babies and young children</td>
<td>Bifidobacterium animalis spp. Lactis BB-12, lactobacillus rhamnosus GG</td>
<td>6 drops daily</td>
</tr>
<tr>
<td>Probiotic chewable support for children</td>
<td>Lactobacillus acidophilus NCFM, bifidobacterium lactis Bi-07, 35 billion live organisms</td>
<td>1-2 cap daily</td>
</tr>
<tr>
<td>Target relief for acute bowel distress</td>
<td>S.5 billion cfu S. boulardii, 3 billion cfu B. lactis HN039, 1 bullion cfu L. rhamnosus HN001</td>
<td>1 cap daily</td>
</tr>
</tbody>
</table>
**Probiotics Protocol (cont'd)**

<table>
<thead>
<tr>
<th>Clinical Focus</th>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target relief for recurring minor GI pain</td>
<td><em>Lactobacillus plantarum</em> 299v Strain, 20 billion live organisms</td>
<td>2 cap daily</td>
</tr>
<tr>
<td>Targeted support for feminine health (vaginal microflora)</td>
<td><em>Lactobacillus rhamnosus</em> GR-1®, <em>Lactobacillus reuteri</em> RC-14®, 2 billion</td>
<td>1 cap daily</td>
</tr>
</tbody>
</table>

*Featuring 10 billion CFU of *Bifidobacterium lactis* B-420™*

**B-420 Regulation of Body Fat Mass and Body Weight**

- The *Bifidobacterium lactis* B-420™ probiotic strain influences the composition of the intestinal microbiome and epithelial barrier function and may enhance satiety signaling, all of which may play a role in the regulation of body weight and fat mass
Conclusion

• 6-month clinical study in obese men and women published in 2017 and showed *Bifidobacterium animalis* ssp. *lactis* 420 had following benefits:
  - Helps control body weight and body weight regulation
  - Helps control body fat
  - Reduced energy intake
  - Promotes short chain fatty acid (SCFA) production
  - Helps control abdominal fat
  - Helps reduce waist circumference

Conclusion (cont’d)

Satiety signaling and energy intake

- B420 animal studies show increase in GLP-1. GLP-1 is an anorectic gut peptide, and shown to increase feelings of satiety
- B420 animal studies show increase in fecal short chain fatty acids (SCFAs). SCFAs such as butyrate shown to increase feelings of satiety
- Clinical study with B420 - daily reported calorie intake was reduced in the group supplemented with the probiotic compared with the placebo group

Intestinal epithelial barrier function

- B420 animal studies indicated B420 has beneficial effect on intestinal barrier function, and leads to reduced bacterial and LPS translocation. Specifically studies showed protection against negative impact of a high fat diet on bacterial and LPS translocation
- Studies indicated B420 supplementation led to reduced endotoxemia and improved intestinal epithelial barrier function. Specifically studies showed protection against negative impact of a high fat diet on bacterial and LPS translocation
- Findings relevant to body weight control and cardiometabolic endpoints because the presence of bacteria and LPS in adipose tissue triggers inflammation, leading to development of insulin resistance and other metabolic abnormalities. Long-term exposure of LPS in circulation led to increased calorie intake and body mass in animal models. A positive correlation between low levels of LPS circulating in the blood (known as metabolic endotoxemia) and higher energy intake seen in human studies

*B. Lactis* B420

- Decrease LPS translocation
- Enhanced epithelial barrier function
- Enhanced tight-junction integrity
- Increase SCFA
- Increase satiety hormones
- Increase GLP-1

“There is no lottery ticket for your health”
- Dr. Robert Silverman

The Triad of Autoimmunity

- Genetic Susceptibility
- Increased Barrier Permeability
- Environmental Triggers

Proposed role of abnormal intestinal permeability in the pathogenesis of autoimmune disease targeting intestinal tissue and different organs

A. Vojdani. Molecular mimicry as a mechanism for food immune reactions and autoimmunity. Alternative Therapies in Health and Medicine, 2015; 21(suppl 1):S34-S45
Leaky Gut May Lead to Autoimmune Conditions

Leaky Gut Vicious Cycle

Leaky Gut May Lead to Autoimmune Conditions

Transmigration of antigen through intestinal barrier, resulting in pain, swelling, tissue damage, and T cell dominance over immune reactivity.

P.J. Rooney et al. A short review of the relationship between intestinal permeability and inflammatory joint disease; Clinical and Experimental Rheumatology 8:75-83, 1990

Leaky Gut Vicious Cycle

Loss of intestinal tight junctions, entry of antigens and peptides, intestinal inflammation, multiple food sensitivities.
INTESTINAL INFLAMMATION

Local activation of intestinal microglia
Enteric nervous system inflammatory neurodegeneration
Brain-gut axis inflammatory neurodegeneration

Production of inflammatory cytokines
Cross blood-brain barrier and activate brain microglia
Brain inflammatory neurodegeneration

• Suppressing or increasing cravings, microbes help the brain decide what foods body “needs”
• Shows a bottom-up communication about diet

Signaling agents of the Brain-Gut Axis

Impact mood
Impact brain neurochemistry
Impact neuronal receptor sites
Impact satiety

Bacterial Metabolites Gut Peptides Cytokines Lipopolysaccharides

Gastrointestinal Tract
Chronic intestinal inflammation alters hippocampal neurogenesis

Chronic intestinal inflammation suppresses hippocampal neurogenesis. Increased levels of pro-inflammatory cytokines have detrimental effects on proliferation of progenitors of neuronal lineage. Deficient hippocampal neurogenesis may underlie increased rate of mood disorder and cognitive impairment observed in IBD patients.

Journal of Neuroinflammation. 2015;12:65

Disorders Associated With Increased Intestinal Permeability

• Celiac disease
• Multiple food / chemical reactivities
• Infections
• Stress
• NSAIDS
• Cystic fibrosis
• Spondyloarthropathies
• Inflammatory bowel disease
• Alcoholism
• Autism
• Childhood Hypersensitivity
• Malignancy
• Neurological treated with cytokine drugs
• AIDS and AIDS
• Environmental illness
• Infections
• Chronic fatigue and immune dysfunction syndrome (CFIDS)
• Fibromyalgia
• Chronic arthritis/pain treated with Acne
• Dermatological hypersensitivity
• Eczema
• Pernicious
• Urticaria
• Diabetes
• Hepatitis
• Hepatic dysfunction
• Pancreatic insufficiency
• And Other Autoimmunity

GI Problems More Common in Autistic Kids

• Norway population-based study: Children diagnosed with autism spectrum disorder (ASD) more likely to have maternally reported gastrointestinal symptoms in their first years of life compared to children with typical development

Bresnahan M, et al. JAMA Psychiatry. 2015. Research supported by the Norwegian Ministry of Health and Care Services, the Norwegian Ministry of Ed. And Research, and the National Institutes of Health/National Institute of Neurological Disorders and Stroke
Role of gut microbiome in Autism

- Gut microbiota associated with Autism
- Gut alters immune system and metabolism
- Higher intestinal permeability with higher antigenic load from GI
- LPS increased in Autism
- Gut microbiome less diverse (ASD)
- Candida twice abundant in Autism

"The autoimmune process can be arrested if the interplay between genes and environmental triggers is prevented by re-establishing intestinal barrier competency."

Lipopolysaccharides (LPS)

- LPS are endotoxins on gram negative bacteria in the gut
- LPS has also been found in particulate matter of some regional air pollution
LPS can cause damage to epithelial cells and tight junctions.

Increased intestinal permeability allows more LPS to enter the bloodstream.

Systemic LPS Effects

Increased LPS in patients with severe autism

Healthy controls | Autism
---|---
Low | High

**Assessing Antigenic Intestinal Permeability**

- Lipopolysaccharides IgG, IgA, IgM:
  - Gut dysbiosis (too much gram-negative bacteria in ratio to gram-positive bacteria)
  - Systemic LPS infiltration
- Occludin/Zonulin IgG, IgA, IgM:
  - Tight junction breakdown
- Actomyosin IgA:
  - Epithelial cell damage


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**Transcellular & Paracellular Routes of Intestinal Barrier Penetration**

![Transcellular & Paracellular Routes of Intestinal Barrier Penetration](Cyrexlabs.com)

- Occludin/Zonulin
- Actomyosin

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**Occludin/Zonulin**
Zonulin controls the tight junction

Actomyosin Network

Immunoglobulins to LPS
- IgG – Chronic issue
- IgA – early onset/reactivated/on-going issue
- IgM – early onset
- Equivocal – mounting issue unless it is IgG then it may indicate healing and antibodies returning to normal levels
Zonulin Antibodies Levels

- Zonulin levels fluctuate in a matter of hours
- The half life of Zonulin is 4 hours
- Studies show significant changes in Zonulin levels between blood draws 2 hours apart
- Multiple draws throughout the day are required to know if Zonulin levels are consistently elevated

- Gut Dysbiosis
- Beginning of Tight Junction Breakdown

- Chronic Gut Dysbiosis
- Mounting Tight Junction Breakdown
- Mounting Epithelial Cell Damage
Chronic/Reactivating Gut Dysbiosis
Early Onset Tight Junction Breakdown
Epithelial Cell Damage

Laboratory Tests

- Intestinal Antigenic Permeability Screen: Occludin/Zonulin, lipopolysaccharides (LPS), Actomyosin (IgA) network. CyrexLabs.com
- Wheat/Gluten Proteome Reactivity & Autoimmunity. CyrexLabs.com
- Gluten-Associated Cross-reactive Foods and Foods Sensitivity. CyrexLabs.com
- Assess Intestinal Dysbiosis (for yeast & bacteria) – organic acid test profile or complete stool analysis. Greatplainslaboratory.com
- Intestinal Permeability Assessment mannitol/lactulose. Genova Diagnostics

Leaky Gut and Leaky BBB

- LPS from bacteria in intestine can be transported in the blood from a patient with Leaky Gut and can enhance immune cell and viral transport across the BBB leading to more extensive damage
- Leaky gut can increase likelihood of brain autoimmunity
- Leaky gut must be diagnosed and repaired
Chronic fatigue syndrome is in your gut

Researchers at Cornell University identified biological markers of the disease in gut bacteria and inflammatory microbial agents in the blood.

A fungus (candida tropicalis) has been identified as a key factor in the development of Crohn’s disease.
Section VI: GI Treatment

**4R Program**

**REMOVE**
- Pathogens, parasites, toxin
- Food allergens
- Gastric irritants

**REPLACE**
- Stomach Acid
- Digestive Enzymes

**REINOCULATE**
- Beneficial bacteria
1. Remove

- Removing offending substances from the diet
- Food allergens and other materials that negatively influence the intestinal environment:
  - Can cause localized irritation
  - Trigger release of damaging chemicals into general circulation
  - Affecting other tissues or organ

1. Remove (cont’d)

- Concentrated aromatic oils:
  - Thyme oil
  - Oregano oil
  - Sage leaf
  - Lemon balm leaf

- For upper respiratory issues/sinusitis
- Aromatic oils = open the bronchial
- Thyme oil – health of GI/upper respiratory
- Sage/lemon balm – herbs that complement and stabilize the fragile essential oils
1. Remove

Concentrated berberine formula for intestinal support

- Berberine HCL
- Oregon grape
- Coptis root
- Chinese herbs, ginger, licorice, skullcap
- For healthy intestinal environment
- Dyslipidemia, dysbiosis
- Best suited for train-wreck patient
- B-bowel issues

Berberine Activates AMPK

- Liver
  - Increases fatty acid oxidation (ketogenesis)
  - Decreases cholesterol synthesis
  - Decreases triglycerides
  - Pancreatic islets
    - Modulates insulin secretion

- Skeletal muscle
  - Increases fatty acid oxidation
  - Increases glucose uptake

- Adipocytes
  - Decreases lipogenesis
  - Decreases lipolysis


“In this study, we report that berberine sulfate is bacteriostatic for streptococci and that sub-MICs of berberine blocked the adherence of streptococci to host cells”

Berberine was shown to possess antimicrobial activity against a wide variety of microorganisms including Gram-negative bacteria, fungi & protozoa.

Result: Tight junction dysfunction can be improved by berberine, thereby demonstrating the therapeutic potential of berberine for intestinal ischemia/reperfusion.

2. Replace

I. Low-gastric acidity:
   - A formulation featuring betaine HCl combined with pepsin to complement the natural production of digestive agents in the stomach.

II. Pancreatic enzyme insufficiency:
   - A formulation that features a comprehensive enzyme complex that helps promote healthy digestive function. Containing protease, amylase and lipase.
3. Reinoculate – Probiotics

- *L. acidophilus* NCFM and *B. lactis* Bi-07 (60 billion live organisms) – designed to relieve recurring bowel distress and related functional discomforts, such as occasional bowel urgency
- Helps relieve abdominal discomfort, bloating, cramping, bowel irritation, and occasional urgent bowel movements

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**L. acidophilus NCFM is one of the most researched strains**

- DNA has been fully mapped
- Safe—Commercially available since the 1970s
- Subject of over 60 publications
- Survives GI transit

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The probiotics (*L. acidophilus* NCFM and *B. lactis* Bi-07) have been studied clinically in numerous models of bowel distress

The similar efficacy, in treating pain, of orally administered *L. acidophilus* NCFM and a standard dosage of morphine suggests that specific modulation of intestinal flora may be a... treatment for abdominal pain, a prominent symptom of irritable bowel syndrome*.


*These observations suggest that inoculation with probiotics can effectively prevent bacteria-induced colitis by limiting enteric bacteria infection and promoting mucosal protective regulatory immune responses.*

This page contains information on the use of Lactobacillus plantarum 299v as a probiotic for treating irritable bowel syndrome (IBS). The text highlights several studies that have found this strain to be effective in improving IBS symptoms.

### L. plantarum 299v – A probiotic for IBS


Over 80+ studies on L. plantarum 299v

#### L. Plantarum 299v RCT (Ducrotté): Clinical Trial Design

**Design**

- Double blind randomized trial of 214 adult patients (n=108 probiotic, n=106 placebo)

**Center**

- Four centers (Mumbai (1), Chennai (2), Bangalore (1))

**Primary endpoint**

- Frequency of abdominal pain episodes

**Secondary endpoints**

- Severity of abdominal pain episodes
- Frequency and severity of bloating
- Frequency and severity of feeling of incomplete evacuation
- Changes in stool frequency

**Inclusion criteria**

- Age 18-70 yrs
- IBS diagnosis based upon Rome III criteria

**Medicinal product, dosage, type of application**

- Lactobacillus plantarum 299v, 10 billion CFU, capsule, 1x daily
- Placebo (potato starch, magnesium stearate), capsule, 1x daily

**Prepared and provided by Rosell-Lallemand Institute (Blagnac, France)**

**Duration of treatment**

- 4 weeks

**Number of visits**

- 7 Total: 4 (1x week for treatment period), 3 (1x week for 3 week follow up period)


L. Plantarum 299v reduces IBS symptoms

- Frequency
- Bloating
- Sense of incomplete evacuation

**L. plantarum 299v may support Gastrointestinal Function via multiple mechanisms**

- Studies in animal models have demonstrated that *L. plantarum* 299v can modulate cytokine production (increase IL-10 and reduce IL-6).
- Studies in human cell lines have demonstrated that *L. plantarum* 299v can modulate mucin gene expression (upregulate Muc2 and 3).
- Studies in ex vivo human colonic mucosal cells have demonstrated that *L. plantarum* 299v can modulate cytokine gene expression in human cells (reduce IL-17A gene expression).

**Randomized controlled trial of probiotics after colonoscopy**

- 20% of patients have on-going abdominal symptoms at day 2 and beyond following colonoscopy
- Probiotic capsule contained *L. Acidophilus* NCFM, *B. lactis* Bi-07
- Double-blind study

**Conclusion:** Study showed significant reduction in the duration of pain post colonoscopy in patients taking probiotic compared with placebo

*ANZ J Surg.* published online July 17, 2015

---

**4. Regenerate/Repair**

**Xanthohumol strong clinical data**

**Brain Health**
- Anti-inflammatory
- Anti-oxidant/polyphenols
- Mitochondrial biogenesis

**Cardiovascular**
- Anti-inflammatory
- Sodium inhibition

**Digestive Health**
- Anti-inflammatory
- Polyphenols

Xanthohumol

**Excellent science:** >250 publications in preclinical science
Xanthohumol modifies kinases in favor of antioxidant protection

- Improves dysfunctional glucose and lipid metabolism
- Results:
  - Dose-dependent decrease in weight gain (60 mg daily)
  - Decreased:
    - Glucose
    - Triglycerides
    - MCP-1
    - LDL-C
    - I-6
    - Insulin

Bioavailable form of curcumin: CurQfen

- Curcumin shows potent anti-inflammatory activity and research suggests it may help reduce inflammation-signaling molecules, such as NF-κB, TNF-α, CCR-2, and PGE2.
- Curcumin also shows potent antioxidant activity and research suggests it may help improve overall redox status through influencing antioxidants Nrf2, GSH-1, and NQO1.
- Delivery of significant concentrations of biologically active free curcuminoids has always been regarded as a major limitation for the efficacy of curcumin supplementation.
- CurQfen is a unique, patented blend of a stable curcuminoid and galactomannan compound (from fenugreek) designed for great bioavailability and more reliable clinical outcomes.

CurQfen: formulated for greater curcumin bioavailability

- In a randomized, crossover study of 50 subjects
  - Single dose of 400mg
  - Curcumin levels were measured over 12 hours
- CurQfen group demonstrated 45.5 times more bioavailability when compared to standard curcuminoids

High-fiber diet keeps gut microbes from eating colon’s lining

Isomalto-oligosaccharide (IMO)
Prebiotic Fiber

- 4 grams of IMO
- IMO is soluble fiber, gentle prebiotic fiber source from tapioca
- Produced short-chain fatty acid (SCFA) the acetate, propionate and butyrate as end products of fermentation
- Inhibits the growth and activities of harmful micro-organisms and contribute to stimulation of the growth of lactobacilli and bifidobacteria

The average American is only eating 10 - 15g of fiber
Recommendation for adults is to consume 25 – 30g of fiber

Paradigm shift

SPM represents a paradigm shift in how we view the regulation of the inflammatory response

Specialized Pro-Resolving Mediators (SPM)

SPMs act to resolve inflammation. Without resolution, even a reduced inflammatory response can become chronic, and full healing and return to homeostasis cannot occur.
SPMs driving reduction in hsCRP and PGE\(_2\): potential mechanisms of action

- Reduction in PMN entering site secreting pro-inflammatory signals including cytokines and PGE\(_2\)
- Lipid mediator class switching during resolution - pro-inflammatory mediators reduce as pro-resolving mediators increase
- Change in macrophage phenotype to more M2/pro-resolving phenotype for reduction in pro-inflammatory cytokines
- Knock-on effect of reduction in pro-inflammatory signal production to lowered hsCRP production by liver

**Arachidonic Acid (AA)**
- SLOX + 5SLOX
- Lipoxins A\(_4\), B\(_4\)

**Free Eicosapentaenoic Acid (EPA)**
- 18-HETE
- 15-HETE
- Resolvin (resolvins)
- Protectins
- Maresins
- Resolvins D3

**Free Docosahexaenoic Acid (DHA)**
- 17-HDHA
- 17 sdOH-DHA
- Resolvins
- NPD1 (protectins)

**Resolution of Inflammation**

- Resolvin D3 multi-level pro-resolving actions are most protective during infection
- D3 mediators produced by resolving exudates stimulates clearance of neutrophils and leukocyte attenuates pro-inflammatory signals
- RVD3 was identified in self resolving exudates during active E.coli infection
- Additionally – reduction of cytokines, chemokines, MMP2 and MMP9
SPMs in Inflammatory Arthritis

- 4-week trial
- SPMs in synovial fluid and plasma were measured before and after trial
- E- and D-series SPMs were present in synovial fluid and plasma of RA patients
- Conversion of SPMs was greater in the synovial fluid than in plasma, indicating that the SPMs work at site of inflammation in addition to working systematically


SPMs – vascular health

- Human aortic branch:
  - DHA and 17-HDHA increased synthesis of D-resolvins
  - 17-HDHA increased specific resolvins to a greater extent than DHA (RvD1 and RvD4)
- Vascular smooth muscle cells/vascular endothelial cells:
  - 17-HDHA had a 6-fold increase in D-series resolvins

FASEB J. Apr 25, 2017

Mounting evidence shows that SPMs have vascular-protective effect

- SPM treatment reduced migration, monocyte adhesion, and pro-inflammatory makers
- Vascular tissue can utilize F.A. of 17-HDHA present within tissue for vascular benefits

FASEB J. Apr 25, 2017
SPMs vs. Omega-3 Fatty Acid to Resolve Inflammation

• SPMs are structurally different from omega-3 FA
• SPMs are functionally different from EPA/DHA
• EPA/DHA may impact initiation phase by competing with FA for enzymes
• EPA/DHA do not have pro-resolving properties of SPMs

Conclusion

Resolution is an active process. Anti-inflammation is NOT equivalent to pro-resolution.

SPMs are lipid compounds isolated in many human tissue during inflammation
• Chemically synthesized in lab and in vivo
• Injected into humans at physiologic doses
• Inflammation resolves faster and mimics natural healing
• Prevents transition to chronic inflammation
• In some tissues, stimulates "regeneration"


Dr. Rob’s GI Restoration Protocols
Remove & Replace – 30 Days

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berberine HCL, Oregon grape, Coptis root, Chinese herbs, ginger, licorice, skullcap</td>
<td>3 TID</td>
</tr>
<tr>
<td>Thyme oil, oregano oil, sage leaf, lemon balm leaf (if pt. has respiratory symptoms)</td>
<td>1 1g TID</td>
</tr>
<tr>
<td>Betaine HCL, peptic</td>
<td>Titrate up to a warming dose</td>
</tr>
<tr>
<td>Protease, amylase, lipase</td>
<td>1 tab w. each meal</td>
</tr>
<tr>
<td>Modified elimination food plan</td>
<td></td>
</tr>
<tr>
<td>EPA/DHA</td>
<td>4 g.</td>
</tr>
</tbody>
</table>
Dr. Rob’s GI Restoration Protocols
Reinoculate & Regenerate Next 30 Days

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powdered nutritional support for inflammation and GI support</td>
<td>Daily</td>
</tr>
<tr>
<td>Specialized Pro-Resolving Mediators</td>
<td>1500 mg acute</td>
</tr>
<tr>
<td></td>
<td>1000 mg sub-acute</td>
</tr>
<tr>
<td></td>
<td>500 mg wellness</td>
</tr>
<tr>
<td>D₃, 5000 (check 25-OH D₃ levels)</td>
<td>Daily with food</td>
</tr>
<tr>
<td>Lactobacillus lantarum 299v</td>
<td>Daily</td>
</tr>
<tr>
<td>Modified elimination food plan</td>
<td>30-60 days</td>
</tr>
<tr>
<td>Alpha-lipoic acid</td>
<td>600 mg daily</td>
</tr>
<tr>
<td>Low-allergy blend of soluble and insoluble fiber</td>
<td>5 g or more daily</td>
</tr>
</tbody>
</table>

Dr. Rob’s 1-Month Gut Program

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berberine HCl, Oregon grape, Coptis root, Chinese herbs, ginger, licorice, skullcap</td>
<td>3 TID</td>
</tr>
<tr>
<td>A formulation for maintenance of good GI health</td>
<td>2 scp. BID</td>
</tr>
<tr>
<td>Specialized Pro-resolving Mediators</td>
<td>1500 mg. daily</td>
</tr>
<tr>
<td>Protease, amylase, lipase</td>
<td>1 tab w. each meal</td>
</tr>
<tr>
<td>L-plantarum 299v</td>
<td>2 daily</td>
</tr>
<tr>
<td>Follow Retain protocol after 1 month</td>
<td></td>
</tr>
</tbody>
</table>

My 6R GI Restoration Program

- **Remove** pathogens
- **Replace** digestive enzymes and stomach acid
- **Reinoculate** with probiotics
- **Regenerate** damaged intestinal mucosa
- **Retest** to see the gains
- **Retain** to create GI supportive lifestyle
### Dr. Rob’s GI Restoration Protocols

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replenish your gut with IMO/(2FL), L-alanyl-L-glutamine</td>
<td>2 scp. once daily</td>
</tr>
<tr>
<td>Specialized Pro-resolving Mediators</td>
<td>500 mg. daily</td>
</tr>
<tr>
<td>50:50 blend 15 billion L. acidophilus/NCFM, B. lactis BI-07</td>
<td></td>
</tr>
<tr>
<td>A low-allergy blend of soluble and insoluble fiber</td>
<td>1 scp. daily</td>
</tr>
<tr>
<td>Dr. Rob’s Super 5</td>
<td></td>
</tr>
<tr>
<td>Modified elimination diet plus foods added through 3 day testing</td>
<td></td>
</tr>
</tbody>
</table>

### Key Targeted Ingredients Address Dysbiosis

- HMO occur naturally in human milk
- HMO have prebiotic effect
- HMOs mimic structures found on surface of intestinal epithelia that bind unwanted bacteria serving as decoy receptors
- HMOs (2'-FL) selectively promote bacterial growth (in vitro) affecting butyrate production

**2'-FL is the most abundant HMO**

- IMO is soluble fiber, well-tolerated prebiotic fiber source from tapioca
- Produces Short-chain fatty acid (SCFA) like acetate, propionate and butyrate as end products of fermentation
- Inhibits growth and activities of harmful micro-organisms and contributes to stimulation of the growth of Bifidobacteria
Butyrate Is a Short Chain Fatty Acid Produced by Bacterial Fermentation with Many Functions

Intestinal Barrier Function
- Inflammatory and Oxidative Stress
- Cell Growth and Differentiation
- Intestinal Motility and Visceral Perception
- Immune regulation
- Ion absorption

Gut Microbes

Butyrate

Propionate

Acetate

Short Chain Fatty Acids (SCFA)


Di-peptide form of L-glutamine (sustamine) for superior absorption

Sustamine® is absorbed up to 224% better than standard L-glutamine®

AUC = Area under the curve

Replenish Nutrients for Those in Need

Healthy Intestines
- 1.5 g L-alanyl-L-glutamine dipeptide for enhanced absorption, stability, & solubility
- 15 g per serving of pea/rice protein blend, including added branched chain amino acids (BCAAs) that may offer an absorption advantage
- 400 IU per serving of vitamin D3, the more bioavailable form of Vitamin D

Intestinal Integrity
- 11.25 mg per serving of zinc as zinc gluconate
- 185.2 mcg per serving of folate as calcium L-5-methyltetrahydrofolate, a body-ready folate
- 1.5 mcg per serving of vitamin B12 as methylcobalamin to enhance absorption

Metabolic Efficiency/Nutritional Insufficiencies
- 1.5 g per serving of 10 g fiber per serving, primarily comprised of gentle prebiotic fibers:
  - PreBiome 2'-FL designed to promote beneficial microbiota and discourage unwanted microorganisms
  - IMOs to further support colonization of healthy microbiota
  - Both nature-identical HMO and IMOs offer a prebiotic approach for greater digestive comfort

Targeted Nutrition
- 7 g per serving, of vegan pea/rice protein blend, including added branched chain amino acids (BCAAs) that may offer an absorption advantage
- Strategic blend of omega-3, -6s, and -9s (MCTs) — all from plant sources
- Sweetened with monk fruit extract and 2 grams of organic cane sugar*
Alpha-linoleic acid (ALA) is an anti-inflammatory agent in inflammatory bowel disease

- ALA supplementation shown to be effective in inhibiting inflammation induced by IL-1β by down-regulating mRNA levels of pro-inflammatory genes including IL-8, COX2, and inducible nitric oxide synthase
- Results suggest that plant derived oil, rich in ALA could ameliorate inflammatory damage in colitis

**Alpha lipoic acid**

- Lowers oxidative stress
- Protects against free radical damage
- Decrease left ventricular hypertrophy (thickening of heart muscle)
- Improves insulin sensitivity and lowers blood sugar
- Chelates metals
- Improved endothelial function
- Lowers blood pressure
- Decreased dementia risk
- Improves the lipid profile
- Activates AMPK, Nrf2, and SIRT1 while inhibiting NF-KB

**Study Links IBS with Vitamin D Deficiency**

"Vitamin D receptor is expressed in the gut and regulates epithelial barrier function and bowel inflammation suggesting that a vitamin D deficiency may directly impact bowel function and hence IBS symptomology"
High-dose vitamin D may boost diversity of the gut microbiome
• Vitamin D3 may increase bacterial richness in the upper GI tract and reduce opportunistic pathogens
• This might in part explain the effects of vitamin D or IBD


CASE REPORTS

70 year-old Female

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>200:1 Anti-Inflammatory Activity</td>
<td>1.0</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>165</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.61</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>61.3</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.75</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>62.5</td>
</tr>
</tbody>
</table>
46 year-old Female

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal Flora</td>
<td>4.9</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>3.7</td>
</tr>
<tr>
<td>Large Intestine</td>
<td>9.0</td>
</tr>
</tbody>
</table>

6 months later

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal Flora</td>
<td>4.9</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>3.7</td>
</tr>
<tr>
<td>Large Intestine</td>
<td>9.0</td>
</tr>
</tbody>
</table>

SIBO

- Excessive bacteria in small intestine
- Small intestine has relatively low levels of bacteria
- Longest section of digestive tract
- Where nutrients are absorbed in the blood stream
- Mal-absorption of nutrients
Stats
IBS – 15% of adults
• Females – 2:1
• Features:
  • Bloating
  • Cramping
  • Constipation/diarrhea
SIBO
• SI devoid of coliform bacteria
• Is a condition of altered microbiome
• Features:
  • Chronic vit. malabsorption
  • Constipation
SIBO is a common occurrence of D-IBS

SIBO symptoms
• Nausea
• Bloating
• Vomiting
• Diarrhea
• Malnutrition
• Weight loss
• Joint pain
• Fatigue
• Rashes
• Acne
• Eczema
• Asthma
• Depression
• Rosacea

SIBO causes & risk
• Diabetes
• Diverticulosis
• Structural defect in small intestine
• Injury
• Fistula
• Intestinal lymphoma
• Scleroderma
• Celiac disease
• Certain Rx medications
• Rosacea
• Aging
SIBO associated complications

• Malnutrition
• Vitamin B12 deficiency
• Anemia
• Poor absorption of fat
• Osteoporosis
• Kidney stones
• Damage to intestinal lining

Test

• Hydrogen/methane breath test – a common method of assessing SIBO
• Hydrogen has greater association with diarrhea
• Methane – almost exclusive association with constipation

Lactobacillus reuteri on methane production

• Study highlights for the first time – beneficial effect of lactobacillus reuteri on chronic constipation via significant decrease of CH4 production

SIBO protocol

Phase I – 30 days
• Bile salts and bitter extracts; 2 tabs with each meal:
  • Helps body break down fats in the diet
  • Supports optimum fat digestion and healthy liver/gallbladder function
• Aromatic oils; 2 sg 3 TID:
  • Kills bad bugs
  • Cleanses bowel of bacteria/viruses/yeast/parasites
• Berberine; 3 tabs 3 TID:
  • Cleanses GI tract killing more bacteria/viruses/yeast/parasites

SIBO protocol (cont’d)

Phase I – 30 days (cont’d)
• Zinc carnosine; 2 tabs TID on empty stomach:
  • Enhances repair of stomach lining
• FODMAP elimination diet - avoid fructose, lactose, fructans, galactans, polyols
Or
• Paleo/keto diet – no more than 50 g. of carbs a day

SIBO protocol (cont’d)

Phase II – 30 days
• Betaine HCl and pepsin; 2 tabs per meal:
  • Supports digestion and breakdown of food
• Broad spectrum of non-animal derived enzymes including acid stable lipase and 3 proteases that function in different pH ranges; 2 tabs per meal
• Continue with bile salts and bitter extracts; 2 tabs per meal
SIBO protocol (cont’d)

Phase II – 30 days (cont’d)
• Add well-rounded dairy-free probiotic – helps gut flora, supports digestion
• Add powdered nutritional support; 2 scp BID
  • Provides strategic macro and micronutrient support for those with compromised gut function
• Modified elimination diet

Probiotics for treating/preventing SIBO

Findings:
• Probiotic supplementation could effectively decontaminate SIBO
• Decrease H2 concentration
• Relieve abdominal pain
• Pooled analysis found probiotics remarkably effective for treatment of SIBO

J Clin Gastroenterol. April 2017

On-going care for health

• Continue with bile salts and bitter extracts; 1 tab per meal
• Add powdered nutritional support - supports intestinal lining and GI health; 2 scp daily
• Continue with probiotic; 1 cap daily
Do you have “leaky skin”?

Effect of gluten-free (GF) diet on autism

In this study:
• GF diet group – GI symptoms and behavioral disorders decreased significantly

Wheat proteins may cause inflammation beyond the gut

• Amylase-trypsin inhibitors (ATIs) found in wheat may potentially lead to the development of inflammation in the lymph nodes, kidneys, spleen, and brain
• They can exacerbate RA, MNS, asthma, lupus, and IBD
• ATIs may contribute to NCGS


Gluten-free gains popularity

• Prevalence of celiac disease remains steady
• More Americans are adopting a gluten-free diet
• 26-30% reduce gluten intake

JAMA Internal Medicine, Sept 2016

Intestinal damage without celiac disease

Conclusion:
- Systemic immune activation in conjunction with compromised intestinal epithelium in the absence of celiac disease
- Sensitivity to wheat:
  - Elevated soluble CD14
  - LPS
  - Fatty-acid binding protein 2

JAMA Intern Med, Apr 2016
Glyphosate (cont’d)

• Compromises your ability to detoxify toxins
• Impairs synthesis of tryptophan and tyrosine, important amino acids in protein and neurotransmitter production

Glyphosate

• Acts as powerful antibiotic
• Slaughters beneficial bacteria in your gut
• Mimics hormones like estrogen
• Impairs function of vitamin D
• Depletes key compounds like:
  • Iron
  • Cobalt
  • Molybdenum
  • Copper

Molecular Mimicry

Antibodies tend to the specific protein sequence of targets. This ensures that, upon and ploy, when you are exposed to allergens, the immune system is prepared to reject them. This may occur when your immune system overreacts to harmless substances (allergens).
Glyphosate-treated wheat

Glyphosate – commonly used as herbicide:
- Active ingredient in Monsanto’s RoundUp
- Shown to severely damage your gut flora and cause gut dysfunction
- Actually patented as an antibiotic
- WHO determined glyphosate as a “probable carcinogen”

Glyphosate-treated wheat (cont’d)
- Use of glyphosate and celiac disease have risen in tandem
- Impairs the villi in your gut
- Inhibits process that normally helps your body digest wheat proteins
- Glyphosate attaches to gliadin – interfering with the protein connections – therefore making the wheat highly indigestible
- Now more likely to cause an immune reaction and gut dysbiosis

Gluten and the Gut
Sources of Gluten

- Gluten is a protein found in wheat, rye, and barley
- It is also commonly found in oats (and sometimes other grains) that become contaminated during processing
- There are also many hidden sources of gluten

Comparison of Gluten-Related Disorders

<table>
<thead>
<tr>
<th></th>
<th>Celiac Disease</th>
<th>Wheat Allergy</th>
<th>Non-Celiac Gluten Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Genetic, autoimmune disorder; gluten ingestion triggers damage to small intestine</td>
<td>Intolerant response to one or more of the proteins found in wheat (can include gluten)</td>
<td>Intolerance to gluten or other wheat components</td>
</tr>
<tr>
<td><strong>Gastrointestinal symptoms</strong></td>
<td>Diarrhea, bloating, abdominal pain</td>
<td>Nausea, vomiting, diarrhea, bloating, irritation of mouth or throat</td>
<td>Diarrhea, bloating, abdominal pain</td>
</tr>
<tr>
<td><strong>Extra-intestinal findings</strong></td>
<td>Weight loss, malnutrition, immune system disorders, arthralgia, joint pain, hair loss, fatigue</td>
<td>Hives, rash, nasal congestion, eye irritation, difficulty breathing</td>
<td>Blotchy, neurological disorders, joint pain, fatigue</td>
</tr>
<tr>
<td><strong>Positive antibody test</strong></td>
<td>Yes</td>
<td>Variable (IgE, IgA)</td>
<td>No</td>
</tr>
<tr>
<td><strong>Abnormal intestinal biopsy</strong></td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Potential Hidden Gluten Sources

- Sauces and gravies (wheat flour often used as thickener)
- Marinades
- Soy sauce = use GF tamari instead
- Ketchup
- Cereal
- Nudels
- Salad dressings
- Yogurt and ice cream (wheat flour often added to prevent ice forming)
- Hot dogs
- Dips
- Mixed spices [Flour often used to prevent caking]
- Candies
- Lunch meats
- Spaghetti sauce
- Seaps
- Tabouleh (contains barley)
- Alternative milks: rice, almond, soy [may contain gluten]
- Instant formula
- Some cereals [those containing caramel coloring = may derive from wheat]
- HVP = hydrolyzed vegetable protein
- Maltos
- Imitation crab
- Miso
- Seafood
- MSG (can be derived from wheat)
- Artificial color
- Etc...
Non-Food Possible Gluten Sources

- Charcoal briquettes
- Envelopes
- Stamps
- Dry wall
- Spray starch
- Play dough
- Glue
- Glue sticks
- Soaps
- Shampoo
- Lotion, hand cream
- Talcum/body powder
- Toothpaste
- Lipstick, lip-gloss/moisturizers
- Makeup
- Medications
- Vitamins
- Herbal supplements

Gluten Digestion

- Humans possess the various digestive enzymes to break down many dietary protein molecules into single amino acids that can be absorbed by the gut (Figure 1).
- Gluten is a protein composite and is made up of gliadins and glutenins in roughly equal parts.
- Gluten is unusually high in the amino acid proline. Partially digested gluten fragments are known as proline-rich peptides (PRPs).
- These inadequately digested PRPs can lead to discomfort associated with some gluten sensitivities (Figure 2).

A. niger prolyl endoprotease (AN-PEP)

- **A. niger prolyl endoprotease (AN-PEP)** is considered a "proline-specific endoprotease" because it digests proteins and peptides over their entire length.
- Other endoproteases include the endogenous digestive enzymes pepsin, trypsin, and chymotrypsin.
- This is in contrast to "exopeptidases", which preferentially break down only the ends of peptide chains.

AN-PEP: Digests Gluten Rapidly

- The speed of protein digestion was tested by incubating AN-PEP with 4 different gluten peptides at pH 4.5.
- The half-life of the reactions ranged from 2.4-6.2 minutes.

<table>
<thead>
<tr>
<th>Gluten Peptide</th>
<th>Half-Life (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Gliadin (Glia-α-9)</td>
<td>3.87</td>
</tr>
<tr>
<td>γ-Gliadin (Glia-γ-1)</td>
<td>2.36</td>
</tr>
<tr>
<td>LMW-Glutenin (Glt-156)</td>
<td>5.10</td>
</tr>
<tr>
<td>HMW-Glutenin</td>
<td>6.19</td>
</tr>
</tbody>
</table>

AN-PEP: Resistant to Stomach Conditions — Acidic pH

- **AN-PEP** exhibited maximum activity at pH 4.5.
- **AN-PEP** retained nearly 100% of its enzymatic activity after 1 hour in the presence of endogenous enzymes.
Enzyme blocks gluten

- Relieves symptoms of gluten intolerance
- AN-PEP (endoprotease) can stop gluten from entering small intestine
- Study revealed that both high-dose and low-dose AN-PEP groups had 85% better breakdown than the placebo group
- *Non-celiac gluten intolerance*

Dr. Rob’s Key Take-Away

- Clinically shown to breakdown gluten before entering the small intestine
- Demonstrated to be effective in acidic condition similar to the stomach
- Digestion of gluten peptides is rapid
- ★ Used when “dining out” in case of accidental, incidental trace exposure to gluten
- ★ (Reality check) May benefit patients who deviate from their gluten-free diet for a special occasion

Novak Djokovic’s Gluten Free Recipe for Success

**Ingredients**
- 1 GF Savvy Nutritionist
- 1 Cooperative patient
- 100% Gluten free diet

**Directions**
- Game.
- Set.
- Match.

**Servings**
- One happy, healthy life
Gut health "leaky gut" (6R program)

1R (1 month)
2R (1 month)

Candibactin AR, BR

SpectraZyme
Complete/Metagest

3R (1 month)
4R (1 month)

UltraFlora Balance
Ultraflora plus 3G0 SPMs

Add if SIBO found

Endotoxin

5R (Retest)
6R (Retain)

GI Replenish
Gluten Digest
Dr. Rob's Super 5

Dr. Rob's Super 5
Micronutrients for Foundation Nutrition

1) Multivitamin/multimineral
2) Omega-3 fatty acids
3) Vitamin D
4) Probiotics
5) Phytonutrient supplements

Why we need to take supplements....
Key Concept

“Food is too weak to replete depleted cells & bodies”

Advances in Therapy, vol. 24 (5), September 2007

Long-term multivitamin use linked fewer heart problems – Harvard study

Multivitamin use for over 20 years associated with a 44% lower risk of major CVD events

Published online ahead of print “Multivitamin use and the risk of CVD in men”

Multivitamin use and risk of CVD in men

Conclusion: In this long-term prospective study in initially healthy men, multivitamin use was associated with a lower risk of major CVD events

American Society for Nutrition Apr. 27, 2016
Phytonutrients clearly influence healthy function and aging
Typical MVM ignores phytonutrients
Phytonutrients help the healthy messages of vitamins and minerals be “heard”


Agricultural Research November 1996

Science is rethinking what daily supplements should be

• Phytonutrients are bioactive food components that have been associated with reduction in chronic disease and preservation of health
• Potential mechanisms:
  • Reducing CVD risk precursors
  • Lowering oxidative stress and inflammation
  • Preserving vascular function
  • Modification of cell signaling pathways
  • Clinicians need to understand importance of phytonutrients and how their mechanisms go beyond simple antioxidant function

Smaller amounts of a variety of phytonutrients have greater beneficial effects than larger amounts of fewer phytonutrients

Smart Evaluations: Total ORAC$_{FN}$

<table>
<thead>
<tr>
<th>Free Radical &quot;Most Wanted&quot; List</th>
<th>Nutrients to counteract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyl</td>
<td>Turmeric, garlic, basil, oregano, cinnamon</td>
</tr>
<tr>
<td>Peroxyl</td>
<td>Broccoli sprout, onion, tomato, carrot, onion, tomato, carrot, spinach, kale, Brussels sprouts</td>
</tr>
<tr>
<td>Peroxynitrite</td>
<td>Acerola, quercetin, acai, mangosteen</td>
</tr>
<tr>
<td>Singlet oxygen</td>
<td>Blackcurrant, blueberry, cherry, acai, blackberry, raspberry</td>
</tr>
<tr>
<td>Superoxide anion</td>
<td>Apple, elderberry, blue corn</td>
</tr>
</tbody>
</table>

Global Advances in Health and Medicine. March 2014

A Phytochemical-rich Multivitamin-multiminerl Supplement is Bioavailable and Reduces Serum Oxidative Stress Markers Lipoprotein, Myeloperoxidase, and Plasminogen Activator Inhibitor-1 in a Four-week Pilot Trial of Healthy Individuals
**Functional Medicine, Inflammation and Chronic Pain: A New Modality for YOU?**

Lipopolysaccharide (LPS) has many deleterious effects and plays a significant role in a number of disease processes by increasing inflammatory cytokine release.

LPS and Muscle Pain

1. LPS: causes inflammation, mitochondrial/muscle impairment, and increased sensitization to pain
2. Bacteria-produced D-lactic acid: neurotoxin and metabolic poison; causes fatigue, muscle pain, and dyscognition
3. Bacteria-produced hydrogen sulfide: neurotoxin and metabolic poison; causes fatigue, muscle pain, and dyscognition
4. Bacteria-produced tryptophanase: leads to tryptophan, and serotonin/melatonin deficiency

Inflammation — Key Component of Myofascial Pain Syndrome

Inflammation is associated with virtually every chronic disease. Inflammation is responsible for the pain and tissue destruction in patients.

Dr. Rob’s Nutritional Take

- Specific nutrients and oxygen are required to sustain a heavily used muscle
- Overuse soft tissue injuries result when supply of nutrients are unable to match demands of muscle/tendon region
- Healthy nutrient supply through diet and supplementation assists the body with natural function and repair processes
A Powerful Combination

- New and improved, enriched form of a hops extract:
  - Designed to provide powerful joint relief without GI side effects
  - Modulates kinase activity in favor of good joint health, including biomarkers such as PGE
- Undenatured Type II Collagen (UC-II):
  - Twice as effective as glucosamine/chondroitin
  - Positively influenced knee extension in patients who experienced joint discomfort
  - Able to exercise longer before experiencing joint discomfort
  - Recover from joint discomfort faster
  - A key protein that supports structure and integrity

Undenatured type-II collagen: Explanation of mechanism

- Three dimensional configuration of glycoproteins in cartilage and ECM triggers T-cell mediated response
- Auto-antigens shown to suppress a variety of induced autoimmune pathologies, including RA & OA
- Interactions between GALT and undenatured type-II collagen facilitates oral tolerance to the antigen
- Undenatured type-II collagen provides epitopes as auto-antigens, shown to deactivate killer T-cell attack on cartilage
Epitope: The part of an antigen recognized by the immune system; antibodies bind to the epitope

Research on a Hops Extract

• Targets the inflammatory signal transduction pathway without affecting constitutive COX-2 enzyme in vitro\(^a\)
• Inhibits markers of inflammation such as PGE\(_2\), MMP-3, IL-6 and IL-8 in vitro\(^b\)
• Reduces swelling in a model of acute inflammation and inhibits bone and cartilage degradation in an animal model of chronic inflammation\(^b\)

\(^a\) Desai A et al. META060 inhibits multiple kinases in the NF-κB pathway and suppressed LPS-mediated inflammation in vitro and in vivo. Inflammation Research 2009;58(5):229-34.

Hop's proposed anti-inflammatory MoA

The presence of THIAA is associated with decreased levels of substances associated with joint discomfort in a dose-dependent fashion
Endotoxemia Contributes to Inflammation and Disease Development

Endotoxemia

- LPS

- Immune cells
- Hepatocytes
- Adipocytes
- Endothelial cells

- PI3K/AKT pathway
- IKK
- NF-κB

- Pro-inflammatory mediators
- Low-grade inflammation, insulin resistance, etc.

O/A joint pain

Selective kinase response modulators affect genetic expression of inflammatory mediators

Selective Kinase Response Modulators affect target kinases implicated in inflammation

External Signals

- Manage Pain & Inflammation

- SKRMS
- THIAA, RIAA

- Selective kinase response modulators

- Pain & Inflammation

- PG2E2
Key nutrients support a balanced response to inflammation through kinase signaling.

Nutritional Approaches for Joint Pain

- THIAA (from hops)
- Undenatured type II collagen
- Magnesium
- Probiotics – L.acidophilus NCFM, B-lactis Bi-07
- Specialized Pro-resolving Mediators (SPMs)

Love it!

Pharmaceutical-grade chondroitin sulfate as effective as celecoxib and superior to placebo in symptomatic knee O/A

Magnesium - an "essential" mineral

- Over 300 enzymatic reactions in the body involve magnesium
- Magnesium is critical to muscle relaxation, energy metabolism, and protein synthesis
- An adult body contains approximately 25 g magnesium
- 50 – 60% present in bones
- Less than 1% is in blood; the rest is stored in soft tissues

The enzymes that use Magnesium are important for many normal functions of the body

- Bone integrity and strength
- Cell Division
- Reduced fatigue, tiredness and helps better sleep
- Electrolyte balance
- Magnesium
- Muscle functions
- Protein synthesis
- Energy-yielding metabolism
- Relaxes nervous system

If your patients:

- Are often stressed
- Have disturbed sleep
- Complain of fatigue and lack of energy
- Are sensitive, nervous and/or irritable
- Consuming a diet low in plant-based foods
- Taking medications that are known to lead to magnesium deficiency
- Experience muscle cramps/spasms
- Experience tired legs
Magnesium deficiency has been strongly associated with migraine attacks

- Recent study by Chiu demonstrates the positive effects of my administration orally for migraine symptoms
- Study: 400-600 mg: magnesium citrate – 8-12 weeks
- Dr. Rob's recommendation: 1200 mg bisglycinate daily - 5-7 days

**Magnesium**

**Conclusion:** Significant inverse correlations between mg intake and:

- Risk of stroke
- Heart failure
- Diabetes
- All-cause mortality

No correlation between increased mg intake and CVD


---

Promotes restful sleep, positive mood, and relaxation

**Magnesium**

Essential mineral involved in many body processes including bone formation, muscle contraction and relaxation, and general nervous system health

**Glycine**

Glycine provides general calming effect on the body and improve the quality of sleep.

**Folate, Vitamin B12 and Vitamin B6**

Folate and vitamin B12 support the metabolism of serotonin, a neurotransmitter associated with mood, sleep, and relaxation.

Vitamin B6 is a factor in the body's conversion of glutamate into GABA, a neurotransmitter with calming and relaxing properties.

**Taurine**

Taurine is essential for cardiovascular, skeletal muscle, the retina, and the central nervous system function.

Promotes restful sleep, positive mood, and relaxation
Middle-aged Executive with Chronic Musculoskeletal Pain

3 Phases of Care

PHASE 1 Acute Phase (first 3-5 days) Protective Phase

PHASE 2 Sub-Acute Phase (day 4-8 weeks) Repair & Remodeling Phase

PHASE 3 Wellness/On-going Care

CHRONIC PHASE
Beyond 3 months On-going Repair & Remodeling
Scar-tissue Adhesions Fibrosis

INJURY
Injury cycle

He who treats the site of pain is lost...

Functional Movement Assessment

Dr. Rob’s Magnificent 7

- Posture/pain
- Overhead squat
- 1-legged squat
- Trunk stability push-up
- Valgus jump test
- Upper/lower muscle firing patterns
- Push-up
Quote

As a rule of thumb, the earlier a musculoskeletal injury is treated, the sooner healing can begin. An untreated injury can easily slide from “acute” into “sub-acute”, and even into “chronic”

Alright lets get ripping!!
Myofascial injury

Regeneration of injured skeletal muscle after the injury. JMTJ Dec 2013

Tero AH Järvinen, 1 Markku Järvinen, 1 and Hannu Kalimo 2

Inflammation is Present in Early Human Tendinopathy

Study provides evidence for an inflammatory cell infiltrate in early mild/moderate human tendinopathy

The American Journal of Sports Medicine, vol. 38, no. 10

The Mature Adult: Aging Tendons and Ligaments

• Several published reports shown increased levels of matrix metalloproteinases (MMPS) lead to degenerative tendon disease
• MMP inhibitors associated with a decrease in tendon dysfunction

Sports Health, Jan/Feb. 2014, p.41-48
Disc Injuries

<table>
<thead>
<tr>
<th>Flexion movement</th>
<th>vs.</th>
<th>Flexion moment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexing the spine</td>
<td></td>
<td>Flexing moment or torque</td>
</tr>
<tr>
<td>Strains layers of collagen in spinal discs</td>
<td></td>
<td>Ab muscle stiffening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No movement</td>
</tr>
</tbody>
</table>

Inflammation

Back pain may raise risk of mental health problems

- 200,000 participants
- People with back pain 2x as likely to experience one of the following:
  - Anxiety
  - Depression
  - Psychosis
  - Stress
  - Sleep deprivation

Interleukin-1β in intervertebral disk degeneration

- Interleukin-1 (IL-1) β has strong pro-inflammatory activity by stimulating the secretion of multiple pro-inflammatory mediators
- IL-1β is highly expressed in degenerative intervertebral disk (IVD) tissues and cells
- Inhibition of IL-1β found to promote extracellular matrix (ECM) repair and protect against disk degeneration

New approach to diagnosing low back pain

- Findings determined serum levels of IL-6 significantly higher in subjects with low back pain compared with control participants
- Participants with low back pain due to spinal stenosis or degenerative disc disease also had higher levels than those with intervertebral disc herniation and controls
- Findings suggest that patients with low back pain have low-grade systemic inflammation
- Biochemical profiling or circulating cytokines can assist in diagnosing those with low back pain

Failed healing of rotator cuff repair

- Found that gene expression related to tissue remodeling, particularly MMP-1 and MMP-9, differs between rotator cuffs that healed and those that failed to heal after orthoscopic repair
- MMP-1 and MMP-9 are highly effective in degrading type-1 and 3 collagen
- Their expression contributes to poor cuff healing
- MMP-1 and MMP-9 expression reflect a highly degenerated tendon or diminished ability to heal

Traumatic and degenerative meniscus tears have difference gene expression

- Traumatic meniscus tears overall exhibited higher inflammatory/catabolic response
- Evidenced by higher levels of chemokines and MMPS

Conclusion: Elevated expression in traumatic tears may be associated with healing potential after surgery as well as future risk of OA in the knee
Causes for insult of the ECM

- Dehydration
- Poor nutrition
- Chronic inflammation
- AGEs
- Toxicity
- Injury

Extracellular Matrix

- Bone
- Ligament
- Tendon
- Cartilage
- Connective tissue
- Skin

- Adhesion
- Mechanical support
- Migration
- Proliferation
- Signaling

- Arthritis
- Atherosclerosis
- Cancer
- Asthma

Extracellular Matrix

- Integrin
- Cell membrane
- Talin
- Actin

Image © Aristo Vojdani, used with permission
The Extracellular Matrix is Composed of Tissues that Serve Multiple Purposes

“ECM is a conglomerate of substances in which biochemicals and biophysical properties allow for the construction, information, mechanical adhesion of cells and proteins, tissue repair, the adhesion, intracellular rearrangement. Kjaer, M. JR

A complex web of connective tissues that
- Provide adhesion to cells
- Act as a structural scaffold
- Actively participate in intracellular signaling
- Translates mechanical loading into cellular response

Key

Extracellular matrix — the fascial system is the largest system in the body and is the only system that touches every other system.
Matrix metalloproteinase (MMPs) enzymes damage collagen and connective tissue

- MMPs are collagen-digesting enzymes naturally produced by the chondrocyte during time of injury
- Poor diet, lifestyle, injury, tissue damage can trigger cell signals which can lead to the over-activated release of MMPs
- Excessive release of MMPs can damage healthy tendon and cartilage tissue

Litherland et al., JBC, Papers in press, March 10, 2008

Matrix metalloproteinases digest collagen and connective tissue

Modulate expression of MMPs to support healthy remodeling of connective tissue

A comprehensive strategy to support the health and integrity of extracellular matrix tissues

Nutrients that impact matrix metalloproteinases:
- HOPS & Berberine synergistically modulate MMP-13
- Selenium to address MMP-1 & MMP-2
- Folic acid to impact MMP-9

Nutrients that affect the lifespan and health of connective tissues:
- niacinamide to address tissue-damaging PARS

Additional nutrients:
- Zinc – to reduce cytokine release
- Biotin – to reduce NF-kappa production
ReCap

- **Phase 1: Acute**
  - Tissue swelling
  - Tissue congestion
  - Pain modulation

- **Phase 2: Sub-acute**
  - Reducing scar tissue formation
  - Aid in connective tissue remodeling
  - Support joint health
  - Reduce risk of re-injury and degeneration

- **Phase 3**
  - Continued connective tissue remodeling
  - Support wellness care:
    - Maintaining foundation nutrition
    - Reducing risk of re-injury

---

Stop doing sit-ups!

- Sit-ups reigning as a workout standard should be ended
- High profile exercise gurus and military experts stopped using sit-ups – poses too great of a risk of back injury
- Navy times called it “an outdated exercise today viewed as a key course of lower-back injuries”
- Canadian armed forces recently cut the sit-up from its fitness tests (concerns over injuries)
- Tony Horton (P90X creator) – no longer does sit-ups or crunches
Stop doing sit-ups! (cont’d)

- Sit-ups can put hundreds of pounds of compressive force on the spine – Dr. Stuart McGill, leader of spine biomechanics
- Dr. McGill found that the forces, combined with repeated bending of the lower back, squeezed the discs out to bulge leading to disc herniation and back pain
- US Army already started to phase out sit-ups for some soldiers
- Navy and marine corps also considering new fitness requirements

The answer: Plank pose

Vitamin D Supplement in patients with CLBP

Conclusion:
Vitamin D supplementation in deficient CLBP patients lead to improvement in pain intensity and functional ability

Vitamin D for disc degeneration (DD)

- Type-II diabetes risk factor for DD
- Diabetes damages small blood vessels
- Adversely affects discs with poor nutrient supply
- Vitamin D reduces inflammation and improves markers of insulin resistance
Vitamin D for disc degeneration (DD) (cont’d)

Study found:
- Degenerative changes in discs with type-II diabetes
- TGF-beta and IGF-1:
  - Were lowered in diabetic group than normal group
  - Highest in group without type-II diabetes
  - Significantly higher in experimental group compared to control group

Flow Chart to Help Doctors Create Protocol

Formulation for pain (acute and chronic)

I. Xanthohumol:
- Anti-arthritis
- Anti-inflammatory
- Antioxidant

II. Curcumin:
- Analgesic
- Anti-arthritis
- Anti-inflammatory
- Antioxidant
Formulation for pain (acute and chronic) (cont’d)

III. Ginger:
- Analgesic
- Anti-arthritic
- Anti-inflammatory
- Antioxidant

IV. Boswellia serrata extract:
- Analgesic: Reduces pain
- Anti-arthritic: Inhibits 5-LOX; Decreases cartilage damage
- Anti-inflammatory/Immunomodulatory effects
- Antioxidant

Conclusion: Curcumin accelerated injured sciatic nerve repair through reducing Schwann cells apoptosis and promoting myelination

Mechanism of Action (MOA) Summary

<table>
<thead>
<tr>
<th>Curcumin</th>
<th>Boswellia serrata</th>
<th>Ginger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition of pro-inflammatory cytokines, chemokines, and transcription factors associated with inflammation and pain</td>
<td>✓ Inhibits PLA2</td>
<td>✓ Inhibits COX-1 &amp; COX-2</td>
</tr>
<tr>
<td>Reduces serum levels of:</td>
<td>✓ Reduces TNF-α, IL-1β, IL-6, MCP-1</td>
<td>✓ Reduces COX-1 &amp; COX-2</td>
</tr>
<tr>
<td>Diminishes chondrocyte production of CXCL8 (IL-8)</td>
<td>✓ Inhibits NFκB</td>
<td>✓ Reduces WBC production of:</td>
</tr>
<tr>
<td>Reduces WBC production of:</td>
<td>TNF-α, IL-12, MCP-1</td>
<td></td>
</tr>
<tr>
<td>Inhibits NFκB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diminishes synoviocyte production of IP-10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Patients are like...

Anti Inflammatory drugs (NSAIDS) cause leaky gut.
Leaky Gut causes inflammation
FDA reverses its position on daily aspirin

FDA website:
“FDA has concluded that the data do not support the use or aspirin as a preventive medication by people who have not had a heart attack, stroke or CV problems, a use that is called “primary prevention”. In such people, the benefit has not been established but risks – such as dangerous bleeding into the brain or stomach – are still present.”

Ibuprofen?
Study published in The European Heart Journal – CV Pharmacotherapy (April 2017) reports that Ibuprofen is associated with a 31% increase risk of cardiac arrest

NSAIDs decrease pain but impair healing.
Nutraceuticals decrease pain and promote healing.

Dr. Robert Silverman, author of Inside-Out Health
….we can take it to the next level
"As a result of the common origins of immune cells and osteoclasts, when chronic inflammation ramps up our immune response, osteoclast activity gets ramped up, too."


INFLAMMATION PROMOTES BONE LOSS

"The receptor activator of nuclear factor κB ligand (RANKL) (along with its receptor), the receptor activator of nuclear factor κB and its natural decoy receptor, osteoprotegerin, are the final effector proteins of osteoclastic bone resorption."

Bone resorption

Peak Bone Mass (PBM)

- Peak bone mass is reached during young adulthood and contributes (positively or negatively) to a person's risk to developing osteoporosis later in life
- A higher PBM during childhood may offset osteoporosis risk in adults
- Optimal calcium intake should begin in childhood

Diet and fracture risk in post-menopausal (PM) women

- Healthy dietary pattern including adherence to Mediterranean diet lead:
  - A role in maintaining bone health in PM women and lower the risk of fractures
  - These women had an absolute risk reduction of 29%

*JAMA Internal Med. May 2016:645-52*

Anti-inflammatory diet reduces bone loss, hip fracture risk in women


**MCHC & calcium study**

- MCHC supplemented group increased bone density by 6.1%; calcium supplemented group showed no significant change; placebo group lost 5.5% of bone density
- Net difference in bone density in MCHC supplemented group over placebo – 11.6%


**Only young bovine bone used**

- MCHC (microcrystalline hydroxyapatite concentrate), produced from New Zealand free-range, pasture-fed cattle
- New Zealand government requires each batch of product be accompanied by veterinary signed certificates verifying safety and disease-free status of bovine source livestock
- MCHC (young bovine bone origin) contains more than just calcium and minerals; it contains both type I and type II collagen, and growth factors that help stimulate production of bone
Gut microbiome and bone health

- Emerging research: prebiotic fibers alter gut microbiome
- Enhances fermentation of fibers
- Leading to production of SCFA
- Enhances calcium absorption
- Positively influencing bone health


Nutritional Therapy for Bone Health

- A Mediterranean style Food Plan
- Nutrients for promoting a healthy gut
- Bone mineralization and density:
  - MCHC, vitamin D, Calcium, Phosphorous

Data shows that over 94% clinicians and 89% patients are interested in non hormonal prescription therapy for perimenopause and menopausal symptoms

• Women suffer needlessly throughout the menopause transition

A revolutionary therapy for the management of symptoms during the menopausal transition (perimenopause) and beyond

Study confirms plant-based therapies offer relief from common menopausal symptoms - JAMA

- The Journal of the American Medical Association (JAMA) recently published findings which reveal plant-based therapies to be associated with the reduction of the frequency of hot flashes and vaginal dryness
- The systematic review and meta-analysis of more than 6,000 menopausal women across 60+ studies, demonstrated that newer plant-based therapies showed significant improvements in the number of hot flashes experienced over a 24-hour period, as compared to conventional therapy
- The findings support the use of plant-based nutritional supplements as an effective tool for the relief of common symptoms of menopause
- The JAMA study included the assessment ERr 731®, an extract of Siberian rhubarb (Rheum rhaponticum L.)

ERr 731 was found to be associated with the reduction of hot flashes
Directions:

• Take ONE tablet with food, and a glass of water the same time of day
• Due to lack of research on this population, do not use if pregnant or nursing
• Like other supplements containing natural selective estrogen receptor modulator (SERM) compounds, Estrovera should be avoided in those with known or suspected estrogen-dependent cancer

Project Implementation

Putting it all together for your SUCCESS

Toxins, Toxins, Toxins

“You can’t be a clean fish in a dirty bowl.”
The Hidden Load
What’s invisible is hurting us!

More than 287 toxic chemicals found in newborn cord blood

Specific genes are turned on and off at certain time intervals, and any disruption of this finely-tuned DNA methylation regulation may persistently alter gene expression. The fetal epigenome is most susceptible during this developmental period to epigenetic modifiers in the maternal environment. An error during such a crucial time might lead to an abnormal phenotypic outcome in the offspring.


Exposure to Toxins

- Polybrominated diphenyl ethers (PBDEs): used as flame retardant
- Bisphenol A (BPA): packaging plastics
- Perfluorooctanoic acid (PFOA): non-stick cookware
- Acrylamide: a) carbs at high temperature; b) coffee
- Mercury: seafood
- Methyl tert-butyl ether (MTBE): a) second-hand smoke; b) gasoline additive
Association between urinary Bisphenol A concentration and obesity prevalence in children and adolescents

**Conclusion:** Urinary BPA concentration was significantly associated with obesity in this cross-sectional study of children and adolescents.

*JAMA* 2012;308(11):1113-1121

Bisphenol A may cause testosterone reduction by adversely affecting both testis and pituitary systems similar to estradiol.


Cash Register Receipts – A Source of BPA

[Link to article](http://dx.plos.org/10.1371/journal.pone.0110509)
BPA is an Ovarian Toxicant

• “I think more scientists working today agree that BPA is an ovarian toxicant” — Dr. Flaws
• Review research published in Environmental Health Perspectives: ovarian toxicity among the most consistent and strongest effects found “in both animal models and in women”

BPA has adverse effects on in-vitro fertilization

Conclusion: Exposure to BPA may lead to reduced quality of embryos during reproduction. Study shows BPA could be the cause for decreases in frequency of implantation pregnancy and live birth rates in couples seeking in-vitro fertilization

BPA alternative disrupts normal brain-cell growth, is tied to hyperactivity

University of Calgary: Thinks it’s research is first to show that bisphenol-S – ingredient in many products bearing “BPA-free” labels – causes abnormal growth surges of neurons in an animal embryo
BPA substitute can trigger fat cell formation: Chemical used in BPA-free products exhibits similar endocrine-disrupting effects

The Endocrine Society, Mar 22, 2016

Mom’s exposure to BPA during pregnancy can put her baby on course to obesity

• Associated measures of obesity in children at age 7
• 94% of pregnant women had detectable levels of BPA


BPA-autoimmunity to brain and nerve tissue

• BPA impacts the brain:
  • Binds to human tissue
  • Can cause immune response that triggers autoimmunity to myelin (coats brain and nerve fibers)
  • Avoid BPA for those with brain inflammation, M/S, autism

Women use **168 chemicals** on their bodies daily

- Average women in the US use 12 personal care products daily
- Contains 168 different chemicals
- Men exposed to 85 chemicals daily
- Women with higher levels experience menopause 2 to 4 years earlier

**Plus One.** Jan 28, 2015.
ABC News. April 27, 2015

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**80% greater autism risk with high prenatal exposure to PCBs**

*Environmental Health Perspectives, August 23, 2016*

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**Phthalates**

**Results:**
- Increasing age and western diets associated with higher concentrations of phthalates
- CVD, type-2 diabetes and high blood pressure increased among those men with higher total phthalate levels
- Elevated phthalate levels increased inflammatory biomarkers

*Medical News Today. July 14, 2017*
Fast food may expose consumers to harmful chemicals called phthalates

Flame retardants harm the thyroid

- Flame retardants (PBDE) – found in old furniture and some clothing; women with high levels at risk for thyroid trouble
- PBDE increased thyroid dysfunction from 48 to 78 percent

US Environmental Protection Agency, 2012. Toxic release inventory national analysis overview

Reported that 3.63 billion pounds of chemicals were disposed of or released to air, water, or land
Toxic Metals

Impact of cadmium exposure on the association between lipopolysaccharide and metabolic syndrome
300% increase in diabetes amongst those in the high cadmium group

Mercury exposure in young adulthood and incidence of diabetes later in life
65% more common in those with highest mercury exposure

Association of urinary metal profiles with altered glucose levels and diabetes risk. A population-based study in China
Aluminum and lead linked to elevated fasting blood sugar

Ingested Toxins

The U.S. allows over 10,000 chemical additives to our food supply

How do I know if I’m Toxic?

Symptoms- (Medical symptom questionnaire): Fatigue, sleep disturbances, GI problems, headaches, allergies, mental fog and anxiety

Physiology- Salivary pH tell us if you have a higher body acidity and increased inflammation
Metabolic Detoxification Questionnaire (MDQ)

A qualitative review of patient systems to be used in conjunction with your physical exam and health history to help you determine severity of patient symptoms and duration of detoxification.

Tracking tool that allows practitioner and patient to establish a baseline and evaluate symptom improvement.

10 and 28-day protocol

Whole Body Alkalization

<table>
<thead>
<tr>
<th>PH Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.6 &amp; below</td>
<td>Dangerous Range. Seek assistance of a licensed professional</td>
</tr>
<tr>
<td>6.0 - 6.2</td>
<td>Unhealthy Range. Consider proper dietary changes</td>
</tr>
<tr>
<td>6.4 - 6.8</td>
<td>Moderate Range. Consider slight dietary adjustments</td>
</tr>
<tr>
<td>7.0 - 7.4</td>
<td>Optimal Range for a 24-hour period</td>
</tr>
<tr>
<td>8.0 - 9.0</td>
<td>Too Alkaline. While not common, this is unhealthy</td>
</tr>
</tbody>
</table>

WHEN PEOPLE SAY THEY DON'T DETOX

STOP! DON'T YOU KNOW YOU HAVE TOXINS?
Reduce Your Exposure

Detox Your Body

The Liver Has Many Functions

The liver works in the body like an oil filter works in a car

Your Liver:
- Processes the body’s stored sugar (glycogen)
- Converts the sugar you eat to usable energy
- Creates bile to aid in the digestion of fats
- Removes hormones (estrogens, epinephrine)
- Converts thyroid hormones
- PRIMARY DETOXIFICATION ORGAN

Remember...

- How well our body detoxifies determines our susceptibility to disease
- If we take in toxins quicker than our body can get rid of them, we are in trouble
- Toxic overload is a silent killer
Phase II Pathways

- **Sulfation** – toxins attach with sulfur compounds. Primary cortisol pathway
- **Glucuronidation** – glucuronic acid combines with toxins. Primarily aspirin pathway
- **Glutathione conjugation** – the attachment of glutathione to toxins to detoxify fat soluble toxins
- **Acetylation** – acetyl co-a is attached to toxins
- **Amino acid conjugation** – conjugation of toxins with amino acid xenobiotics
- **Methylation** – involves conjugating methyl groups to toxins. **estrogen**

10-Day DETOX

1) Nutritional Detox Powder

**Regulating nutrients:**
- L-Glycine
- Magnesium
- Support optimal function of Phase I and Phase II enzymes

**Antioxidants for support of Phase II:**
- Comprehensive vitamin profile, including vitamins A, C, E and a broad spectrum of B vitamins help neutralize reactive intermediary compounds
- Pantothenic acid supports the production of ATP to power the reactions
Leading edge nutrients

- Xanthohumol
- Broccoli sprout and floret powder, broccoli seed extract
- Superoxide dismutase (SOD)
- Isomaltooligosaccharides (IMO)
- N-acetylcysteine (NAC)

Nrf2 on Cellular Antioxidants and Detoxification

There are no drugs that up-regulate Nrf2 but there are several natural ingredients which do

Nrf2 – Nuclear factor erythroid-2

- Activates transcription of 500 genes
- Most are cytoprotective functions
- Detoxification of both xenobiotics/toxic metals
- Antioxidant activities – over 2 dozen genes
- Produce anti-inflammatory changes
- Improves mitochondrial function

Metabolic Detoxification
The power of Keap1/Nrf2 activation

- Cruciferous vegetables such as broccoli accumulate significant concentrations of glucoraphanin (a glucosinolate)
- Glucoraphanin is converted in vivo to biologically active sulforaphane (an isothiocyanate). This conversion requires myrosinase enzyme
- Sulforaphane (SF) is a potent activator of the body’s own antioxidant and detoxifying enzymes via the Keap1/Nrf2 pathway and is the compound responsible for the many positive health benefits associated with Broccoli consumption

```
Glucoraphanin + Myrosinase → Sulforaphane + Glucose
```

Broccoli sprout extract helps type-2 diabetes

- **Sulforaphane** leads to significant improvement in fasting blood glucose levels (type-2 diabetes)
- Reduces amount of glucose produced by cultured liver cells
- Reverses abnormal gene expression in the liver

*Science Translational Medicine, 14 June 2017 (Ref)

Sulforaphane ameliorates obesity

Based on its two functions:
- Energy consumption by browning of adipocytes
- Reduction of metabolic endotoxemia through improving gut bacterial flora

**Results:**
- 15% lower weight gain vs. placebo
- Visceral fat reduction
- Blood glucose level improvement

*Nrf2 pathway*
Metabolic Detoxification
The Importance of Acid-Alkaline Balance

"Metabolic detoxification using a high vegetable diet in conjunction with supplementation of an effective alkalizing compound, such as potassium citrate, may shift the body's reserves to become more alkaline."

Metabolic Detoxification
The importance of metallothionein for support of heavy metal metabolism

Support metabolism of heavy metals but do not facilitate excretion of certain healthful minerals (calcium, magnesium, selenium, zinc)

Body's natural mechanism for eliminating heavy metals

Metallothionein binds to heavy metals in the cell, transports heavy metal out of the cell to the liver, conjugated with glutathione (phase II detoxification) transformed to mercapturate, excreted via urine or stool.
10-Day Detox

2) A capsular formulation to support detoxification: supports detoxification. Provides bifunctional support to enhance the activities of several liver detox enzymes while promoting balanced activity of Phase I and Phase II detox pathways.

3) Eating plan: a modified elimination diet rich in vitamins, minerals, and phytonutrients reduces the allergen and toxin load, helping the body to detoxify efficiently:
   a) Listing of foods to choose from for Days 1 – 10
   b) Sample recipes/menu plan for each day
   c) 3 meals a day

Nutrients that balance Phase I & Phase II enzymes
- Ellagic acid from pomegranates
- Catechin from decaffeinated green tea
- Watercress glucosinolates

Support multiple Phase II detoxification pathways
- Sulfation: N-acetylcysteine, Sodium Sulfate
- Acetylation: Vitamin B5, Magnesium
- Methylation: Vitamin B12, Choline, 5-MTHF

Antioxidant and overall liver function support
- N-Acetylcysteine
- Silymarin
- Vitamin C & Vitamin A

Additional Daily Support
Addition of a daily phytonutrient supplement recommended to support balanced clearance of toxins.

Take a Probiotic to Detoxify the Body

• Two new studies: taking a probiotic can help body detoxify
• Nutrition journal:
  1) Probiotics help detoxify body of heavy metals, free radicals, and dangerous bacteria by enhancing natural antioxidant status in body
  2) Probiotic also significantly increased glutathione status (the number one internal antioxidant in the body) and decreased malondialdehyde

10-Day Detox Protocol

• Nutritional Detox Powder: 2 scp. BID
• A capsular formulation to support detoxification: 2 caps BID
• Modified elimination diet
• Probiotic – lactobacillus acidophilus, NCFM, b. lactis BI-07: 1 cap daily
  • 15 or 60 billion live organisms

pH Helps to Defeat Pain and Inflammation

Dr. Rob’s Take

• Muscle/joint disorders may develop from:
  • Improperly managed inflammation
  • Acid/alkaline imbalances
• The body has a choice to drop toxins off at a storage depot if the liver cannot dispose of the toxins at the time
• Handy place: a) fat cells; b) collagen (extracellular matrix)
• Fat cells enlarge and water infiltrates the surrounding extracellular matrix
Next step towards your goal...

- Continue detox
- Estrogen detox
- Heavy-metal detox
- Gut restoration
- General wellness
- Body-composition/weight loss

On-going detox

Formula for Balanced Clearance of Toxins Through Phase I and Phase II

Daily bifunctional support for detoxification:
- Supports the balance between Phase I and Phase II
- Provides nutrients used to support multiple Phase II detoxification pathways
- Silymarin and other traditional herbs provide antioxidant activity and supports overall liver function
Glutathione: Antioxidant and detoxifying function

- Help reduce free radical formation
- Function in the regeneration of glutathione
- Aid in phase II detoxification

Bifunctional Modulators support balance between Phase I and Phase II

- Inhibit overproduction of Phase I enzymes and up-regulate production of Phase II enzymes with:
  - Decaffeinated green tea catechins
  - Ellagic acid
  - Watercress glucosinolates

Antioxidants
The missing piece to support glutathione

- Help reduce free radical formation
- Function in the regeneration of glutathione
- Aid in phase II detoxification

Glutathione: Antioxidant and detoxifying function

- GST - glutathione-S-transferase
- GSSG - glutathione disulfide
- GSH - glutathione reduced
- NADPH - Nicotinamide adenine dinucleotide phosphate reduced
- NADP+ - Nicotinamide adenine dinucleotide phosphate oxidized
- SOD - Superoxide dismutase
Kidney Detoxification/Health

- Formulated with NAC, targeted vitamins, and traditional Chinese herbs to help protect kidneys from oxidative stress
- Promote healthy kidney detoxification
- Support cardiovascular health for individuals with renal stress concerns
- Designed to help protect kidneys from oxidative stress

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<tr>
<td>Vitamin B6</td>
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<tr>
<td>Folate (as calcium-L-5-methyltetrahydrofolate)</td>
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<tr>
<td>Vitamin B12 (as methylcobalamin)</td>
<td>1250 mcg</td>
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<tr>
<td>Cordyceps (Paecilomyces hepiali) mycelium extract (standardized to 4% cordycepic acid and 0.25% adenosine)</td>
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<tr>
<td>Chinese salvia (Salvia miltiorrhiza) root</td>
<td>200 mg</td>
</tr>
<tr>
<td>N-AcetylCysteine</td>
<td>200 mg</td>
</tr>
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</table>

Provide your patients with a powerful formula for balanced daily detoxification

- Bifunctional detoxification support:
  - Methylated vit. B12, folic acid with nutrients to balance phase I and phase II
  - Antioxidant protection and detoxification support:
    - Vit. C, selenium, niacin (niacinamide), n-acetyl-L-cysteine (NAC), broccoli extract
    - Kidney detoxification and kidney health:
      - Vit. B6, B12, Folate, cordyceps, Chinese salvia, NAC
  - Once daily convenient packet

Heavy Metal Detox
Heavy Metal Formula

- Zinc (as zinc citrate).................................................. 5 mg
- Andrographis (Andrographis paniculata)........... 150 mg
- Turmeric (Curcuma longa) Rhizome Extract..... 158 mg
  [standardized to 95% (150 mg) curcuminoids]
- Proprietary Blend of Hops (Humulus lupulus)... 2645 mg

Heavy-Metal Detox – On-Going Care

1) One packet to provide on-going liver and kidney detoxification
2) Supports the genetic expression of enzymes involved in the metabolism of heavy metals (3 tabs BID)
3) Minimum 30 days

Liver Detoxification of Estrogens

- Metabolism of estrogen takes place primarily in the liver
- Promoting favorable phase I and phase II estrogen clearance is key for female performance and long-term health

Birth control pills + Hormone Replace Therapy = exogenous estrogen
Estrogens, whether you make them or take them,  
Or whether you have been unknowingly intoxicated by them,  
You need to get rid of them every day . . .  
IN A HEALTHY WAY!

**Estrogen Elimination Basics**

Problems with detoxification occur when:
1) Nutritional (micro or macro) deficiencies lead to poorly performing enzymes
2) Genetic alterations lead to poorly performing enzymes
3) Estrogen elimination is impaired through constipation or increased beta-glucuronidase
4) Underlying liver or gall bladder disease

**Action of Beta-Glucuronidase**
30-Day Female Estrogen Detox

- Women’s estrogen detox formula: 2 scps BID
- Detox support capsules: Provides bifunctional support to enhance the activities of several liver detox enzymes while promoting balanced activity of Phase I and Phase II detox pathways (3 caps BID)
- Methylation support formula: Involves conjugating methyl groups to toxins and SAMe (2 tablets on empty stomach)
- Probiotic: lactobacillus acidophilus, NCFM, b. lactis BI-07: 1 cap daily
- Eating Plan: a modified elimination diet rich in vitamins, minerals, and phytonutrients reducing the allergen and toxin load, helping the body to detoxify efficiency.

Promoting Weight loss without Supporting Detox is Malpractice!

Persistent Organic Pollutants

Weight Loss May Push Toxins Into Bloodstream

“Serum concentrations of most POPs were higher in those with long-term weight loss”
Juicing and other fasting programs can actually deprive your body of essential nutrients needed to support detoxification.

Detoxification – 21st Century Model

- Body’s innate process of removing or altering metabolic wastes and acquired toxins
- Enables the body to perform its life processes unencumbered by detrimental elements and disruptive molecules
- Body’s natural innate processes to “recycle” or “take out the trash”

Assault on The King

- 20th century detox – effective
- No longer effective in the 21st century
- World changed
- In the past – 20th century toxins could easily be removed
- But today, the toxins we are exposed to are more potent

The detox that is necessary now should be more powerful and multidimensional
Assault on The King

- Today - more direct damage occurring inside the cells
- Game changed from fat cells/EC Matrix to the intracellular life process
- In chess terms, 20th century toxins assaults - fielded by pawns
- 21st century assaults - directly impacting the King

The Best Way to Detox

- Support the liver
- Assist the body to remove toxins from the storage depots (fat cells and extracellular matrix)
  - Support the intracellular processes (methylation, ATP production, free-radical quenching, telomere repair, membrane fluidity)

Protocols for cell membrane fluidity:
- Alpha-lipoic acid
- Omega-3 fatty acids
Healthy, Lean, Strong

91 year-old Betty Calman shows off the peacock pose.

Are You Kidding Me?

- Tampons and pads are regulated by the FDA as medical devices.
- Medical devices are not required to disclose ingredients.
- Tampons – made from cotton, rayon, pulp fiber.
- 94% of cotton in U.S. = GMO!

Are You Kidding Me? (cont’d)

- These materials may contain toxic disinfection by-products:
  a) From chlorine bleaching
  b) Dioxins, furans, DBP
  c) Pesticides from non-organic cotton
- FDA recommends that tampons be free of dioxine, etc...
- It is not a requirement.
- Studies have shown the toxins are present in brands studied.
Clear white tampons and pad

• All fibers must be bleached
• Chlorine creates toxic dioxin
• Dioxin collects in your fatty tissues
• EPA called dioxin a serious public health threat with no “safe” level of exposure

Clear white tampons and pad (cont’d)

• Low or trace levels of dioxins lead to:
  • Abnormal tissue growth in the abdomen and reproductive organs
  • Abnormal cell growth throughout the body
  • Immune system suppression
  • Hormonal and endocrine system disruption

FYI

• Feminine-care products are classified as “cosmetics” by FDA
• Means no specific tests are required to demonstrate their safety
• Avoid fragranced tampons
• Use “unscented” products
• Chlorine-free or unbleached tampons/pads
• Use organic – chemical-free (non-GMO particles)
Try This...

• Burn an organic tampon/pad – it burns slow and clean
• Burn a commercial brand (undisclosed ingredients)

  Creates black smoke and thick residue
  Indicates the pad has dioxins

Post Detox...

1) Energy levels (fatigue), skin, hair, overall look
2) Musculoskeletal:
   a. O.A.
   b. Muscle aches
   c. Fibromyalgia
3) Weight loss/body composition
4) Academic improvement
5) Combination with gut protocol
6) Heavy metal
7) Hormone issues
Case scenario

• Elevated HbA1C
• One major cause is an unrecognized B6 deficiency
• Test xanthurenic organic acid test
• Patient takes B6 and no improvement
• **Zinc deficiency**
• When a hidden zinc deficiency is present, the body cannot convert B6 to its active form
• This is essential in normalizing the glycosylated hemoglobin

Case scenario (cont’d)

• Elevated stored phthalates in the body interfere with zinc metabolism
• Root-cause resolution HbA1C – B6 deficiency – zinc deficiency – stored phthalates

“....one third of what we eat keeps us alive.
Two thirds of what we eat keeps doctors alive”
Unknown

YOU ARE WHAT
YOU EAT
Laboratory Tests to Consider

- Systolic and diastolic blood pressure
- ESR (erythrocyte sedimentation ratio) (to detect certain inflammatory diseases, e.g., RA, polymyalgia, rheumatica)
- Levels of vitamins (C, B₆, B₁₂, folic acid)
- Liver enzyme panel
- CRP (C-reactive protein)
- AA/EPA ratio (analysis of fatty-acid) – ideal ratio 1.5
- Homocysteine
- ANA
- Tissue pH (urine/saliva) – 7.0 optimum reading
- BIA (body composition, phase angle, hydration status)
Laboratory Tests to Consider (cont'd)

- Fasting glucose, 2-hour glucose
- Fructosamine
- Hemoglobin A1C
- Fasting insulin
- Fibrinogen – increased in diseases involving tissue damage or inflammation
- Cholesterol:
  - Traditional - outdated
  - Exercise physiology evaluation:
    - Strength, balance, flexibility, aerobic capacity, endurance
  - Vitamin D

Leading-edge cholesterol tests

- Total cholesterol - Total amount of cholesterol in your blood which includes mainly two forms, your 'good' HDL cholesterol and your 'bad' LDL cholesterol
- Triglyceride – Major form of fat stored in the blood
- HDL-C - 'Good' cholesterol in your blood made up of many different particles; five major particles are important to heart disease risk
- ApoA-I - Protein that is located in your 'good' HDL cholesterol

Leading-edge cholesterol tests

- LDL-C - 'Bad' cholesterol in your blood
- Lp(a) - A particle similar to LDL; your level of Lp(a) is determined by your genes. You want a low amount
- ApoB - Protein that is located in your 'bad' LDL cholesterol
- sdLDL-C - Small, dense form of your 'bad' LDL cholesterol; increased levels indicate build up of fatty materials in your arteries
Lipoprotein-A

- Estimated that 1 in 5 people globally have inherited Lp(a)
- 63 million in the U.S.
- If you have high Lp(a) each of your children has at least a 50% chance of inheriting it

The Risk is in the LDL Particle Number

- 1st ring: Large LDL (Pattern A)
- 2nd ring: Small LDL (Pattern B)
- LDL Cholesterol Balance

HDL/Total cholesterol ratio

- 0.24 or higher is ideal
- Under 0.24 – low
- Less than 0.10 – very dangerous
Triglyceride/HDL ratio

- New benchmark for assessing health
- People with highest triglyceride/HDL ratio were 16 times more likely to develop HD
- Ideal ratio 2:1

Journal Circulation

Triglyceride/HDL

- 2 or less is ideal
- 4 – high
- 6 – much too high

<table>
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<tr>
<th>Ratio</th>
<th>Risk Level</th>
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<td>1:1 or Less</td>
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<tr>
<td>2:1</td>
<td>Low Risk</td>
</tr>
<tr>
<td>3:1</td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>4:1</td>
<td>High Risk</td>
</tr>
</tbody>
</table>

Inflammation Testing

- MPO — myeloperoxidase – early indicator of patient’s CVD risk:
  - Elevated MPO indicates presence of unstable plaque in the artery wall
- HOMA-IR — homeostatic model assessment of insulin resistance. Marks for both the presence and extent of any insulin resistance that the patient might currently express:
  - Fasting blood sugar and responsive insulin
- Lp-PLA2 — assess risk of CAD, stroke:
  - An enzyme that appears to play a role in inflammation of blood vessels
Cholesterol: The Good, the Bad, and the Healthy Diet

Cholesterol: a friend or a foe? Is cholesterol a cause of heart disease or a misunderstood messenger?

Cholesterol Facts:
- Cholesterol is a part of every cell membrane
- Cholesterol is a precursor of:
  1. Steroid Hormones (Estrogen, Testosterone, Progesterone, Cortisol)
  2. Bile Acids (fat digestion)
  3. Vitamin D (osteoporosis)
  4. Cholesterol only appears to be problematic when oxidized

Swenson FL. The role of the cholesteryl ester transfer protein in lipoprotein metabolism. Diabetes Metabolism Review. 1991;7:139-153
Free Radicals and Oxidative Stress

• "...it is the oxidation of LDL, which is now believed to be the focal pivotal step in the process of atherosclerosis."

• "Preventing the oxidation of LDL may be the most powerful means of preventing cellular injury leading to atherosclerosis."

Sinatra ST, DeMarco J. Free radicals, oxidative stress, oxidized low-density lipoprotein (LDL), and the heart: antioxidants and other strategies to limit cardiovascular damage. Conn Med 1995; 59 (10):579-88

ApoB/ApoA-I Ratio: Strong New Risk Factor for CVD

An elevated apo B/apo A-I ratio may constitute a cardiovascular disease risk factor. The results indicate that the apoB/apoA-I ratio is a simple, accurate, and new risk factor for CV disease — the lower the apoB/ApoA-I ratio, the lower the risk.

Apo A's remove lipids, Apo B's deposit lipids

Legend:
TG: Triglycerides
Chol: Cholesterol
Blood cells
Blood flow
Apo B, Apo A animation
Credit: Jeff Bland, Ph.D.
Elevated Cholesterol Is An Important Risk Factor For Heart Disease And Stroke

Raised total cholesterol is highly prevalent, affecting 13.4% of US adults²

The prevalence of high cholesterol increases with age


Clinical Biomarkers Plot the Trajectory of Cardiovascular Risk

The Interaction of Dyslipidemia and Oxidative Stress/Inflammation, Contribute to Vascular Disease

Cardiometabolic syndrome

• Inflammation – free radicals, high blood sugars, stress, blood-clotting problems
• E.g.
  • Chronic inflammation lowers testosterone production – body produces more cholesterol
  • Autonomic nervous system problem – more cortisol = requires more cholesterol

Cholesterol is like the body’s “band-aid” – when there is inflammation it tries to patch things up

Status – they lower inflammation and also act as antioxidants

• Should you fast before a cholesterol test
• Has been “preferred”
• Repeated studies found no clinically significant differences between fasting and none fasting
Rethinking heart health

Myths:
• High cholesterol is the root cause of CV disease
• LDL cholesterol is bad
• Eating cholesterol and saturated fat raises blood-cholesterol levels
• Statins save the lives of healthy people w/o heart disease

New statin guidelines

• Everyone 40 and older should be considered for the drug therapy

My answer:
Statins have important side-effects (under reported by big pharma). Ultimately humans are not predestined to heart attack in middle-age as populations worldwide have shown. Let's first consider everyone eligible for a therapeutic lifestyle program.

Statins increase risk of diabetes

• Study of almost 26,000 healthy people, those taking statins were 87 percent more likely to get type-2 diabetes

• Randomized controlled trial of 153,840 women, those who took statins were 48% more likely to get type-2 diabetes
www.theNNT.com

• Independent group of doctors and scientists created platform for reviewing literature on various medical topics
• No pre-existing heart disease who took statins for 5 years:
  • Helped prevent heart attack – 1 in 104
  • Helped prevent stroke – 1 in 134
  • 1 in 10 had muscle damage and pain
  • 1 in 50 developed diabetes
  • Slightly better numbers if had a previous heart attack

Global study lays groundwork for daily statin usage to prevent heart disease

• Researches are suggesting the daily usage of statins to lower blood pressure and cholesterol
• Over 5.6 years:
  • 3.7% (10mg statin) had heart attacks, strokes or heart-related deaths
  • Compared to 4.8% of those who took a placebo
  • They claim a 24% reduction in risk
• New guidelines increased the number of Americans eligible for statins by 20 million people

Are you kidding me?!

The trial was **funded** by Canadian Institutes of Health and Research and **AstraZeneca**, the pharmaceutical company that makes the statin **Crestor**, which was used in the study
Fitness downside to statins

- Statin shown to make exercise more difficult and less beneficial
- Activity levels consistently declined throughout experiment
- Lost grip strength
- Large muscles fatigued earlier
- Exercise vs. no exercise

PLOS One, Dec 2016
NY Times, Jan. 4, 2017

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Muscle rupture associated with statin use

**Conclusion:** Data suggests that use of statins is associated with muscle rupture

[Image of muscle rupture]

Br J Clin Pharmacol, Apr 13, 2016

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Statin Use Increases Odds of Back Disorder: Cohort Study

- Statins use increased odds of:
  - Spondylosis
  - IVD disorder
  - Herniated disc
  - Spinal stenosis

JAMA Internal Medicine, May 1, 2017
Yo-yo dieting may increase risk of heart disease death

- Women of normal weight who subsequently experienced yo-yo effect were 3.5 times more likely to die from sudden cardiac arrest than women whose weight remained stable.

American Heart Association, Nov. 15, 2016

European Society of Cardiology Annual Meeting, Italy. Aug 28, 2016

Mediterranean diet compare their 37 percent lower risk of HA to a 24 percent lower risk for those taking statins.

Management of Dyslipidemia is Critical for at Risk Patient Groups

**Powdered nutritional support** to help manage distinctive nutritional requirements of patients with dyslipidemia.

**Powdered medical food** can be used by individuals with:
- Cardiovascular disease
- Metabolic syndrome
- Obesity and/or central adiposity
Powdered Nutritional Support

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<tr>
<th>Ingredient</th>
<th>Benefit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smart Macronutrient Profile</td>
<td>• Balanced macronutrient ratio to support healthy metabolic controls</td>
<td>Babault et al., Int J Sports Physiol Perform. 2015;10(3):265.</td>
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<tr>
<td>XNT ProMatrix® (xanathumol)</td>
<td>• XNT ProMatrix increases bioavailability by 81% over 6-hour period.</td>
<td>Metagenics data on file.</td>
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<td>Flax seed</td>
<td>• Plant-based omega-3 fatty acids</td>
<td>Ursoniu, et al., Clin Nutr, 2015</td>
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<tr>
<td>Flax seed</td>
<td>• Plant-based omega-3 fatty acids</td>
<td>Metagenics data on file.</td>
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</tbody>
</table>

Xanthohumol – Cardiovascular Models

Xanthohumol has been shown in pre-clinical models to have a protective effect in the development of atherosclerosis in susceptible disease models.1,2

Pre-clinical research shows xanthohumol modules lipid metabolism through reducing lipid synthesis in the liver1

In an animal model, xanthohumol significantly lowers body weight and plasma glucose levels.3

• The suppression of postprandial hyperglycemia may be due to xanthohumol’s effect in inhibiting the enzyme α-glucosidase.4

• The suppression of postprandial hyperglycemia may be due to xanthohumol’s effect in inhibiting the enzyme α-glucosidase.4

• Concentrated source of xanthohumol allows lower daily dosage for beneficial effect.1

• 1700 mg per day reduced plasma LDL by 24.4% in conjunction with dietary intervention (Figure 1).5

• REDUCOL® has been shown to alter cholesterol synthesis, helping to reduce plasma cholesterol.6

Selecting A Non-GMO, Soy-free, Evidence-based Phytosterol: REDUCOL® (80% B-sitosterol)

5. Selecting A Non-GMO, Soy-free, Evidence-based Phytosterol: REDUCOL® (80% B-sitosterol).
Due to Structural Similarity, Plant Sterols Compete with Cholesterol for Absorption in the Intestine

Cholesterol displaced from the micelles is not absorbed and is excreted in the stool. When added to the diet, phytosterols can inhibit the absorption of cholesterol, likely through the disruption of the intraluminal solubilization step. Subsequent change in cholesterol synthesis contributes to the plasma cholesterol balance.

IMOs: a Source of Prebiotic Soluble Fiber for Lipid Management

1 serving provides 5 g of soluble fiber from iso-malto oligosaccharides (IMOs)

- Supplementation with IMOs has been shown to:
  - Reduce total cholesterol\(^2\)
  - LDL cholesterol\(^3\)
  - Plasma triglycerides\(^1\)
  - Increase HDL cholesterol\(^1\)
- Increased production of short chain fatty acids (SCFA)\(^4\)
  - This is relevant to subjects with metabolic dysfunction, as SCFA stimulate gut peptides involved in satiety and insulin secretion\(^5\)

In clinical trials,
10 g IMO daily for 4 weeks

- Reduced total Cholesterol, plasma TG and improvements in HDL (+39 %)
- Increased SCFA production

Introducing the perfect 10

Omega 7 + 3 Combination = Heart Health
Perfect 10 – for Heart Health

• Delivers a powerful combination of purified omega-7 and omega-3 fatty acids to provide targeted support for cardiovascular health
• The unique levels and ratios of omega-7 and omega-3 fatty acids are designed to reduce serum triglycerides and blood levels of CRP

Purified Omega-7

• Each softgel provides 105mg of palmitoleic acid from omega-7, purified to remove palmitic acid
• Palmitic acid is a saturated fatty acid which has negative effect on important aspects of metabolic syndrome
• Many unpurified palmitoleic acid preparations, such as those from sea buckthorn, may contain high concentrations of palmitic acid

Concentrated Omega-3

Provides a concentrated dose of 500mg of combined EPA and DHA in each enteric, easy-to-swallow, softgel with a natural lemon flavor
Health Benefits of Omega-3s

• Widely studied, with over 20,000 published scientific papers that support health benefits
• Benefits include support for cardiovascular health, healthy brain development and improve cell membrane structure

Omega-3 Health Benefits

A large, consistent beneficial effect of omega-3 fatty acids was found for triglycerides

Omega-3 fatty acid

• Omega-3 FA able to stimulate activation of brown and beige adipose tissue
• This allows for the development of new therapies for obesity and other metabolism diseases

EPA/DHA reduce risk of CHD

Study showed:
“6% reduced risk among RCTs, coupled with an 18% risk reduction in prospective cohort studies – tell a compelling story about the importance of EPA/DHA for CV health”
“This provides a most comprehensive quantitative assessment”

Other findings:
• 16% decrease with high triglycerides
• 14% decrease with high LDL

Mayo Clinic proceedings, Jan. 2017;82(1):15-29

Consumption of omega-3 linked to lower risk of fatal heart disease

JAMA Internal Medicine, June 2016

Omega-3 fatty acids aid healing after heart attack

• High dose of omega-3 FA (4 g. daily) from fish oil for 6 months after heart attack improved function of the heart and reduced scarring in the undamaged muscle

Circulation, August 2016
**Case Study: 44 Year Old Male**

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</tr>
<tr>
<td>Lp[a]</td>
<td>27</td>
</tr>
<tr>
<td>HbA1c</td>
<td>6.4</td>
</tr>
<tr>
<td>HOMA-IR</td>
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</tr>
<tr>
<td>Glucose</td>
<td>114 (fasting)</td>
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**4 Weeks**

<table>
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<tbody>
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<td>Weight</td>
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<tr>
<td>Total Cholesterol</td>
<td>248</td>
</tr>
<tr>
<td>LDL</td>
<td>148</td>
</tr>
<tr>
<td>HDL</td>
<td>37</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>140</td>
</tr>
<tr>
<td>Apo B</td>
<td>119</td>
</tr>
<tr>
<td>Apo A-1</td>
<td>150</td>
</tr>
<tr>
<td>Lp[a]</td>
<td>24</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.9</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.6</td>
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<tr>
<td>Glucose</td>
<td>100 (fasting)</td>
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### 8 Weeks

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<tr>
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</tr>
<tr>
<td>LDL</td>
<td>114</td>
</tr>
<tr>
<td>HDL</td>
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<tr>
<td>Triglyceride</td>
<td>126</td>
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<tr>
<td>Apo B</td>
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<td>Apo A-1</td>
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<tr>
<td>LPLA</td>
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<tr>
<td>HDLMMAR</td>
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<td>Glucose</td>
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### 12 Weeks

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<tbody>
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<tr>
<td>Total Cholesterol</td>
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<tr>
<td>LDL</td>
<td>98</td>
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<tr>
<td>Triglyceride</td>
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</tr>
<tr>
<td>Apo B</td>
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<tr>
<td>Apo A-1</td>
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<td>LPLA</td>
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<tr>
<td>Glucose</td>
<td>86 (fasting)</td>
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</tbody>
</table>

### Dyslipidemia Protocols

1. Powdered nutritional support – 2 scp BID
2. Paleo/Mediterranean diet
3. Omega-3 FA – 2 sg BID or omega 7 + omega 3 – 2 sg BID
4. Lactobacillus acidophilus NCFM/B.lactis Bi-07 – 1 daily
5. Specialized pro-resolving mediators – 2 daily