Waging A War Against Obesity with Fasting Protocols and Nutraceuticals

Dr. Tim Schroeder, PharmD, FAARFM, ABAAHP, MS, MBA
Executive Leadership / Vice President / General Manager / Compounding & BHRT Expert / Private Pilot
Disclosure Statements:

• No financial disclosures to report at this time.
• This material is provided for educational and informational purposes only to licensed health care professionals. This information is obtained from sources believed to be reliable, but its accuracy cannot be guaranteed. Herbs and other natural substances are very powerful and can occasionally cause dangerous allergic reactions in a small percentage of the population.
• Patients undertaking a weight-loss program should be under the care of a health care professional at all times.
• The use of any specific product should be in accordance with the manufacturer’s directions.
My Journey in Functional Medicine
Paradox!!!
Learning Objectives:

• Discuss weight loss as a multi-factorial problem

• Review metabolic targets and labs in weight loss management

• Define autophagy

• Outline the physiology, phases and types of fasting

• Summarize compounding and nutraceuticals options for weight loss
Pre-Assessment Questions

• Which of the following supplement (mineral) has over 300 biochemical reactions in the body:
  o A. Ashwagandha  
  o B. Potassium  
  o C. Magnesium  
  o D. L-theanine  

  Hint – minerals in the human body include calcium, potassium, magnesium, sodium, and phosphorus.

• 8-OHdG (deoxyguanosine) is a reliable marker for oxidative stress?
  o True or False?
Billboard Signs: Weight-Loss Highway

https://www.d4creative.com/soza

Obesity Epidemic

• Obesity is one of the greatest public health challenges of the 21st century

• There are 1.6 billion adults currently classified as being overweight and 500 million as obese worldwide.

• Obesity is the leading cause of DM2 and DM2 is the leading cause of:
  - Renal failure requiring transplant or dialysis
  - Blindness (in western world)
  - Cardiac disease
  - Amputations

Obesity Epidemic continued

- Economic cost of diabetes - 2012 versus 2017 (in USA)
  - 2012 – estimated cost of diagnosed $245 billion
    ($176 billion direct costs and $69 billion in reduced productivity)
  - 2017 – estimated cost of diagnosed $327 billion
    ($237 billion direct costs and $90 billion in reduced productivity)

  An Increase of $82 Billion!

• Obesity is associated with a constellation of metabolic abnormalities
  o Insulin resistance
  o B-cell failure
  o Dyslipidemia
  o Low HDL
  o Increased LDL particles
  o Increases free radical production (ROS)

What else should be on this list?
Obesity Epidemic continued

• Being overweight or obese increases the patient’s risk of developing the following cancers:
  o Postmenopausal breast cancer
  o Endometrial
  o Esophageal
  o Gallbladder
  o Kidney
  o Pancreatic
  o Thyroid

https://www.sunstar.com.ph/article/1777390
Obesity Epidemic continued

• Historical view of Obesity
  o Lifestyle choice
  o Character flaw
    • Lack of willpower
    • Psychological issue

• Current perspective
  o Not simply a problem of eating too much
  o Inflammation closely associated
    • Adipose tissue
  o Probably several dozen or more clinically meaningful types
  o Multi-factorial disorder
Adipose Tissue

• Once considered storage depots for energy, adipocytes are now recognized as active endocrine cells that have several roles:
  o Regulation of metabolism
  o Energy intake
  o Fat storage


Greenberg, AS. et al., “Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr 2006;83(suppl.):461S-465S.
Endocrine Effects of Adipose Tissue

- Fat cells secrete Adipokines – impacts appetite, balance, immunity via TNF-alpha and IL-6, blood pressure, lipid metabolism, insulin sensitivity

- Bottom Line – weight gain leads to dysinsulinemia and can lead to inflammation, elevated lipids and blood pressure

Adipose Tissue

Lean adipose tissue

Obese adipose tissue

Adipokines (adiponectin, resistin, leptin)

Pro-inflammatory molecules (TNFα, IL-6, NO)

Weight gain

ATM activation switch

Alternatively activated

Classically activated

Adipose Tissue

Jung UJ, et al. Obesity and its metabolic complications: the role of adipokins and the relationship between obesity, inflammation, Insulin resistance, dyslipidemia and nonalcoholic fatty liver. Int J Mol Sci. 2014; 15(4);6184-6223
Weight Loss as a Multi-Factorial Problem

It’s not just about calories in vs. calories out.
Weight Loss as a Multi-Factorial Problem

- Detoxification
- Inflammation
- Sleep deprivation
- Gut Microbiome
- Yeast
- Fiber
- Water
- Exercise
- Hormones
- Food
  - Artificial sweeteners
  - Food addictions
  - High fructose corn syrup

Weight Loss as a Multi-Factorial Problem

- **Neurotransmitters**
  - Epinephrine
  - Norepinephrine
  - Serotonin
  - Dopamine
  - GABA
  - Glutamate
  - Histamine

- **Neural pathways involved in regulating food intake and energy control**
  - Gut Hormones
    - Ghrelin
    - Cholecystokinin
    - Peptide YY

Hedonic Reward-based

Billboard Signs: Weight-Loss Highway
Types of Bariatric Surgery

- **Restrictive**
  - Adjustable gastric Banding (Lap Band), Gastric Sleeve

- **Malabsorptive**
  - Bilopancreatic diversion with or without duodenal switch

- **Combination**
  - Gastric Bypass (Roux-en-Y), Duodenal switch

- 1992 ~16,000; 2003 ~103,000; 2009 ~ 220,000
- Average cost $17,000 to $28,000
- Recidivism after Bariatric Procedures is a problem
Bariatric Surgery Complications

- Deficiencies in certain micronutrients
- Dumping
- Osteoporosis
- Skin wrinkles
- Weight gain
- Psychological problems
- Increased suicidality
Labs for Weight-Loss Testing
Labs for Weight-Loss Testing

- Due to time constraints, if you would like my entire slide deck on Labs for Weight-Loss testing please email me.
Labs for Weight-Loss Testing

**CONVENTIONAL MEDICINE**
- Disease Oriented
- Doctor Centered
- Everyone is Treated the Same
- Specialized
- Diagnosis Based on Symptoms
- Early Detection of Disease

**FUNCTIONAL MEDICINE**
- Health Oriented
- Patient Centered
- Holistic
- Looks at Underlying Cause of Disease
- Biochemical Individuality
- Preventative Approach

https://southjordanwellness.com/functional-medicine/
Labs for Weight-Loss Testing

• Cost of Lab Testing
  o Cash pay versus insurance
  o Most insurances will not pay for functional-type lab testing

• Core testing – CMP and CBC
  o Helps determine basic foundation of health and looks at:
    • Blood parameters
    • Organs of detoxification
    • Blood sugar and insulin regulation
    • Electrolyte balance

• Functional Medicine tests + standard PCP labs
Labs for Weight-Loss Testing
• Lab values (ranges) can be improved by
  o Dietary and lifestyle changes
  o Exercise regimen
  o Dietary supplements
  o Rx medications/surgery when necessary

• Factors affecting lab values
  o Sex
  o Age
  o Race
  o Medical history
  o Sleep and stress levels
  o Not following testing requirements
Labs for Weight-Loss Testing

- CBC
- CMP
- Urinary pH
- Salivary pH
- Gamma glutamyl transferase (GGT)
- Fasting glucose
- Insulin
- Hemoglobin A1c
- 2 hour post prandial
- Thyroid panel
- Stress/Cortisol salivary and serum

- Vitamin D
- RBC Chromium
- RBC Magnesium
- NMR lipoprotein
- 8-deoxyguanosine (8-OHDG)
- Adiponectin
- Leptin
- CRP
- Hormones (Testosterone, Estrogens, Progesterone, DHEA)

Insulin Resistance…
Labs for Weight-Loss Testing

- Urinary and Salivary pH
  - pH critical in determining biochemical balance
  - Optimal salivary pH = 7-7.2 (trending low 6.1-6.9, trending high 7.3-7.8)
  - Optimal urinary pH = 6.5-7 (trending low 6-6.49, trending high 7.1-7.2)
  - The more acidic (lower pH) = more inflammation
    - Mitochondria less efficient
    - Joints and tissues stressed
  - More lactic acid produced at lower pH
  - A trending high or high pH means body too alkaline
    - Digestive issues (hypochlorhydria)
    - Detoxification and drainage problems (liver, lymph, kidney)
Cortisol and Weight Gain
- Chronic stress directly related to weight gain
  - “Stress eating”
- Imbalances in hypothalamic-pituitary-adrenal (HPA) axis leads to:
  - Increased cortisol output
  - Insulin resistance
  - Inflammation
  - Sleep problems
  - Hormonal imbalances
  - Weight gain
- Increased visceral “belly” fat
Labs for Weight-Loss Testing

- Cortisol Level: Triggers
  - Wired and Tired
  - Tired and flat
  - Poor sleep
  - Poor performance
  - Weight gain around the abdomen
  - Mind racing “chatter”
  - Immune problems
    - Allergies and Asthma
    - Inflamed joints
    - Poor exercise recovery
• Serum cortisol Ranges
  o 8 am serum cortisol range 4.3 – 22.4 mcg/dL
    • Alert low = <4.3
    • Trending low 4.4-9.9
    • Optimal = 10.17
    • Trending high = 17.1-22.4
    • Alert high = > 22.4

• Salivary – 5 Point cortisol Ranges
  o Look for patterns in graphs
    • High levels in evening can be indicative of sleep problems
    • “Adrenal fatigue” look for flattening of the cortisol pattern
Labs for Weight-Loss Testing

Salivary Cortisol and DHEA

Cortisol
Reference Range
1 Hour After Rising
7AM - 9AM:
0.27-1.18 mcg/dL
11AM - 1PM:
0.10-0.41 mcg/dL
3PM - 5PM:
0.05-0.27 mcg/dL
10PM - 12AM:
0.03-0.14 mcg/dL

DHEA 7am - 9am

Hormone | Reference Range | Reference Range
------- | --------------- | ---------------
DHEA 7am - 9am | 71-640 pg/mL | 194
DHEA: Cortisol Ratio/10,000 | 115-1,188 | 234

https://www.revitalizemed.com/saliva-testing-get-skinny-hormones/adrenal-chart/
Labs for Weight-Loss Testing

https://www.womenshealthmag.com/uk/health/mental-health/a708722/cortisol-test/
Labs for Weight-Loss Testing

• Most Americans are vitamin D deficient; Vitamin D has a role in 4000 reactions in the body
• Obesity is associated with low vitamin D deficiency
• Optimal vitamin D level = 50-80 ng/mL
  o Trending low = 20-49.9
    • 5,000 IU Daily
    • Recheck in 90 days
  o Alert low = <20
    • 5-10,000 IU daily
    • Recheck in 90 days
  o Alert high =>100
    • Can lead to toxicity including calcium deposits in soft tissue
• If taking Vitamin D supplements and no effect on lab, add vitamin A to improve absorption.
Labs for Weight-Loss Testing

- **RBC Magnesium**
  - Magnesium is necessary for over 300 biochemical reactions
  - Over 75% of Americans are Magnesium deficient
  - Deficiency reported in overweight and obese individuals
  - Important in:
    - Muscle and bone health
    - Immune health
    - Sleep
    - Nervous system/brain
    - Energy production
    - Blood glucose and insulin regulation
  - Perform RBC magnesium levels
    - Ranges: (4 - 6.4 mg/dL)
      - Alert low <=5
      - Trending low 5 - 5.6
      - OPTIMAL = 5.7 - 6.2
      - Trending high = 6.3 - 6.4
      - Alert high =>6.2
• 8-OHdG (deoxyguanosine)
  o Reliable marker for oxidative stress
  o Correlated to DNA damage
  o Range 0-54.1 ng/mL
    • OPTIMAL = 0-35
    • Trending high = 35.1-54.1
    • Alert high => 54.1

Key Metabolic Targets in Weight Loss

Key Metabolic Targets in Weight Loss

- **PGC-1alpha** – perhaps the most important metabolic target for obesity and glucose regulation. This is the co-regulator of OXPHOS relationships and is decreased in obese and type 2 diabetic patients. **Key to mitochondrial energy production** which is the primary cellular target that is disturbed in obese and Type 2 diabetics, as well as cancer chemistry.

- **PPAR alpha** – this signaling substrate allows for the efficient burning of fat for energy.

- **PPAR gamma** – this causes insulin sensitization and enhances glucose metabolism. This is a common target for drug development for glucose regulation.


Key Metabolic Targets in Weight Loss

- **GLP-1** - Glucagon like peptide triggers satiety and delays gastric emptying. This compound signals the hypothalamus for controlling appetite.

- **Leptin** – released to signal to brain that you are full. Obese people have disorder of leptin signaling.

- **Cortisol** – the key stress hormone that disrupts insulin and glucose regulation, triggers chronic inflammation and disrupts sleep.
  - Adrenal fatigue
Key Metabolic Targets in Weight Loss

• Serotonin – is essential to maintaining satiety, and for positive mood.

• Dopamine – responsible for managing the reward cascade system, which supports cravings, helps with focus and satisfaction.

• NF Kappa Beta – the principle inflammatory compound that is responsible for initiating the inflammatory chemical production from cells including COX 1,2.

• Vitamin D – plays a critical role in insulin regulation and immune modulation. It is a co-factor in expression of insulin receptors.
Roadblocks to Weight Loss:

• Insulin resistance
• Mitochondrial dysfunction
• Inflammation in muscle cells
• Gut imbalances
Insulin Resistance

- Key metabolic function of Insulin
  - Stimulating glucose uptake in Skeletal muscle and adipocytes
  - Upregulating the synthesis and storage of glycogen in skeletal muscle
  - Downregulating glucose production (gluconeogenesis) in the liver
  - Inhibiting the breakdown of fat (lipolysis) in adipocytes

Insulin Resistance

Mitochondrial Dysfunction
Mitochondrial Dysfunction

• Mitochondrial dysfunction has been implicated in the pathogenesis of insulin resistance
  o Insulin resistance linked to Type 2 diabetes mellitus

• Mitochondrial are dynamic organelles
  o Adapt to short and long-term metabolic perturbations
  o Undergo fusion and fission cycles
  o Biogenesis governed by PGC-1alpha

Mitochondrial Dysfunction
Mitochondrial Dysfunction

Muscles = Energy Currency of the Body

Physical Activity – Glucose Utilization

• Greatest volume of glucose utilization occurs in skeletal muscles
  o Glucose transport into myocytes is an important factor in whole body glucose disposal and insulin activity

• Aerobic Activity
  o Myocytes will use both the stored glycogen and the contraction-stimulated glucose transport for energy

• Physical activity has a two-fold effect on myocytes
  o Acute stimulation of insulin-independent glucose disposal into the myocyte triggered by muscle contraction
  o Depletion of glycogen stores in muscle tissue
Inflammation in Skeletal Muscle

Inflammation in Skeletal Muscle

# Inflammation in Skeletal Muscle

<table>
<thead>
<tr>
<th>Myokines</th>
<th>Major autocrine, paracrine, or endocrine effects on metabolism and inflammation</th>
<th>Regulation in SM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IL-6</strong></td>
<td>Promotes muscle hypertrophy&lt;br&gt;Acutely: enhances insulin sensitivity and insulin-stimulated glucose uptake; promotes lipolysis and FA oxidation in myocytes, adipocytes, and whole body (19, 20, 22–25); inhibits inflammation (19, 26)&lt;br&gt;Chromically: induces insulin resistance; promotes inflammation in skeletal muscle and liver (162, 163)</td>
<td>Increased with exercise (19, 20), decreased in obesity and T2D (30, 31), increased in obesity and T2D (32–34)</td>
</tr>
<tr>
<td><strong>IL-8</strong></td>
<td>Induces angiogenesis and leukocyte recruitment (19, 24)</td>
<td>Upregulated with exercise (19, 20), increased in obesity with T2D (34)</td>
</tr>
<tr>
<td><strong>IL-15</strong></td>
<td>Promotes muscle hypertrophy; reduces lipid deposition in white AT (19, 24)</td>
<td>Increased with exercise (19, 20); increased in obesity with T2D (34); no change in obese subjects with insulin resistance (164)</td>
</tr>
<tr>
<td><strong>TNF-α</strong></td>
<td>Inhibits insulin sensitivity and insulin-stimulated glucose uptake; impairs mitochondrial ultrastructure and functions; proinflammatory in myocytes, adipocytes, and immune cells (40–45)</td>
<td>Increased in obesity with insulin resistance or with T2D (31, 34, 35, 38)</td>
</tr>
<tr>
<td><strong>GROα</strong></td>
<td>Induces immune cell infiltration; proinflammatory (34)</td>
<td>Increased in obesity with T2D (34)</td>
</tr>
<tr>
<td><strong>MCP-1</strong></td>
<td>Induces immune cell infiltration; proinflammatory (34, 35, 37, 76)</td>
<td>Increased in obesity with insulin resistance or with T2D (34, 35)</td>
</tr>
<tr>
<td><strong>RANTES</strong></td>
<td>Induces immune cell infiltration; proinflammatory (35, 77)</td>
<td>Increased in obesity with insulin resistance (35)</td>
</tr>
<tr>
<td><strong>FGF21</strong></td>
<td>Induces white AT browning; protects from diet-induced obesity and insulin resistance (29, 165)</td>
<td>Increased with stress, insulin challenge, obesity, and T2D (165)</td>
</tr>
<tr>
<td><strong>Irisin</strong></td>
<td>Induces white AT browning; increases myocyte proliferation, GLUT4 expression, and mitochondrial uncoupling and biogenesis (24, 27–29)</td>
<td>Induced with muscle contraction (28); decreased in obesity (166)</td>
</tr>
<tr>
<td><strong>Myonectin</strong></td>
<td>Promotes FA uptake by adipocytes and hepatocytes with reduction of circulating FFAs (167)</td>
<td>Increased with exercise; decreased in obesity (167)</td>
</tr>
<tr>
<td><strong>Myostatin</strong></td>
<td>Inhibits muscle hypertrophy; maintains metabolic homeostasis and modulates AT function and mass (19, 24)</td>
<td>Decreased with exercise; increased in obesity (19, 168)</td>
</tr>
</tbody>
</table>

Gut Microbiome Imbalances and Obesity

- Obesity characterized by low grade inflammation
- Gut microflora imbalances linked to inflammatory conditions, obesity and type 2 diabetes
- Probiotics dampen inflammatory signaling
- Obese individuals commonly have imbalances in microflora
- GUT health important in metabolic homeostasis
- Serotonin made in the gut

What Drugs Commonly Affect the Microbiome?

- Antibiotics
- NSAIDS
- Corticosteroids
- OCs/HRT
- PPIs/H2 blockers
- Metformin
- Statins
- Antipsychotics
- Opioids

What Drugs Commonly Affect the Microbiome?

- Study tested 1,100 drugs on 40 representative GUT bacterial strains
- 25% of drugs affected bacterial growth in vitro
- Possible new source of antibiotic resistance
- Nutrients that support Gut Health
  - Berberine
  - Probiotics
  - Glutamine
  - Zinc carnosine

Body’s way of cleaning house – innate recycling
Define Autophagy

- Literally “self-eating” coined by Nobel-Prize scientist Christian de Duve
  - Auto “self”
  - Phagein “to eat”

- Different from Apoptosis (programmed cell death)

Role of Autophagy (Why do we care?)

- Autophagy has a variety of physiological and pathophysiological roles:
  - Starvation adaptation
  - Intracellular protein and organelle clearance
  - Development
  - Anti-aging
  - Elimination of microorganisms
  - Cell death
  - Tumor suppression
  - Antigen presentation
  - Important in inflammation and immunity

Autophagy - How do we trigger it?

- Intermittent fasting
- Lower carb intake – ketosis
- Regular exercise
  - AMPK and mTOR regulate autophagy
Fasting

• “The best of all medicines is resting and fasting,”
  Benjamin Franklin (1706-1790)

• “A little starvation can really do more for the average sick man than can the best medicines and the best doctors,”
  Mark Twain (1835-1910)
What is Fasting?

• Generally defined as the abstinence or limitation of food, drink or both
• One of the most ancient and widespread healing traditions in the world
• Hippocrates (c 460-370 BC) – treatments included fasting and apple cider vinegar
• Greeks called fasting the “physician within”
• Religions use fasting for spiritual purposes
Fasting vs. Starvation

• Fasting is completely different from starvation in one crucial way: **CONTROL**.

• Starvation is the involuntary abstention from eating. It is neither deliberate nor controlled. Starving people have no idea when and where their next meal will come from…

• Fasting is voluntary. Food is readily available, but you choose not to eat.

Who Should NOT Fast?

- Those who are severely malnourished or underweight
- Children under eighteen years of age
- Pregnant women
- Breastfeeding women

- Always seek the advice of a health-care professional before attempting fasting…
Fasting Myths

- Fasting puts you in “starvation mode”
- Fasting makes you burn muscle
- Fasting causes low blood sugar
- Fasting results in overeating
- Fasting deprives the body of nutrients
- “It’s just crazy”

Physiology of Fasting

- Two-compartment model of energy production; if glucose is not available, then fat is burned for fuel
  - Glucose
  - Fat

- Periods of low food availability part of human history

- Fed State vs. Fasted State
Two-Compartment Model

[Diagram showing the two compartments: Body Fat (left) and Insulin/Glycogen (right). The diagram illustrates the flow of calories in and out, with an emphasis on the relationship between insulin and glycogen.]
5 Stages of Fasting

1 – Feeding

2 – Post-absorptive phase

3 – Gluconeogenesis

4 – Ketosis

5 - Protein conservation phase


5 Stages of Fasting


5 Stages of Fasting

1. Feeding
   - During meals insulin levels raised
   - Allow uptake of glucose into tissues – muscle, brain
   - Used directly for energy
   - Excess glucose stored as glycogen in liver


5 Stages of Fasting

2. Post-Absorptive Phase
   - 6-24 hours after initiation of fasting
   - Insulin levels begin to fall
   - Breakdown of glycogen for glucose – energy
   - Glycogen stores last approx. 24 hours
5 Stages of Fasting

3. Gluconeogenesis
   - 24 hours – 2 days post initiation
   - Increased PGC-1alpha liver expression
   - Liver manufactures glucose from amino acids = gluconeogenesis
   - In non-diabetic, glucose levels fall but stay within normal range
5 Stages of Fasting

4. Ketosis
   - 2-3 days post initiation
   - Low insulin levels stimulate lipolysis
   - Triglycerides broken down into:
     • Glycerol
     • Pyruvate
     • Lactate
   - Fatty acids used for energy; not for brain
   - Ketone bodies that cross Blood Brain Barrier are used by brain


5 Stages of Fasting

4. Ketosis
   o Post 4 days of fasting
   o 75% of brain energy provided by ketones
     • Beta-hydroxybutyrate
     • Acetacetate
   o Levels can increase of 70 x during fasting


5 Stages of Fasting

5. Protein Conservation Phase
   - >5 days post initiation
   - High levels of growth hormone maintains muscle and lean tissues
   - Energy from free fatty acids and ketones
   - Increased norepinephrine to maintain metabolic rate


Types of Fasting

- Time Restricted Eating (TRE)
- Intermittent Fasting (IF), Alternate Day Fasting (ADF)
- Short Term Fasting (ST): <3 consecutive days
- Prolonged Term Fasting (PF): > 3 consecutive days


Types of Fasting

• Time Restricted Eating (TRE)
  o Food is ingested in a window of time during the day
  o Fast/refrain from eating other hours of day
  o Ex: 12 hours per day of no food
  o Ex: Eat between 12 pm and 7pm; fast the remaining hours
  o This type of fasting is used mostly for weight loss


Types of Fasting

- Intermittent Fasting (IF)
  - Most common type
  - Example – 5:2 diet
  - Fasting on 500 calories for women and 600 calories for men on 2 non-consecutive days a week
  - Ex: Monday and Friday
  - Used for weight loss, improved metabolism


Types of Fasting

- Periodic Short Term or Prolonged Fasting
  - Short Term (ST) or Prolonged (PF), Periodic Fasting
    - ST <3 consecutive days
    - PF 3 or more days
    - PF stresses body more and produces more profound results
  - Stimulates protectionist and rejuvenation modes
  - Strive and thrive


Fasting Mimicking Diet (FMD)

- Developed by Dr. Valter Longo, University of Southern California
  - Author of The Longevity Diet
- Periodic Fasting
- Involves severe caloric restriction for 5 days out of the month
- Uses 770-1100 calorie plant-based nutrients


Benefits of Fasting

• It’s free, saves money on food, and is flexible
• Improved insulin sensitivity
• Improved thermogenesis
• Increased PGC-1alpha
• Rids body of excess fluid
• Decreased inflammation
• Stimulates brain derived neurotrophic factor (BDNF)
• Weight loss
• Cancer protective


Meal Frequency and Timing

Weight-Loss Nutraceuticals

Med for horses not bodybuilders...

Buyer beware!!!!!
Weight-Loss Nutraceuticals

• Check for interactions with Rx meds.
  o **Due diligence** is mandatory!
  o Check if patients are on SSRIs, MAOIs, TCAs
  o Triptans

• Not all supplements are created equal
  o Check for standardization
    • Example – Green Tea 50% - 70% EGCG (epigallocatechin-3-gallate) content
Weight-Loss Nutraceuticals

• Targeting specific approaches for weight loss
  o Dopamine and serotonin support
  o Glucose regulation
  o Cortisol/stress management
  o Thyroid support
  o Sex hormone support
Weight-Loss Nutraceuticals

Dopamine and Serotonin Support

• Theacrine – 1,3,7,9 tetramethyluric acid
  o Purine alkaloid similar to caffeine in structure
  o Reported to improve dopamine levels, modulates other neurotransmitters, decreases ROS and Inflammatory Cytokines centrally
  o Improves Focus and Concentration
  o Dosing
    • Up to 300 mg orally per day


Weight-Loss Nutraceuticals

Dopamine and Serotonin Support

- Mucuna (Mucuna pruriens) – Velvet Bean
  - Contains L-Dopa
  - Improves dopamine pool
  - Helps improve the reward cascade and improves satiety
  - Dosing - 150-200 mg BID (50-98% extracts)

L-Tyrosine
  - Precursor for catecholamines (dopamine, norepinephrine, epinephrine)
  - Helps improve thermogenesis
  - Helps support dopamine pools
  - Dosing – 1500 mg BID

5-Hydroxytryptophan (5-HTP)
  - Amino acid precursor for serotonin
  - Manufactured from L-tryptophan
  - Supports serotonin pools
  - Dosing – 50-100 mg TID

Weight-Loss Nutraceuticals

Dopamine and Serotonin Support

• Evodia
  o Stimulates tryptophan hydroxylase 2 (THP2)
  o Converts tryptophan to 5-HTP
  o Increases serotonin pools
  o Helps improve insulin sensitivity
  o Dosing - 150 mg daily (standardized to 98% evodiamine)

Capsinoids – cayenne pepper (Capsicum sp.)
  - Improves fat burning – thermogenesis
  - Stimulates Transient Receptor Potential Vanilloid 1 (TRPV1) channel – capsaicin receptors in the gut
  - Increased skeletal muscle activation via uncoupling protein-3 (UCP-3)
  - Enhanced white “belly” fat lipolysis
  - Improved lipid oxidation
  - May suppress appetite
  - Dosage = 3 caps in AM


Weight-Loss Nutraceuticals

Thermogenic / Fat-burning support

- **Green Tea (Camellia sinensis) Leaf**
  - Antioxidant – 20 times more potent than Vitamin E
  - Decreased muscle inflammation and improved recovery times in exercise
  - Reported to improve
    - Immunity
    - Performance and endurance
    - Mental Clarity
    - Lipolysis – fat metabolism
  - Dosing - 500 mg daily (250) BID of a least 50% EGCG content


Weight-Loss Nutraceuticals

Glucose Regulation

• Chromium Picolinate
  o Dosing - 200 mcg daily with a meal
• Alpha Lipoic Acid (ALA)
  o 1500 mg daily for weight loss
  o 300 mg BID for general support
• Cinnamon bark
  o Dosing - 500 mg BID
• Thai ginseng
  o Dosing - 100 mg daily (4% 5,7 dimethoxyflavones (DMF))

• Magnolia and Phellodendron combination — marketed for stress-related appetite control and reduction of stress-related fat deposition.
  o Helps decrease food cravings associated with increased stress
  o Helps normalize cortisol and DHEA levels, including exercise induced
  o Dosing - 250 mg orally 3 times a day

Weight-Loss Nutraceuticals

Stress/Anxiety

• **L-theanine**
  - Promotes relaxation without drowsiness
  - Dosing - 100 mg orally 1-3 times daily

• **Ashwagandha (Withania somnifera) root**
  - Herbal adaptogen that enhances the body’s resilience to stress
  - Antioxidant properties
  - Dosing - 500 mg orally daily
Weight-Loss Nutraceuticals

Thyroid Support

• Selenium
  o Supports Immunity and Antioxidant
  o Cofactor in conversion of T4 to T3
  o Dosing - 200 mcg daily with a meal

• Bladderwrack (Fucus vesiculosus)
  o Iodine up to 6000 mcg/gm plant

• Coleus (Coleus forskohlii) root
  o Used in Ayurveda and Chinese Medicine
  o Promotes fat oxidation and may help improve free testosterone
  o Dosing - 500 mg bid of 10%
Weight-Loss Nutraceuticals

Hormone Support

• DIM (diindolylmethane)
  o Found in cruciferous veggies
  o Advanced metabolite of indole-3-carbinol
  o Helps convert active estrogens into 2-hydroxyestrone
  o May act as weak estrogen and improve free testosterone levels
  o Decreased risk of hormonally related cancers, including breast, prostate and thyroid
  o Dosing - 100 mg BID; add I3C (indole-3-carbinol) 200 mg BID for extra support


• Eurycoma (Eurycoma longifolia) root
  o Tongkat ali or “Malaysian ginseng” – used in SE Asian cultures for improved testosterone levels, libido
  o Reported to improve testosterone levels (free and total) in men and women
  o Also improves testosterone/cortisol ratio
  o Dosing – 100-200 mg BID (50:1 w/v)


Weight-Loss Nutraceuticals

Detoxification Support

• Milk Thistle (Silybum marianum)
  o Hepatoprotective
  o Improves glutathione stores
  o Improves phase 1 detoxification
  o Dosing - 175 mg BID – standardized to 80% (140 mg) Silymarin

• Shatavari (Asparagus racemosus)
  o Antioxidant flavonoids
  o Nephroprotective
  o Improved diuresis
  o Also improves Th1/Th2 balance
  o Dosing - 250 mg BID standardized to 50% saponins
Weight-Loss Nutraceuticals

General Support

• Magnesium
  o Critical in over 300 biochemical reactions in the body
  o Low levels correlate to insulin resistance/type 2 diabetes
  o Low levels Mg found in obese/overweight individuals
  o Dosage – Check RBC magnesium level
    • 400-800 mg daily chelate
    • Dose at night, if sleep is a problem
  o *Weight loss clinics will give IM magnesium injections – 1 cc
    50% Magnesium sulfate. Patients will experience severe pain
    without lidocaine being added to the IM shot.


Weight-Loss Nutraceuticals

• What body builders are using:
  o Bacopa Monnieri (BM)
    • Helps Improve:
    o Memory
    o Cognition
    o Attention
    • Works similar to MAOI and AChE inhibitors
    • Dosing - 500 mg per day
  o Rhodiola Rosea (RR)
    • Helps improve:
    o Stress
    o Anxiety
    o Depression
    • Works similar to MAOI inhibitor.
    • Dosing - 500 mg per day
Compounding Options

- Weight loss options available from a compounding pharmacy
  - Insulin resistance:
    - Metformin 250 mg/Chromium 200 mcg/ALA 250 mg
  - Cravings:
    - Phentermine (18-37.5 mg)/Topiramate (20-30 mg)/Naltrexone 4 mg
    - Topiramate 30 mg/Naltrexone 4 mg
    - Chromium 200 mcg / Naltrexone 4 mg
    - Add Theacrine or 5-HTP
  - Erectile dysfunction
    - Tadalafil 7 mg
Compounding Options

• Patient specific options available from a compounding pharmacy
  o Filler options:
    • Magnesium glycinate
    • Indole-3-carbinol
    • DIM (diindolymethane)
    • Gluten Free/Allergenic/dye free filler
    • E4M – extended release filler
Compounding Options - Peptides

- 7000 naturally occurring peptides
- Selective signaling molecules
- Pharmacological profile and intrinsic properties
- 140 peptide therapeutics
- 60 US Food and Drug Administration (FDA) – approved peptide medicines
- World Market in 2011 – 14.1 billion
- Metabolic diseases and Oncology

For more information on peptides: peptidesociety.org
Compounding Options - Peptides

- Peptides for weight loss
  - GHRP
  - GHRH/GHRP
  - AOD9064
  - Frag 176-191
  - Melanotan II
  - PEPCK
  - Dihexa
  - GLP-1R Agonist

<table>
<thead>
<tr>
<th>Purpose</th>
<th>GHRH/GHRP/BPC</th>
<th>Dosing</th>
<th>Benefits</th>
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<tbody>
<tr>
<td>Introduction 2 wks</td>
<td>GHRP</td>
<td>50 mcg Bedtime</td>
<td>Sleep, bone mineral density, well being</td>
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<td>Anti-Aging</td>
<td>GHRH/GHRP</td>
<td>100mcg Bedtime</td>
<td>Sleep, recovery, well being, bone mineral, receptor entraining</td>
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<td>100mcg Bedtime</td>
<td>Fatty acid release,</td>
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<td>Progressive Fat loss</td>
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<td>100mcg Bedtime</td>
<td>Fat loss, Enhance fasting</td>
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<td>BPC-157</td>
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<td>100mcg Morning</td>
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<td>100mcg 3 hrs later</td>
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<td>Injury</td>
<td>GHRH/GHRP</td>
<td>100mcg Bedtime</td>
<td>Recovery, Increased healing injury, IGF-1,</td>
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<td>BPC-157</td>
<td>2 more dosing 3 hr split</td>
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<td>100mcg</td>
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<td>Split dosing 600mcg</td>
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Compounding Options - Peptides

- GHRH
  - Semorelin
  - GRF 1-29
  - Mod GRF 1-29 (CJC 1296 without DAC)
  - CJC-1296 with DAC
  - Tesamorelin
- GHRP – Ghrelin like
  - Hexarelin
  - GHRP – 2
  - GHRP-6
  - Ipamorelin

- Most common peptides used for weight loss includes Ipamorelin, CJC-1296, Tesamorelin, and Semorelin
Post-Assessment Questions

• What is the optimal Vitamin-D level (ng/mL)?
  o A. <20
  o B. 20-49.9
  o C. >100
  o D. 50-80

• What is the dosage of selenium for thyroid support?
  o A. 300 mcg
  o B. 200 mcg
  o C. 200 mg
  o D. 300 mg

• When recommending any type of supplements to a patient, due diligence is mandatory for checking interactions?
  o True or False?
Questions?
My Contact Information

Tim Schroeder
Pharm D
FAARFM, ABAHP
MS, MBA

Connect with me on LinkedIn