



Functional Medicine Approaches to Manage Metabolic Syndrome and Obesity

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- Notice of Requirements For Successful Completion
 - Please refer to learning goals and objectives
 - Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
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 - Participants will be notified by speakers to any product used for a purpose other than for which it was approved by the Food and Drug Administration.
 - All nutraceuticals discussed although recognized in medical journals are not FDA approved

Ali Miller, RD, LD, CDE

- Background in Integrative naturopathic approaches using Food-As-Medicine
- Clinically using ketogenic diet and functional medicine since 2009
- Naturally Nourished Podcast, Virtual Practice & Supplement Line*
- Author of *Naturally Nourished: Food-as-Medicine for Optimal Health* (2015), *The Anti-Anxiety Diet* (July 2018), and *The Anti-Anxiety Diet Cookbook* (Sept 2019)



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DISEASES (above the water line): Diabetes, Cancer, Heart disease, Arthritis, Auto-Immune diseases, Fibromyalgia, Obesity.

UNDERLYING CAUSES (below the water line): Inflammatory imbalances, Structural imbalances, Immune imbalances, Digestive, absorptive, and microbiological imbalances, Hormonal imbalances, Detoxification, Mitochondrial dysfunction, Toxic chemical exposure.

Functional Medicine: Treating the ROOT Cause (circled in blue)

Underlying influencers to consider:

- Microbiome and gut metabolites
- Endocrine disruptors and detoxification mechanisms
- Antioxidant capacity and nutrient deficiency
- Insulin resistance and frequency



Examine Probiotics, Detoxification, Intermittent Fasting, and Nutritional Ketosis as therapeutic approach

Defining the Epidemic in the US

- More than 100 million in the US now living with Diabetes or Prediabetes
- More than 1/3 of population has prediabetes
- Age 45-64 17% diagnosis of DM2
- 9.4% of population with diagnosis with one out of four untreated or managed
- Estimated \$327 billion in 2017, 26% increase in 5 years

Year	Obesity prevalence (%)	CHO intake (g/d)
1960	~10	~350
1971	~12	~380
1977	~15	~400
1990	~22	~450
2000	~30	~500

Adapted from Lee S Gross et al., The American Journal of Clinical Nutrition, 2006, 73(3), 776-8

Current Treatments

- Metformin: increases tissue sensitivity to insulin, reduces liver glucose production
 - GI distress, mitochondrial disruptor
- Sulfonylureas: increase insulin secretion (glucotrol, glipizide)
 - Hypoglycemia, weight gain
- GLP-1 receptor antagonists: slow digestion, lower BG, weight loss (byetta, Victoza)
 - Dizziness, nausea, vomiting
- SGLT2 inhibitors: prevent kidneys from reabsorbing sugar (Invokana, Farxiga)
 - Yeast infection, UTI



GET TO THE ROOT!! WHY?

Treatments or Drivers of Illness?

- Digestive distress
- Headaches, swelling, muscle function
- Megaloblast anemia
- Mitochondrial dysfunction
- Folate and B12 deficiency
- Depression, Anxiety, Cognitive decline



- Comorbidity:
- Vascular function
 - Neuropathy
 - Gastroparesis
 - Kidney damage
 - Hypertension
 - CVD

Defining the Microbiome

- 100 trillion cells of bacteria and yeast
- Birth and breastfeeding as thumbprint, bacteria and HMO to selectively support
- Symbiosis
 - Lactobacillus and Bifidobacterium
 - Diurnal metabolism and digestive regularity
 - S2F1 -> Bifidate
 - Synthesize nutrients, high amounts of K, B, biotin
 - GABA and serotonin
- Dysbiosis
 - Klebsiella, Citrobacter, pathogenic strains
 - Bleeding, IBS, dermatitis, fatigue
 - Unmanaged blood sugar contributes
 - excessive epinephrine
 - secretory Iga

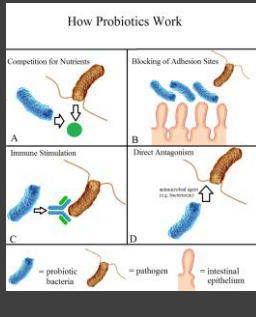
Research looking at sterilized microbiome from stress and a sterilized or dysbiotic state can have negative impact on metabolism.

"It has become increasingly apparent that amount and nature of calories taken up by the intestine are strongly impacted by the microbiota colonizing it"

Development of obesity and insulin resistance heavily connected to microbiome!
Molecular Metabolism, September 2016

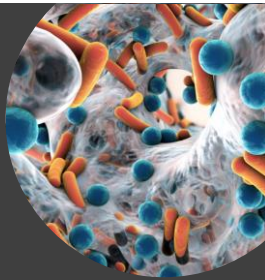
Contributors to microbiome

- Supporters of Symbiosis:
 - Prebiotic dietary fibers
 - Sunchoke, jicama, asparagus, onion, garlic, banana, cabbage
 - Aid in SCFA production, enhance Cal/Mag absorption, lowers serum cholesterol
 - Probiotic-rich foods
 - Kefir, yogurt, raw aged cheese
 - Cultured vegetables
 - Kombucha
- Supporters of Dysbiosis:
 - Stress → Sterilizes
 - Antibiotic use
 - Other medications: birth control, PPI/antacids, Non-caloric sweeteners
 - Elevated blood sugar levels
 - High sugar refined carbohydrate diet



Probiotics: 1st line of defense

- Drug-resistant organisms on increase
- 80% of immune function is directly related to intestinal health
- Increase adhesion proteins in epithelial, reducing permeability
- Decrease inflammation and can treat inflammatory conditions
 - Gastroenteritis, IBD, IBS, H-pylori, Ulcerative Colitis, Crohn's, DM1
- Natural Antibiotics
 - Synthesize/secrete antibacterial compounds
 - Reinforce barrier function of intestine
- Anti-carcinogenic
 - Modify the ability of microflora to produce carcinogens
 - Inhibition of genotoxicity of known carcinogens (in vitro and in vivo)
 - Probiotics can prevent DNA damage and mutations
 - Dysbiotic bacteria can activate procarcinogens to DNA reactive agents



Probiotics: Mechanisms for Metabolism

- Reduce inflammation and oxidative stress
- Aid in secretion of post-prandial insulin but not of fasting
 - Receptor activation and recognition by microorganisms from the intestinal lumen trigger inflammatory responses
- Regulate immune response that damages beta-cells of pancreas

PLoS One. 2016; 11(7):e0157241. doi:10.1371/journal.pone.0157241

PMCID: PMC4868111

Effect of Probiotics on Glycemic Control: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials

Yafeng Yuan^{1,2}, Jia Sun^{1,2}, Jia He², Fanwen Chen², Ruiqiang Chen^{1,2}, and Liang Chen^{1,2}*

17 randomized controlled trials were included, 17 fasting blood glucose, 11 fasting plasma insulin, 8 homeostasis model assessment of insulin resistance

Probiotic consumption, compared with placebo, significantly reduced fasting glucose, fasting plasma insulin, HOMA-IR



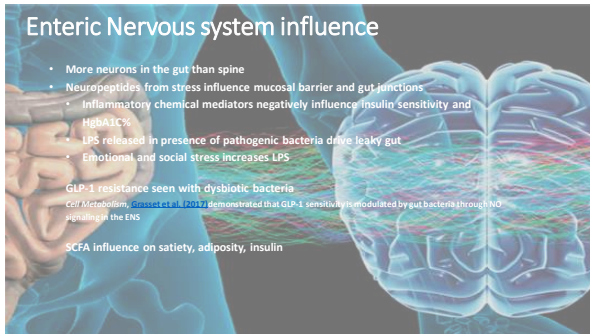
Enteric Nervous system influence

- More neurons in the gut than spine
- Neuropeptides from stress influence mucosal barrier and gut junctions
 - Inflammatory chemical mediators negatively influence insulin sensitivity and HbA1C%
- LPS released in presence of pathogenic bacteria drive leaky gut
- Emotional and social stress increases LPS

GLP-1 resistance seen with dysbiotic bacteria

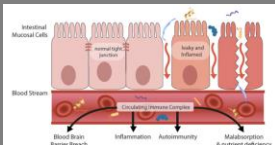
Cell Metabolism, [Gross et al. \(2017\)](#) demonstrated that GLP-1 sensitivity is modulated by gut bacteria through NO signaling in the ENS

SCFA influence on satiety, adiposity, insulin



Leaky gut and Metabolism

- Intestinal permeability →
- antigen exposure →
- immune reactions (b-cell damage) →
- cytokine production (reduced insulin sensitivity)

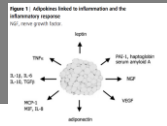


Vaarala O, Atkinson MA, Neu J (2008) **The "Perfect Storm" for Type 1 Diabetes: The Complex Interplay Between Intestinal Microbiota, Gut Permeability, and Mucosal Immunity.** Diabetes Journal, (57)10(2555-2562).

Brain, Behavior, and Immunity
Volume 22, Issue 4, August 2003, Pages 268-275

Influence of depressive mood on the association of CRP and obesity in 3205 middle aged healthy

Weight loss improves disease activity in patients with psoriatic arthritis and obesity: an interventional study.



Assessing the microbiome and Gut integrity

- L-Glutamine: 2-3g/day aids with intestinal enteropathy and as GLP-1 secretagogue
 - Aids in reduced sugar cravings
 - Supports muscle mass
 - Aids in immunological processes
- Stool test
 - Secretory IgA
 - Lipopolysaccharide
 - Buiptate
 - Microbiology assessment
- Probiotic challenge
 - 50:50 blend of live lacto: bifido strains increasing in 3 day increments to assess tolerance at 15-60 billion CFU

Bone broth as medicine

- Rich in glycine, glutamine, collagen
- Aids in leptin release in brain
- Curbs cravings
- Promotes immunity
- Aids in gut restoration



Resetting imbalance

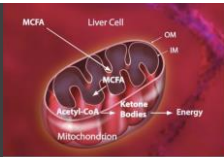
PLDW prior to Pollination

- Support Dysbiotic Cleanse
 - Berberine
 - Caprylic Acid
 - Oil of oregano
 - Garlic
 - Colloidal silver
- Break biofilms for best outcomes
 - Complex protective networks of bacteria
 - Proteolytic Enzymes (protease, papain, bromelain, trypsin, etc.)
 - Break down inflammatory proteins and biofilms leading to exposure
 - N-acetyl cysteine
 - Detoxification
 - encapsulation of endotoxins, prep for removal
- FAM to Support Gut Flora
 - Reduce refined sugar, processed carbohydrates
 - Ample prebiotic fibers
 - Live active cultures: kimchi, sauerkraut, kombucha, keifer, yogurt, pickled veg



MCT rich coconut oil

- High in saturated fat, pref. for cooking at higher temperatures
- Provides satiety and stabilizes blood sugar
- Monolauric acid antifungal/bacterial/antiviral
- High content of MCTs promote ketosis
 - MCFA (MCT) can cross inner mitochondrial membrane without carnitine
 - Provide satiety and stabilize blood sugar
 - anti-inflammatory
 - promote ketosis and fat burn
 - Support brain health



MCFA= medium chain fatty acids, OM = outer membrane, IM = inner membrane
 Adapted from: Bach AC & Babban VN. The American Journal of Clinical Nutrition 2010; 92:1010-14

“Food is a double edged sword where foods can provide nourishment as anti-inflammatory support to glucose regulation as well as send chemical disruption signals for endocrine system and metabolic function.”



Endocrine disruptors

*Hormone-mimicking compounds that act the similar or different on a receptor with potential to have more pronounced influence

- *Plastics
- *Pesticides
- *Perfumes

*6 billion pounds produced in our environment annually: POPs, Dioxins, PCBs, BPA

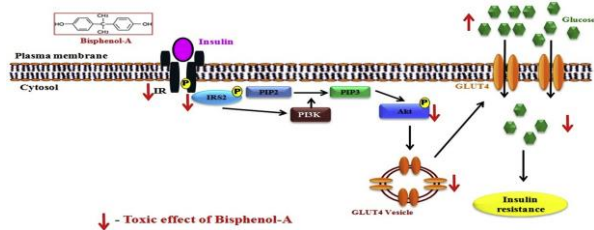
*Toxic food additives → GRAS law only 1/3 of 10k chemicals in food system have been tested





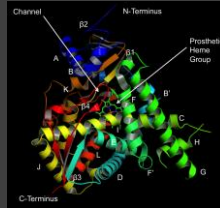
Insulin resistance with endocrine disruptors and other mechanisms of toxicity

Chemico-Biological Interactions March 2017



Detox phase 1: Activation

- Lipid soluble toxins from endotoxins and exotoxins get converted to intermediary compounds; cytochrome p450
 - Oxidation
 - Reduction
 - Hydrolysis
 - Hydration
 - Dehalogenation



Nutrients to support:

- Vitamin A
- B Vitamins
- Glutathione
- BCAAs
- Flavonoids
- Vitamin C
- Vitamin E
- Copper
- Selenium
- Zinc
- Manganese
- CoQ10
- Thiols (garlic, alliums, crucifers)
- Silymarin (milk thistle)



Phase 1 Detox: Activation



Detox phase 2: Encapsulation

- Conjugation enzymes support conversion from activated intermediary metabolites to harmless excretion products
 - Glucuronidation
 - Sulfation
 - Glutathione conjugation
 - Acetylation
 - Amino-acid conjugation
 - Methylation



1/24/2016 2015-07-07 707699
 Published online 2015 Jan 16; doi: 10.1155/2015/707699
 PMID: 26187267
 Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application
 Romilly E. Hodges¹ and Deanna M. Mrazek^{2,3,*}

Nutrients to support:

Glycine

Taurine

Glutamine

Cysteine

Methionine

N-acetylcysteine

Glutathione



Phase 2 Detox: Encapsulation



Phase 3: Excretion

• Conjugated compounds are excreted by kidneys and bladder or intestines and stool predominantly with some exiting via sweat

- Serum → Kidneys → Urine
- Bile → Intestines → Feces/Stool





Phase 3 Detox:Excretion

Nutrients to support:

Fiber

Fluid

Bitters (ACV, dandelion)

Diuretics (cucumber, celery)



Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application

Exposures	Food, Beverage, or Microbiome Component	Type of Study	Design and key references	
Cancer	Fruit/vegetables in diets	Clinical	Approximately 7 and 14 servings of vegetables/vegetables including fruits, beans, lentils, and other. Each category (total grams) and fruit intake (grams) observed	
		Observational	-13 g/d of fruits/vegetables [1][2] 4-7 cups of vegetables/vegetables including 1 cup of soluble fiber, 1 cup of beans and lentils, 2 cups of fruits/vegetables, and 1 cup of fruit [3][4]	
	Fractionation vegetables	Clinical	Approximately 7 and 14 servings of vegetables/vegetables including fruits, beans, lentils, and other. Each category (total grams) and fruit intake (grams) observed	
	Alkaline vegetables	Clinical	150 g cooked Brussels sprouts [1][2]	
		Clinical	1.5 kg fresh chives, 1.5 cup of fresh kale, 10 g garlic, and 1 cup of fresh onion [1][2]	
	Bromelain	Clinical	1 g/d bromelain [1][2] over 8-day trial	
		Observational	-High intake [3][4]	
	Cancer, liver, pancreas, eye, and liver disease	Citrus	Observational	-High intake [1][2]
			Interventional	200 mg bromelain/600 mg vitamin C [2][3]
		Garlic	Interventional	18 or 200 mg garlic [4][5]
Interventional		100 mg [6] or 400 mg [7] 4 times weekly [2]		
Risk of		Interventional	20 g [8] or 40 g [9] over 8-day trial	
Health outcomes		Interventional	150 mg [10] or 300 mg [11] 4 times weekly [2]	
Single intervention		Interventional	100 mg [12] or 400 mg [13] 4 times weekly over 8-day period [2][3]	
Combinations		Interventional	Bromo-299 [14]	
Observational		Interventional	Established of a specific [15] food, and/or [16] [17]	
Biologics		Interventional	Resection on early [18] [19] [20] [21] [22] [23] [24] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55] [56] [57] [58] [59] [60] [61] [62] [63] [64] [65] [66] [67] [68] [69] [70] [71] [72] [73] [74] [75] [76] [77] [78] [79] [80] [81] [82] [83] [84] [85] [86] [87] [88] [89] [90] [91] [92] [93] [94] [95] [96] [97] [98] [99] [100]	

"designing clinical recommendations to maximize the effects of food and reduce the impact of toxins is essential" J Nutr Metabolism 2015

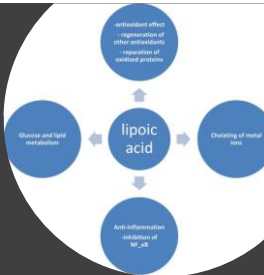
Mechanism of action of Antioxidants

- Scavenge free radicals
- Reduce oxidative stress
 - Lowers risk of cataract, neuropathy, enhances circulatory function
- Prevent cell destruction
- Enhanced glucose utilization
- Reduced glycation
- Reduced inflammatory process



Role of Antioxidants in detox and metabolic disease

- CoQ10: 100-300mg
 - Mitochondrial function
 - Enhanced glucose uptake
- Alpha Lipoic Acid: 300mg (with 4000mcg biotin)
 - Water and fat soluble function; functions in oxidized and reduced form; Myelin sheath regenerator
 - prevents beta cell destruction, enhances glucose uptake, and its antioxidant effects may be particularly useful in slowing the development of diabetic complications such as diabetic neuropathy; Frontiers of Pharmacology 2011
- Cysteine replete glutathione along with glycine
 - 2 g taurine/200-400mg magnesium glycinate
- Vitamin C
 - 1g/day reduces blood glucose and lipids; buffered for bowel tolerance



Remove Inflammatory Foods

- Gluten→ hybridized, higher in gliadin, zonulin increase driving leaky gut, glietomorphin (blood-brain barrier)
- Casein/Dairy→ low stomach acid, poor digestion, and inflammation in the GI tract, opioid activity
- Digestaid Enzyme has DPPIV for caseomorphin and glietomorphin metabolism!
- Corn
- Soy
- Sugar
 - increased IGF-1, insulin resistance, hyperglycemic response



Food Matters

- Practicing MEDICINE without providing resources for a healthy diet is INCOMPLETE and COUNTERPRODUCTIVE
- Can't overmedicate excess carbohydrates →
 - Solution for diabetics is reducing their carb intake for glycemic control not upping their hypoglycemic or exogenous insulin
- Processed refined carbs leave us OverFED yet Malnourished!
 - It is NOT just empty calories, deleterious effects need to be discussed!!!
 - Depletes minerals, B-vitamins
 - Drives gut and microbiome distress
 - Proinflammatory
 - Hyperinsulinemia



Naturally Nourished Optimal Eating

- Rich in anti-inflammatory compounds:
 - Omega-3s: wild fish, pasture-raised egg yolk, flax
 - Sea Vegetables
 - Berries
 - Tropical fruit
 - Herbs/Seasonings
- Vascular support
- Antioxidant support
- Traditional foods diet/Paleo approach
 - Low-carbohydrate meal plan 60-90g carbs/day
 - Ketogenic 15-60g carbs



Restore Micronutrient Status

Chromium
Helps with insulin activity. Deficiency can lead to insulin resistance and hyperglycemia. Found in whole grains, nuts, and fruits.

Biotin
Essential for glucose metabolism. Deficiency can lead to insulin resistance. Found in eggs, nuts, and vegetables.

Magnesium
Essential for insulin action. Deficiency can lead to insulin resistance. Found in leafy greens, nuts, and whole grains.

Zinc
Essential for insulin action. Deficiency can lead to insulin resistance. Found in nuts, seeds, and whole grains.

Lipidic Acid
Essential for insulin action. Deficiency can lead to insulin resistance. Found in fatty fish, nuts, and seeds.

Glutathione & Cysteine
Essential for insulin action. Deficiency can lead to insulin resistance. Found in eggs, nuts, and whole grains.

Coenzyme Q10
Essential for insulin action. Deficiency can lead to insulin resistance. Found in fatty fish, nuts, and seeds.

Vitamin B12
Essential for insulin action. Deficiency can lead to insulin resistance. Found in meat, fish, and dairy.

Vitamin B3
Essential for insulin action. Deficiency can lead to insulin resistance. Found in meat, fish, and whole grains.

Vitamin D
Essential for insulin action. Deficiency can lead to insulin resistance. Found in fatty fish, eggs, and fortified foods.

Vitamin E
Essential for insulin action. Deficiency can lead to insulin resistance. Found in nuts, seeds, and whole grains.

Vitamin C
Essential for insulin action. Deficiency can lead to insulin resistance. Found in fruits and vegetables.

Inositol
Essential for insulin action. Deficiency can lead to insulin resistance. Found in whole grains, nuts, and seeds.

Carotenes
Essential for insulin action. Deficiency can lead to insulin resistance. Found in leafy greens, carrots, and tomatoes.

Glutamine
Essential for insulin action. Deficiency can lead to insulin resistance. Found in eggs, meat, and whole grains.

- Inadequate intake
- Increased demand
- Inability to absorb
 - GI
 - Rx interaction
 - CoQ10 and statin
 - Magnesium and B12 → diuretics and PPI
 - Increased homocysteine and CVD
- Inability to use
 - Genetic SNP

Restore Micronutrient Status

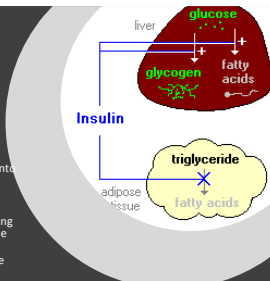
- **Antioxidants:** Berries, Cacao, Roots, Herbs, Teas and Coffee
- **Magnesium:** dark chocolate, nuts, seeds, leafy greens, avocados, and beets
- **CoQ10/Zinc:** oysters, liver, beef and lamb, egg yolk, fish, pork, turkey, pumpkin seeds, sesame seeds, dark chocolate, nuts

Enhanced Antioxidant status

- Turmeric: curcuminoids 2g dosage
- Blend of boswellia, ginger, cinnamon, ginseng
- Berberine: independent hypoglycemic impact and antiviral antifungal; 400-1000 mg
- Eat in variety of preparation forms
- Different environments influence nutrients differently
 - Cooking reduces Oxalic acid
 - Magnesium is better absorbed
 - Acid → Increases minerals
 - Vitamin C converts ferric Fe3+ to ferrous Fe2+ iron
 - Lemon with spinach
 - Carotenoid and Lycopene bioavailability increase with heat and fat
 - Ghee on roasted carrots
 - Olive oil on roasted tomatoes

Why Insulin matters?

- Just as profound as the effects on carbohydrate metabolism are the effects on fat metabolism!
- Insulin is proinflammatory
- Stimulates body fat storage and elevates triglycerides
- Insulin promotes synthesis of fatty acids in the liver
 - stimulatory to synthesis of glycogen in the liver as it accumulates to high levels (roughly 5% of liver mass), additional glucose taken up by hepatocytes is shunted into pathways leading to synthesis of fatty acids, as lipoproteins delivered to tissues including adipocytes, which use them to synthesize triglyceride.
- Insulin inhibits breakdown of fat in adipose tissue by inhibiting the intracellular lipase that hydrolyzes triglycerides to release fatty acids.
 - Insulin is involved in further accumulation of triglyceride in fat cells.



From a whole body perspective, insulin has a fat-sparing effect. Not only does it drive most cells to preferentially oxidize carbohydrates instead of fatty acids for energy, insulin indirectly stimulates accumulation of fat in adipose tissue.

Ketosis novelty or treatment?

1923 Dr. Justin Elliot Diabetic diet and Dr. Fredrick Allen: meats, poultry, game, fish, clear soups, gelatin, eggs, butter, olive oil, coffee, tea* and contained approximately 5% of energy from carbohydrates, 20% from protein, and 75% from fat

54 participants with DM2 A1c improved greater over 1 year with low carb non-calorie restricted over low-fat calorie restricted (1)

28 participants veteran hospital outpatient (2):

Hemoglobin A_{1c} decreased by 16%

Diabetes medications were discontinued in 7 participants, reduced in 10 participants, and unchanged in 4 participants

The mean body weight decreased by 6.6%, Fasting serum triglyceride decreased 42%

1. Stern L, Iqbal N, Seshadri P, Chizzaro RL, Daily DA, McGroarty L, Williams M, Grovety EJ, Somsho P. *Ann Intern Med*. 2004 May 18; 140(10):778-85.
 2. Yancy WS, Foy M, Chaleckii AM, Vernon MC, Westman EC. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutrition & Metabolism*. 2005;2:34. doi:10.1186/1743-7075-2-34.

Using Nutritional Ketosis

- Ketone bodies block hunger signals aids with GLP-1 and leptin
- Muscle sparing mechanisms
- Reduced adipokine signals with less body fat
- Enhanced fat metabolism upon glycogen depletion only occurs with carb restriction
- Implement meal plan at <30g CHO/day
 - Once body adapts can increase to <50g CHO/day
 - Provide adequate protein and antioxidant support with vegetables
 - 80-100g protein/day
- Intake of minimum 1/2 body weight in fluid oz of water



- HOW you "keto" MATTERS!
 - Avoid of toxins, additives, preservatives
 - High Antioxidant
 - Fiber: nuts, seeds
 - Greens
 - Sulfate: broccoli, cauliflower, brussels
 - QUALITY of animal fats & protein
 - No non-caloric sweeteners

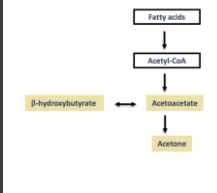
Why Carb restriction is key?

- Diets with high-starch, low-fiber ratio are associated with a higher risk of type 2 diabetes (1)
- High carbohydrate intakes (≥ 74 En%) may increase the risk for metabolic syndrome, while moderate fat intakes (≥ 20 En%) may reduce the risk for metabolic syndrome in women (2)
- In a study with type 2 diabetics, a low-carbohydrate ketogenic diet led to greater improvements in glycemic control, and more frequent medication reduction/elimination than the low glycemic index diet (3)
- The low-carbohydrate ketogenic diet has also been shown to induce significant weight loss and improve fatty liver disease (4)
- Low-carbohydrate diet is associated with better vigilance attention and reduced self-reported confusion (5)

1. Alessi HB et al. American Journal of Clinical Nutrition 2015;102(6):1543-53
2. Park S et al. International Journal of Food Sciences and Nutrition 2017;68(4):479-487
3. Westman EC et al. Nutrition & Metabolism 2008; 19(5):36
4. Tendler D et al. Digestive Diseases and Sciences 2007; 52(2):589-93
5. D'Anici KE et al. Appetite 2009; 52(1):96-103

What are ketones?

- Normal physiological process body is adapted to produce
 - In absence of carbohydrates via carb restriction or fasting, liver produces ketones from fat
 - Acetone, Acetoacetate, BHB



- Ketone benefits
 - Cellular protection
 - Enhanced signaling
 - Reduce oxidative stress
 - Reductions in insulin
 - Regulation of BG levels

J Nutr Metab. 2018 Feb 11;2018:157945. doi: 10.1155/2018/157945. ©Wiley 2018
Nutritional Ketosis and Mitohormesis: Potential Implications for Mitochondrial Function and Human Health.
Milner VJ, Williams GJ. *Wiley*. 2018.

Mechanisms of ketosis

- Supports mitochondria
- Enhance GABA activity, anxiolytic
- Lower DHEA for PCOS and infertility
- Uses fat as fuel reduces muscle wasting with significant weight loss
- Aids in healthy brain function as ketones are more sustained fuel
- Ketosis can improve insulin function in the body
- Ketosis can decrease LDL, Triglycerides, total cholesterol
- Ketone bodies block hunger signals
- Altered adipokine signals with increased body fat



Distinguishing from Ketoacidosis

Blood Levels	Normal Diet	Keto Diet	Ketoacidosis
Glucose	80-120	65-80	>300
Insulin	6-23	6.6-9.4	0
KB conc	0.1	0.5-2.5	>25
pH	7.4	7.4	<7.3

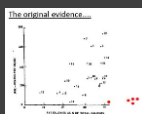
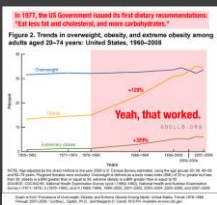
- Nutritional ketosis occurs with carb **RESTRICTION** and reduced blood sugar levels
 - No pH change
 - No threat to kidney function
- Ketoacidosis occurs at unmanaged carb intake with **ELEVATED** blood sugar levels

Lipid hypothesis and Saturated Fat myths

1960s Ancel Keys Seven Countries Study (out of 22)
When in doubt get back to known mechanisms of action!

Saturated fat:
Comprises 50% of our cell membranes
Heat stable
HDL increase
Reduction of Lp(a)
Supports bone health
Lung surfactant is 100% saturated fat
Brain composition
Neve signaling
Immune support

Rank	Food	Calories	Cholesterol	Saturated Fat	Trans Fat
1	Butter	119	215	72	0
2	Cheese	115	210	65	0
3	Whole milk	122	35	5	0
4	Whole milk	122	35	5	0
5	Whole milk	122	35	5	0
6	Whole milk	122	35	5	0
7	Whole milk	122	35	5	0
8	Whole milk	122	35	5	0
9	Whole milk	122	35	5	0
10	Whole milk	122	35	5	0



the Masai, Inuit, and Tokelau

Benefits of Intermittent Fasting

- Intentional avoidance of intake also known as time-restricted eating TRE; Mimics ancestral approach
- Weight loss maintenance and body fat burn
 - Increased HGH
 - Improved leptin signaling
 - Reduced insulin
- Enhances cognitive function and brain health
 - increases your BDNF, which supports brain connectivity and new neuron growth.
- Reduced inflammation
 - "autophagy" to clear out old and damaged tissues and cells; when body has body a break from the constant effort of digesting food it focuses more energy on repair alleviating inflammation in the body.
- Cardiovascular support
 - Reductions in blood pressure
 - Studies have shown that 70 days of alternate-day fasting can reduce LDL cholesterol by 25 percent.

Defining Intermittent Fasting

- 12/12
- 16/8 typically 12-9pm or 9am-5pm eating window
- 20/4 or warrior diet
- 24
- 5/2 with 2 days as VLCD 500 (f) 600 (m)
- No insulin stimulation = blood sugar regulation = less cravings and consistent energy
- Insulin goes down, body able to access fat as fuel
 - Sustainable
 - Free!
 - Muscle sparing

During pure/water fasting:
 Water
 Salt
 Coffee, Tea
 Electrolytes

Fat Fast: coconut oil, grassfed butter

Bone Broth fast: glycine supports

Tea benefits:
 EGCG
 Appetite suppressant
 Gut and Detox support
 L-theanine



Other Considerations for ketosis?

- Work with clients to cope with side effects while entering process
 - Electrolytes; salt!
 - Hydration status
 - Digestive enzyme with lipase, ox bile, HCl-
 - Melatonin
 - L-carotene
- Monitor labs: fasting insulin, uric acid, GGT, CMP, CBC, lipids with particle size, hgbA1C, leptin, adiponectin,
 - Reductions in: Fatty Liver, Insulin Resistance, Inflammation
 - Leptin levels may drop too low concerning for cycling women

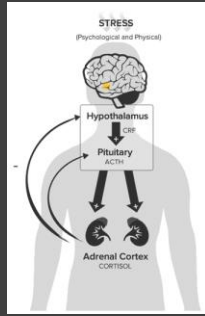
Ketosis as Medicine for mood and Anxiety?

- Elevated blood sugar levels >2x more likely to develop depression and anxiety
- Ketones promote mood stabilizers and metabolic regulators:
 - GABA
 - HGH
 - Leptin
 - Mitochondrial fuel
 - high octane brain fuel



Stress and blood sugar balance

- High stress levels stimulate nervous and endocrine system increasing blood sugar levels, hindering digestive function (increasing toxicity), etc.
- HPA-axis involved with metabolism, hormonal balance, cortisol, inflammation, hyperinsulinemia
 - Glucocorticoid impact
- Develop coping mechanisms for stress to regulate blood sugar levels
 - What is your coping mechanism?
 - Is it healthy/sustainable/realistic?
 - Can you modify for stressor or stimulus?
 - Cognitive restructuring/ Control the Reaction
 - 4-7-8 Breathing



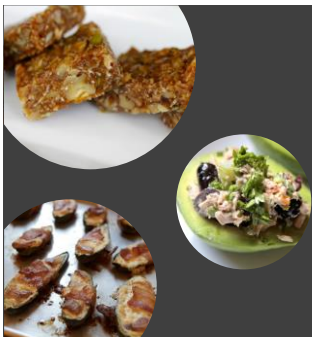
Stress blood sugar connection support!

- Nervines: chamomile, oat pod, schisandra berry
- Adaptogens: panax ginseng, ashwagandha, holy basil, cordyceps
- L-theanine: modulates NT, alpha brain waves
- Adrenal support with glandular and B6, B5 to calm nervous system
- Vitamin C



Keto-friendly nutrient dense snacks

- Prosciutto wrapped asparagus
- 6 olives + 2 oz in house roasted turkey
- Bell Peppers + Spicy Cashew "Cheese"
- Celery + 1.5 tbsp tahini
- Kale chips
- ¼- ½ Avocado sprinkled with roasted Sunflower Seeds
- Nori sheet with avocado and lox



Functional Approaches to Metabolic conditions

- Start with foundational diet to minimize demand of insulin while working to sensitize receptors
 - Low glycemic or ketogenic base
 - Education on diabetic exchanges and carb control
 - Limit non-caloric sweeteners
- Consider Ketosis and Intermittent fasting
- Determine point of functional support entry!
 - Microbiome: GI distress, skin conditions, yeast infection, antibiotics history
 - Detox support work environment, chronic fatigue, other endocrine disorders
 - Microtrauma: athletic, mother, accident/injury, hair/diet/nail health, stress demands
 - HPA-axis: stress impacts digestion, blood sugar, hormones, inflammation, sleep, mood and more!

Consider advanced labs to confirm the "why" and support with therapeutic food and supplementation

Case Study: Leslie

- Executive, travel, high stress, successful
- November 2017 HgbA1c 9.9%
- CRP 19.1
- LDL Particle 2100
- Metformin 1000mg BID
- Recently added Januvia 100mg at rise
- IBS, chronic constipation
- Fatigue, brain fog, insomnia
- Stressed and tired AND stressed and wired



Case Study: Leslie Interventions November

- Magnesium Glycinate 250mg Myo-inositol 2g 2 scoops at rise, 2 scoops at bed
- L-glutamine 2500mg with DGL and aloe 1 scoop at bed
 - Gut integrity, BG regulation, sugar cravings
- Buffered vitamin C 500mg 1 at breakfast 1 at lunch
- EPA-DHA 860mg/580mg 1 at breakfast 2 at dinner or bed
- Adaptogenic blend (rhodiola, ginseng, cordyceps) 1 at breakfast, 2 at afternoon (or lunch) this one is important to
 - protect thyroid in times of stress and supports metabolism and energy!
- Methyl-folate 1mg, methylcobalamin 1mg, Sam-E 400mg 1 at rise
 - mood stability and serotonin support)

Case Study: Leslie Interventions November

- Low glycemic diet: No Naked Carbs!
- Whole food approach no processed products
- Eggs 5x/wk
- Probiotic rich food 5x/wk
- <75 g carbs daily, consistency of eating 3-4 hours, fat increase 70-80g
- Increased water 3 L daily
- Walking over lunch hour, minimum 30 min daily
- Meditation app
- 4-7-8 breath
- Sleep hygiene

Case Study: Leslie Interventions April

- Probiotic challenge fail in Feb, 6 week Dysbiosis/yeast cleanse March
 - Berberine 250mg 2 at breakfast, 2 at dinner
 - Digestaid 1 at meals
 - 50:50 blend lactobacillus and Bifidobacterium 1 at rest
 - 1 10g scoop collagen daily
 - Continued from November supplements
- Energy improving, down 13 pounds, libido up, medications reducing

Shift to nutritional ketosis <30g carbs
Intermittent fasting as a tool to use 3 days out of the week to accelerate fat burn

Case Study: Leslie Results



- Stopped Januvia January 20th 2018
- Reduced Metformin to 500 BID April 2018
- July 2018 HgbA1C 5.2% (from 9.9%)
- LDL Particles 1068 (from 2100)
- CRP 11.8 (from 19.1)
- Off All Diabetic Rx August 2018

- 22 pound weight loss
- 5% body fat loss

Case Study: Leslie interventions July

- Mediator Release Test, 170 foods/chemicals for cytokines, prostaglandins, inflammatory chemical release
- Not IGG or IGE
- 3 months off all moderate: YELLOW
- 6 months off all reactive: RED
- Added proteolytic enzymes and botanicals that were non-reactive
- CRP 4.7 October 2018



What is Food-as-Medicine?



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Questions?

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