Diabesity: A Functional Medicine Approach for Obesity & Diabetes

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Kripalu
Obesity or “Diabesity”
The Continuum Concept
Diabesity: Is Sugar Toxic?
What is Diabesity?

Condition of metabolic imbalances ranging from mild insulin resistance to end stage diabetes.
Animal Study

High GI

Low GI

Animal Study: Islet Abnormalities

Gastric Bypass
What Epigenetics Really Means
The Gene-Environment Connection
What is Diabesity?

- Condition of metabolic imbalances ranging from mild insulin resistance to end stage diabetes
- Is all overweight and obesity driven by insulin resistance?
- What causes insulin resistance?
- How can you correct insulin resistance?

Francine Kaufman, MD coined the term “diabesity”
Diabesity is a Chronic SYSTEMIC Disease: Causes vs. Effects

- Heart Disease
- Cancer
- Diabetes
- Alzheimer’s
- Arthritis
- Autoimmune
- Depression
Living in Harmony with Our Genes
A Role for Sweet Taste - Calorie predictive relations in energy regulation by rats


- Rats fed yogurt – sugar or saccharin sweetened over 14 days
- Results – artificial sweetener
  - Total food consumption increased over 14 days
  - Increase weight gain and body fat
  - Body temperature and thermogenesis decreased
  - Consumed LESS calories but gained more weight
Food is information. It regulates gene expression.

NUTRIGENOMICS
Beyond Food as Calories
Mechanisms and Causes vs. Risk Factors

**Risk Factors**
- Hyperinsulinemia
- Hyperglycemia
- Hypertension
- Dyslipidemia
- Coagulopathy

**Treatments**
- Actos, Avandia, Biguanides
- Oral hypoglycemics, insulin
- Anti-hypertensives
- Statins, fibrates
- ASA, clopidogrel
...THE TOP PRESCRIPTION IS FOR YOUR ARTHRITIS, BUT IT MAY CAUSE A HEART ATTACK. THE SECOND PRESCRIPTION SHOULD PREVENT A HEART ATTACK, BUT IT COULD DAMAGE YOUR LIVER. THE THIRD SHOULD PREVENT LIVER TROUBLE, BUT IT MAY DESTROY YOUR SPLEEN. THE FOURTH PROTECTS THE SPLEEN BUT HAS BEEN KNOWN TO EAT AWAY THE PROSTATE. THE FIFTH.....
Mechanism and Causes vs. Risk Factors

**Causes**
- Allergens
- Pathogenic Microbes
- Toxins
- Stress
- Nutrient deficiencies/excesses

**Treatment**
- Allergy elimination
- Ecological balance
- Detoxification
- Mind body/Cognitive Tx
- Diet and Nutrient therapy
Epigenetics: Feeding Your Genes
What Epigenetics Really Means
The Gene-Environment Connection
A Roadmap for 21st Century Wellness and Health Care
Addressing Clinical Imbalances

- Nutritional/Lifestyle
- Immune/Defense & Repair
- Digestive/Assimilation
- Detoxification/Biotransformation & Elimination
- Mitochondrial/Energy
- Hormonal/Communication & Circulation
- Structural Integrity
- Mind/Body/Soul/Community
Diabetes, HTN, Hyperlipidemia

- 59-year-old black woman, college dean
- Dx 1997 HTN
- Dx 1999 with Type 2 DM
- Dx 2000 obstructive sleep apnea
- Dx 2003 hyperlipidemia
- HbA1c 10.3
- Fatigue – can’t drive or watch TV
- Ravenous hunger
- Weight 190lbs, BMI 35, BP 160/104
History

• Medications
  – Lipitor 20 mg qd, Glyburide 5 mg bid, Metformin 1500 mg/d, Metoprolol 25 mg, Lotrel 10/20, ASA 81mg and MVI

• Social
  – 4–6 drinks/wk, nonsmoker, single

• Exercise
  – Irregular

• Diet
  – Microwave oatmeal, apple, chicken salad, chicken, peanuts, candy and chocolate at night
Laboratory Evaluation

- Urine 3+ glucose, FBS 312, **HbA1c 10.1**
- 25 OH vitamin D 17 ng/ml (nl 30-100)
- ALT 56, microalbumin neg
- TC 186, HDL 54, LDL 122, TG 101
  - Small LDL (1320/1608) and HDL particles
- CRP 0.7, Hcy 6.4, fibrinogen 311, Lp(a) 423
- Lipid peroxides 2.2 nmol/mL (nl <1.5)
- Organic acids
  - Lactate, B OH butyrate, and **Krebs cycle** metabolites abnormal (CoQ10), B vitamin deficiencies
Functional Assessment

• Hormonal Imbalances/Communication
  – Type 2 DM – insulin resistance
  – Hypertension
  – Hyperlipidemia - small LDL particles
  – Sleep apnea
• Impaired Detoxification/Biotransformation
  – NASH
• Mitochondrial/Energy
  – Mitochondrial dysfunction and COQ10 deficiency
  – Oxidative stress
• Nutritional Imbalances
  – Vitamin D deficiency
Dietary Recommendations

- Protein in morning (shake or eggs)
- Only WHOLE grains – no flour or sugar
- 50 grams fiber
- Increase omega-3 fats
- Reduce red meat
- No processed food, junk food, trans fats, juices, or sodas
- No HFCS or artificial sweeteners
- Smaller, more frequent meals
Treatment

• Medications:
  – Niacin 500 mg
  – Reduced Lipitor from 20 to 10 mg
  – Eliminated glyburide
  – Eliminated beta-blocker
Nutritional Supplements

- Whole soy protein shake with plant sterols
- Glucomannan (konjac root) 4 caps before meals
- Multivitamin
- Omega-3 fatty acids 1-2 gms bid
- R-lipoic acid, chromium, magnesium and biotin
- RIAA – protein kinase modulators or SKRM’s (Acacia)
- Cinnamon
- Mitochondrial support
  - CoQ10, N-acetyl-cysteine (NAC), acetyl-L-carnitine, alpha lipoic acid, creatine, magnesium malate, PC, Na succinate
- Vitamin D 5,000 U daily
Results: 1 Year

- BMI 35 to 31 (lost 20 lbs)
- BP 160/104 to 127/79
- HbA1c 10.1 to 5.9
- OSA resolved
- Increased energy, no cravings, exercising
- FBS 321 to 111
- LDL from 122 to 71 (small particles from 1320 to 615)
- Vitamin D from 17 to 62
Diagnosis: Testing

• 2 hour post 75 gm glucose load GTT with INSULIN levels
• Or 30 min post 75 gm glucose load insulin and glucose
• NMR lipid profile (Liposcience or Labcorp)
• TG/HDL ratio > 4
• Other tests: per system or cause
Normal Glucose Tolerance?

Severe Hyperinsulinemia
and Insulin Resistance
Limitations of Diagnostic Criteria
The Multiple Dimensions of Insulin Resistance

- 51 year old obese businesswoman
- Smoker 1 ppd
- Minimal alcohol and caffeine intake
- No sugar but very high refined CHO diet
- No regular exercise
- Early menopause at 40 on tibolone (Livial) - gained 45 lbs
- Fatigue
- Severe GERD
- No family history of diabetes
“Normal” GGT

- Normoglycemia
- (96, 115, 103)
- Hyperinsulinemia
- (35, 224, 106)
Initial Evaluation

- hs-CRP 4.9 mg/L
- HbA1C 5.7%
- TC 292, TG 112, HDL 33, LDL 235,
- TC/HDL 8.85 (nl < 3), TG/HDL 3.3
- GGT 201 (nl < 60)
- HCY 9.0, Lp(a) 34, Fibrinogen 324
- H. pylori antibodies 3.3
- VO2 Max 63% predicted
Core Clinical Imbalances

• Nutritional Imbalances
  – High CHO diet – bread, potatoes, pasta
• Immune/Inflammatory/Defense & Repair
  – High CRP, VAT, adipocytokines
• Hormonal & Metabolic/Communication
  – Hyperlipidemia, estrogen (ERT), dyslipidemia (low HDL)
• Digestive/Assimilation
  – H. pylori, GERD
Core Clinical Imbalances

• Detoxification/Biotransformation
  – High GGT (toxic exposure), NASH (fatty liver)

• Mitochondrial Imbalances/Energy
  – Low VO2 max, sedentary, fatigue
  – smoker
Treatment:
Take Out Bad Stuff & Add Good Stuff

- **Nutritional Balance**
  - Low GL, high PI, high fiber diet, eat early and often
  - Multivitamin, EPA/DHA

- **Digestive Balance**
  - H. pylori treatment (triple therapy) and probiotics

- **Hormone Support**
  - Stopped hormone therapy (DEXA - T score 114%)
  - Glucomannan for insulin/lipid balance
  - Red rice yeast
Treatment:
Take Out Bad Stuff & Add Good Stuff

• Detox/Biotransformation Support
  – Dietary detoxification support (crucifers, etc.)
  – Silymarin (milk thistle)

• Energy and Mitochondrial Support
  – alpha lipoic acid
  – Regular exercise
Results: 3 Months Later

• Quit smoking
• No GERD
• Lost 46 pounds in three months
• TC/HDL ratio decreased 8.85 to 3.8
• Fasting insulin 35 to 18
• GGT 201 to 111
• CRP 4.9 to 1.2
MONDAY MORNING
this is what it looks like
Goof Proof Health

Good Health Made So Simple
Mom, Dad or even a Sixth Grader
Can Understand It!
Lifestyle 2.0

• Get Healthy Together – Get Connected
• Take out the Bad Stuff & Put in the Good Stuff
• Eat real food, eat early, eat often
  – Try an elimination diet and add detox and anti-inflammatory foods
• RX: multivitamin, vitamin D, omega 3 fats and extra chromium, biotin and magnesium
• Add glucomannan and alpha lipoic acid
• Get Moving – aerobic, interval and strength training
• Breathe and Dance and Play and Be...
Food as Medicine
Food as INFORMATION
Beyond Calories
“The fox knows many little things, but the hedgehog knows one big thing.”

*Isaiah Berlin*
MONDAY MORNING
this is what it looks like
THE
BLOOD SUGAR SOLUTION

The UltraHealthy Program for Losing Weight, Preventing Disease, and Feeling Great Now!

• Reverse prediabetes and diabetes
• Eliminate the leading causes of heart disease, cancer, and obesity
  • Increase your energy
  • Cure your sugar cravings and get thin fast
Goof Proof Health

Good Health Made So Simple
Mom, Dad or even a Sixth Grader
Can Understand It!
Nutrigenomics
GOOF PROOF YOUR KITCHEN

GET RID OF METABOLISM BLOCKERS
INGREDIENTS: ENRICHED BLEACHED WHEAT FLOUR [FLOUR, FERROUS SULFATE, “B” VITAMINS (NIACIN, THIAMINE MONONITRATE (B1), RIBOFLAVIN (B2), FOLIC ACID)], SUGAR, CORN SYRUP, WATER, HIGH FRUCTOSE CORN SYRUP, PARTIALLY HYDROGENATED VEGETABLE SHORTENING (CONTAINS ONE OR MORE OF: SOYBEAN, CANOLA OR PALM OIL), DEXTROSE, WHOLE EGGS. CONTAINS 2% OR LESS OF: MODIFIED CORNSTARCH, CELLULOSE GUM, WHEY, LEAVENINGS (SODIUM ACID PYROPHOSPHATE, BAKING SODA, MONOCALCIUM PHOSPHATE), SALT, CORNSTARCH, CORN FLOUR, CORN DEXTRINS, MONO AND DIGLYCERIDES, POLYSORBATE 60, SOY LECITHIN, NATURAL AND ARTIFICIAL FLAVORS, SOY PROTEIN ISOLATE, SODIUM STEAROYL LACTYLATE, SODIUM AND CALCIUM CASEINATE, CALCIUM SULFATE, SORBIC ACID (TO RETAIN FRESHNESS), COLOR ADDED (YELLOW 5, RED 40). MAY CONTAIN PEANUTS OR TRACES OF PEANUTS.
INGREDIENTS: ENRICHED BLEACHED WHEAT FLOUR [FLOUR, FERROUS SULFATE, “B” VITAMINS (NIACIN, THIAMINE MONONITRATE (B1), RIBOFLAVIN (B2), FOLIC ACID)], SUGAR, CORN SYRUP, WATER, HIGH FRUCTOSE CORN SYRUP, PARTIALLY HYDROGENATED VEGETABLE SHORTENING (CONTAINS ONE OR MORE OF: SOYBEAN, CANOLA OR PALM OIL), DEXTROSE, WHOLE EGGS. CONTAINS 2% OR LESS OF: MODIFIED CORNSTARCH, CELLULOSE GUM, WHEY, LEAVENINGS (SODIUM ACID PYROPHOSPHATE, BAKING SODA, MONOCALCIUM PHOSPHATE), SALT, CORNSTARCH, CORN FLOUR, CORN DEXTRINS, MONOLITHIN, NATURAL LACTATE, SODIUM SELENATE, CALCIUM SULFATE, SORBIC ACID (TO RETAIN FRESHNESS), COLOR ADDED (YELLOW 5, RED 40). MAY CONTAIN PEANUTS OR TRACES OF PEANUTS.
HIGH FRUCTOSE CORN SYRUP
Toxic Sugars

- High fructose corn syrup - Super sugar
  - Rise in HFCS parallels rise in obesity
  - Unknown in our diet in before 1970, now the most common sugar consumed
  - Sweeter and cheaper than sugar
  - Uncontrolled entry into bloodstream and cells
  - Provides no feedback to brain to reduce hunger
  - Increases appetite and sugar cravings
  - Major cause of inflammation and fatty liver
  - Major cause of elevated cholesterol and triglycerides
Trans Fats

• Trans or hydrogenated fats - Super fats
  – Developed as butter alternative
  – Preserves foods, kills people
  – Labeling just started in Jan 2006
  – Turns on weight gain genes
  – Blocks metabolism and reduces fat burning
  – Impairs blood sugar metabolism causing diabetes
  – Increases cholesterol
  – Increases inflammation
  – Promotes heart disease, cancer and dementia!
<table>
<thead>
<tr>
<th>Additive</th>
<th>Where used</th>
<th>Potential problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>E102 - tartrazine</td>
<td>Sweets, biscuits, mushy peas</td>
<td>Hyperactivity, asthma, rashes</td>
</tr>
<tr>
<td>E124 - ponceau 4R</td>
<td>Sweets, biscuits, drinks</td>
<td>Allergy, intolerance</td>
</tr>
<tr>
<td>E110 - sunset yellow</td>
<td>Sweets, ice cream, drinks</td>
<td>Gastric upset, allergy</td>
</tr>
<tr>
<td>E122 - camoisine</td>
<td>Biscuits, jelly, sweets, ready meals</td>
<td>Allergy, intolerance</td>
</tr>
<tr>
<td>E104 - quinoline yellow</td>
<td>Sweets, smoked haddock, pickles</td>
<td>Hyperactivity, asthma, rashes.</td>
</tr>
<tr>
<td>E129 - allura red</td>
<td>Soft drinks, cocktail sausages</td>
<td>Some evidence of hypersensitivity</td>
</tr>
<tr>
<td>E211 - sodium benzoate</td>
<td>Soft drinks, baked goods, lollies</td>
<td>Hyperactivity; asthma</td>
</tr>
</tbody>
</table>
Food as Medicine: Nutritional Balance

- Macronutrient composition
  - Protein, fats and CHO effects on cell signaling and gene expression
- Macronutrient quality
  - Phytonutrients and glycemic load
- Meal timing and frequency
- Quality vs. Quantity
- Food addiction – Implications?
Cutting Cravings
TEN TIPS TO BOOST YOUR METABOLISM
DRINK THE POUNDS OFF

MAGIC WEIGHT LOSS DRINK
SHAKE UP YOUR METABOLISM
MANAGING YOUR BLOOD SUGAR

INSULIN

EXERCISE

DIET
GET SUPER THIN WITH SUPER FIBER
PGX:

KONJAC or

GLUCOMA

NNAN
Turn Up Your Metabolic Fire

• Keep up a slow burn all day
• Power up your metabolism with protein
EAT EARLY AND EAT OFTEN
SAY NO TO SUMO!!
WHEAT BELLY??

GET THE BEAT ON WHEAT
Glutamine, 5HTP, Chromium, B complex, etc.

Featured Kits

Craving Control Kit

- Break the cycle of relentless food cravings
- Balance neurotransmitter levels that lead to cravings
- Control your appetite by slowing the absorption of fats and sugars
THE BLOOD SUGAR SOLUTION

The UltraHealthy Program for Losing Weight, Preventing Disease, and Feeling Great Now!

- Reverse prediabetes and diabetes
- Eliminate the leading causes of heart disease, cancer, and obesity
  - Increase your energy
  - Cure your sugar cravings and get thin fast
Core Imbalances & Diabesity

- Immune/Defense and Repair
- Hormonal/Communication
- Digestion/Assimilation
- Detox/Biotransformation
- Energy/Mitochondrial
- Mind/Body/Soul/Community
Nutrigenomic Index
Whole, unprocessed predominately plant based diet

- Low Glycemic Load (low/no flour, sugar, grain)
- Proper Fatty Acid Composition (ω 3:6 ratio)
- High Phytonutrient Density
- Healthy Protein (plant or grass fed)
- High Micronutrient Density
- Low Allergenic Burden (gluten, dairy, etc.)
- Low Toxic Burden (pesticides, hormones, GMO, etc.)
- Healthy pH Balance
- Healthy Salt-Potassium Ratio
- High Fiber Content
Nutritional Support: Metabolic Tune Up: The Basics

• Multivitamin and micronutrients
  – Chromium, Mg, Zn, Biotin, B complex (methylation – folate, B₁₂, B₆)

• Essential Fats
  – EPA/DHA, GLA (gamma linolenic acid)

• Vitamin D₃
  – Gene response modulator
Nutritional Support: Advanced

- **Hormonal Support**
  - Glucomannan!!!! – konjac root fiber
- **Mitochondrial support**
  - Carnitine, coenzyme Q10, alpha lipoic acid
  - Amino acids
- **Detoxification Support**
  - NAC (n-acetyl-cysteine), silymarin
- **Phytonutrients and herbs**
  - SKRM’s (hops and heartwood), curcumin, ginseng, bitter melon, green tea, fennugreek, gymnemna
How to work with your doctor to get what you need

www.drhyman.com
WARNING

CHALLENGES AHEAD
Overcoming Challenges

- Cravings and food/substance addictions
- Lack of time, lack of planning
- No support from family or friends
- No support group
- Social gatherings and eating out
- Emotional eating and stress
- Cost of food
- Lack of cooking skills
SOLIDARITY
It's good to have friends.
Food as Medicine: Nutritional Balance

• Macronutrient composition
  – Protein, fats and CHO effects on cell signaling and gene expression

• Macronutrient quality
  – Phytonutrients and glycemic load

• Meal timing and frequency

• Quality vs. Quantity

• Food addiction – Implications?
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• Healthy Salt-Potassium Ratio
• High Fiber Content
Macronutrients
What to Eat

- Low glycemic index and glycemic load diet
- High fiber - 50 grams
- Increased omega 3 fatty acids, monounsaturated fats
- Colorful diversity of low glycemic vegetables and fruits
- Increased intake of nuts, seeds and legumes
- Non GMO traditional soy foods
- Lean animal protein (wild?)
- Whole grains (minimal flours)
Macronutrients
What Not to Eat and When

• Minimize or eliminate refined flours and sugars
• Minimize caffeine and artificial sweeteners
• Eliminate trans fats and minimize saturated fats (<5% of calories)
• Combine protein, fat and carbohydrates to reduced glycemic load
• Increase meal frequency and decrease meal quantity
• Eat breakfast and don’t eat 2-3 hours before bed
Nutritional Support: Metabolic Tune Up: The Basics

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  - Cr, Va, Mg, Zn, Biotin, B complex (methylation – folate, B12, B6)
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  - Gene response modulator
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- Immune/Defense and Repair
- Hormonal/Communication
- Digestion/Assimilation
- Detox/Biotransformation
- Mitochondrial/Energy
- Mind/Body/Soul/Community
Inflammation
Inflammation and Obesity
Cause and Effect

Inflammation in the Metabolic Syndrome

Women’s Health Study:
n=14,719

C-reactive protein (mg/L)

Number of Components of the Metabolic Syndrome

Ridker Circulation 2003;107:391-397
The Causes of Inflammation

• Diet
  – Sugar
  – Trans and saturated fats
  – Polyunsaturated omega 6 oils (except GLA)
• Allergens (IgG, IgE - food and environmental)
• Stress
• Lack of exercise
• Toxins (metals, petrochemicals or POP’s)
• Infections (microbesity?)
Hormonal and Autonomic Dysfunction
Hormonal/Autonomic Dysfunction

- Hypercortisolemia (24 hour urine, elevated morning cortisol)
- Reduced heart rate variability
- Women: PCOS, DHEA-S, LH:FSH > 3:1, hair loss, infertility, menstrual irregularities
- Men: low testosterone in men
- Altered thyroid function
- HPA axis and appetite regulation
Digestive Imbalances
Leaky gut and diabetes mellitus: what is the link?

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Summary
Diabetes mellitus is a chronic disease requiring lifelong medical attention. With hundreds of millions suffering worldwide, and a rapidly rising incidence, diabetes mellitus poses a great burden on healthcare systems. Recent studies investigating the underlying mechanisms involved in disease development in diabetes point to the role of the dys-regulation of the intestinal barrier. Via alterations in intestinal permeability, intestinal barrier function becomes compromised whereby access of infectious agents and dietary antigens to mucosal immune elements is facilitated, which may eventually lead to immune reactions with damage to pancreatic beta cells and can lead to increased cytokine production with consequent insulin resistance. Understanding the factors regulating the intestinal barrier function will provide important insight into the interactions between luminal antigens and immune response elements. This review analyses recent advances in the mechanistic understanding of the role of the intestinal epithelial barrier function in the development of type 1 and type 2 diabetes. Given our current knowledge, we may assume that reinforcing the intestinal barrier can offer and open new therapeutic horizons in the treatment of type 1 and type 2 diabetes.

Keywords: Barrier function, diabetes mellitus, gastrointestinal tract, insulin resistance.

Introduction
According to the reports of the World Health Organization (WHO), globally an estimated 220 million people are suffering from diabetes mellitus (1). Without further actions or interventions, this number is likely to double by the year 2030. In the past decades, the prevalence of both type 1 and type 2 diabetes mellitus has dramatically increased, resulting from changes in diet, reduced physical activities and exposure to certain environmental factors described in the ‘hygiene’ and ‘overload’ hypotheses (2). Certainly, as type 1 and type 2 diabetes are multifactorial diseases, genetic factors consisting of multiple susceptibility genes as well as environmental influences contribute to disease development. In a number of countries, type 2 diabetes mellitus has become the most prevalent type of diabetes in children (3). The dramatic rise in prevalence will have impact on the socioeconomic perspective of the population. For instance, the WHO estimates that in the coming 5 years, China will lose over 300 billion dollars income because of heart disease, stroke and diabetes (1).

Diabetes affects the gut: there is ample evidence that diabetes mellitus affects gastrointestinal morphology and function. Conversely, the gut affects diabetes: several recent publications provide evidence that an altered bowel function contributes to the pathogenesis of diabetes mellitus. In this respect, the intestinal barrier is particularly relevant with focus on intestinal permeability (IP), immune response and intestinal microbiota. Intestinal barrier function is compromised in various gastrointestinal disorders such as inflammatory bowel disease, celiac disease, non-alcoholic steatohepatitis/non-alcoholic fatty liver disease (NASH/NAFLD) and irritable bowel disease, but also in autoimmune and systemic diseases (4). This review explores the...
The Microbiome and Obesity: Is Obesity Linked to Our Gut Flora?

Franklin Tsai, MD, and Walter J. Coyle, MD

Introduction

The human body harbors a large contingent of microorganisms, but nowhere is there more abundant and intricate host-microbial interaction than in the colon. There are about 10^{14} microbes per deciliter, which makes it the most biodense niche known [2•]. Genetic material from these bacteria represents 100-fold more genes than the entire human genome [3••]. We are just beginning to unravel the complex relationships between the human host and our colonic petri dishes. Recent literature has focused on the link between our metabolism and the gut flora. In this article, we summarize some of the studies that have advanced the understanding of the microbiome and its effects on metabolism, obesity, and health.

The prevalence of obesity among US adults has more than doubled since 1980 [4]. Currently, 65% of the adult population are overweight and 32% are obese [4,5]. Furthermore, the prevalence of obesity among children has more than tripled since 1980, suggesting that this problem continues to worsen [4]. Obesity is associated with medical conditions including type 2 diabetes, cardiovascular disease, obstructive sleep apnea, and multiple malignancies. A strong correlation exists between obesity and increased mortality risk [6]. The enormous costs of obesity and its comorbidities to our already overburdened health care system are alarming.

Multiple factors drive the obesity epidemic, including genetic and environmental contributions such as increased food availability, high-fat diet, widespread use of high-fructose corn syrup, and physical inactivity [7•]. For each individual, weight is determined by poorly defined interactions among genetic predisposition and social, dietary, behavioral, and environmental factors. Epidemiologic evidence suggests that the constant increase in obesity cannot be fully accounted for by genetics, food availability, and behavioral changes alone [8]. There is increasing evidence that our gut microbiota plays a critical role in energy balance and metabolism, implicating it as a major factor in the development of obesity.

We have only recently begun to appreciate the importance of the symbiotic relationship with our microbial inhabitants. These consist mostly of anaerobic bacteria, but also archaeal spp, yeasts, and parasites, collectively known as microbiota [1]. Although the upper gastrointestinal tract is sparsely populated because of the luminal medium and propulsive forces (10^4–10^5), the human colon has the highest density of any known natural bacterial ecosystem (10^{11}–10^{13}), harboring at least 1000 and potentially as many as 36,000 species [2•,9]. This impressive bacterial load is equal in mass to a single kidney and as metabolically active as the liver [10]. Indeed, 90% of the cells in our body are microbial, such that we may be viewed as passengers in our mobile colonic petri dishes.
Digestive Dysfunction

- Food allergens/sensitivities
- Gluten enteropathy and inflammation
- Small bowel bacterial overgrowth
- Parasite, worms, yeast
- Increased permeability
- **Metabolic endotoxemia** – LPS bind to lymphocytes, increase cytokines leads to insulin resistance
IgG Food Allergy and Weight

- 30 obese and 30 normal children
- Obese children had 3 fold higher CRP, 2.5 fold higher level of IgG antibodies to 277 foods
- Obese children had increased carotid intimal thickness

Wilders-Truschnig M, et. al. IgG Antibodies Against Food Antigens are Correlated with Inflammation and Intima Media Thickness in Obese Juveniles. Exp Clin Endocrinol Diabetes. 2007 Dec 10
Food Allergy and Weight
An Unrecognized Epidemic

• Detoxification/elimination diets
• Food sensitivities and allergies
• Celiac and gluten intolerance
• Inflammation and allergy
Testing for Gut Dysfunction

- Celiac panel
- IgG food sensitivities
- Digestive stool analysis +/- PCR
- Dysbiosis markers on organic acids
Treatment Gut Dysfunction

4 R program – Textbook of Functional Medicine

1. Remove allergens, toxins, microbes
2. Replace enzymes, HCl, pre-biotics
3. Re-innulate with probiotics
4. Repair with nutrients (Zn, A, n3, GLA, glutamine, etc.)
Detoxification Imbalances
Obesogens: 73% increase in obesity in 6 month old babies since 1980
Toxins and Diabesity

- Environmental Health Perspectives: PCB’s and chlorinated pesticides increase risk of diabetes
- JAMA: Arsenic increases risk diabetes
- JAMA: Bisphenol A increase risk for CV disease, diabetes and elevated GGT
- Toxic evaluation: heavy metals, POP’s

Obesity is not a single clinical condition. Obesity is a complex chronic disease resulting from the interplay among genetics, environment, and lifestyle. Emerging scientific concepts provide a new basis for understanding the multiple causes of obesity as well as the underlying mechanisms involved in weight dysregulation. While most obesity can be effectively treated for compliant patients, using a focused lifestyle intervention based on whole foods, low glycemic index, plant-based diet combined with exercise and stress management, there are patients who do not respond predictably to normally successful interventions. A novel hypothesis linking environmental and internal toxins to disruptions of key mechanisms involved in weight regulation may yield new treatment strategies.

The key biological systems involved in obesity (and all diseases) that are altered by toxins are the neuroendocrine-immune system, and mitochondrial energetics and redox status. Obesity provides an illustrative example of how therapeutic tools for disease treatment and therapy can be used to improve patients’ health and quality of life. A new experimental and methodological approach can be applied to any chronic disease and provides an opportunity to integrate fragmentary scientific discoveries into a cohesive whole that creates a new clinical roadmap.

This paper will explore a novel hypothesis that links obesity and toxins. We will discuss how one particular disease and the effect of one or more toxins can create a clinically relevant, integrative view of obesity. Alterations in thyroid metabolism and receptor function, central appetite dysregulation, inflammation’s influence on insulin and leptin resistance, impaired mitochondrial oxidative metabolism, and oxidative stress-mediated effects via nuclear factor kappa B (NFkB) are all mechanisms by which toxins cause alterations in metabolism and influence weight regulatory mechanisms.

These systems are not discrete entities but systems in the true sense of the word—interacting, interactive, dynamic, overlapping networks of biochemical and physiological information spaces of functional relationships. Multiple patterns of genetic, physiological, and biochemical dysfunction are linked to obesity, including genetic polymorphisms, inflammation, mitochondrial dysfunction, oxidative stress, neuroendocrine-immune dysfunction, especially autoimmune dysfunction involving the hypothalamic pituitary-adrenal axis, nutritional deficiencies or excesses, and toxins. The nature, cause, and remediation of obesity can be seen in the path of any one of these patterns. The focus here will be on how toxins modulate their influence through all these mechanisms.

**Genetic Regulation and Toxins: Underlying Mechanisms**

The influence of toxins on metabolism occurs through 3 key mechanisms: hormonal regulation, neuroregulatory mechanisms, mitochondrial function, and oxidative stress. Toxins can alter the hormonal regulation of weight, a process that involves thyroid, leptin, insulin, adiponectin, resistin, sex hormones, and gut hormones, including ghrin, peptide YY (PYY), and cholecystokinin (CCK). Toxins, alter thyroid hormone metabolism and receptor function leading to lowered metabolic rate. Important neuroregulatory mechanisms affected by toxins include hypothalamic satiety modulation through effects on peripheral and central inhibitory and stimulatory stimuli, including corticotrophin releasing factor (CRF), endocannabinoids, and amylin (GLP-1). Stress-induced adrenocorticotropic hormone (ACTH) also alters appetite and weight control mechanisms. Toxins can influence weight through toxic mediated increases in inflammatory cytokines (TNF-α, IL-6) on the immune modulator-activating receptor (CD155) family of cellular receptors, promoting insulin resistance, and the melanocortin receptor (MC) system altering central appetite regulation. Counter-regulatory signals triggered by inflammation such as suppression of cytokine signaling (SOCS) induce leptin resistance. Toxins alter mitochondrial energetics by damaging enzymes involved in fatty acid oxidation and mitochondrial biogenesis. Oxidative stress influences weight via NFκB mediated disruption of gene transcription that controls insulin resistance and inflammation. Other mechanisms may include direct effects of toxins on hepatic substrate of lipid and glucose metabolism, and on inflammatory cytokines.

**Can Energy Molecules Cause Obesity?**

It is clear that ingesting foreign molecules can lead to obesity, including medications. While most drugs are not truly toxins, certain drugs can have toxic effects and cause weight gain—psychotropic medications in particular have been shown to promote weight gain. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit, lithium, valproate, metformin, dopamine, and some selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, clozapine, and paroxetine have all been shown to promote weight gain through various mechanisms. Heres using on demand and used to increase appetite in cancer patients. Billions of dollars are pouring into obesity drug research to find the magic molecule that will burn fat or reduce appetite. However, affecting the pathway in a complex cellular system will likely fail because of coordination counter-regulatory mechanisms. It is clear that medications can affect our weight and may play a role in obesity for some people, but it is important to recognize that if medications influence weight, then certainly other foreign chemicals, including environmental toxins, can cause weight gain.

Environmental toxins interfere with metabolism, oxidative hepatic detoxification systems, disrupt central weight control systems, promote insulin resistance, alter circadian rhythms, activate the stress response, interfere with thyroid function, increase inflammation, damage mitochondria, and lead to obesity. Most researchers have largely ignored the effects of environmental chemicals on metabolism. Still, a few researchers have started connecting the dots linking environmental toxins with obesity, specifically the role of endocrine disruptors such as phthalates and bisphenol A.
Toxin Mediated Obesity: Potential Mechanisms

- **Thyroid** dysfunction: thyroid metabolism, receptor function
- Central **appetite** dysregulation
- Inflammatory **cytokines** and insulin & leptin resistance
- Impaired **mitochondrial** function and oxidative metabolism
- **Oxidative stress** mediated effects via NFκB
Enhancing Detoxification

- Minimize exposure to toxins by eating organic foods, filtering water, avoiding large fish, filtering air.
- Sweat and circulate! Use of sauna or steam.
- Use foods that help detoxify - the cruciferous veggies (broccoli), watercress, green tea, cilantro, dandelion greens, pomegranate.
- Use detoxifying herbs such as milk thistle and green tea.
- Use supplements to support detoxification such as vitamin C, n-acetylcysteine, lipoic acid, and probiotics.
- Treat heavy metal toxicity
- Tests for detoxification genes (SNP’s) and heavy metals and persistent organic pollutants (POP) may be helpful
Dangers of Sarcopenia

The True Cause of Aging
Age-related changes in muscle mass in thigh cross-sectional area of two people with similar BMI
“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”
An optimum intake of micronutrients and metabolites, which varies with age and genetic constitution would tune up metabolism and give a marked increase in health, particularly for the poor and elderly, at little cost.

Psycho-spiritual Imbalances
REFRIGERATOR RIGHTS—THE MISSING LINK IN HEALTH, DISEASE, AND OBESITY

Mark A. Hyman, MD

Breath therapy, water gardens, and yoga. The thread connecting these various healing techniques is the concept of allostatics—the ability to achieve stability through change. Restoring allostatics, the balance that prevents the chronic activation of the stress response, is critical in addressing the epidemic of stress-related disorders. Hans Selye, MD, MD, who first described the stress response, understood the inherent paradox that the physiologic systems triggered by stress can both protect and damage the body. The effect of stress is mediated through the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis when it interacts with the cardiovascular, metabolic, and immune systems in response to internal or external stressors. The consequences of unrelenting stress on our health is perhaps the most challenging and clinically difficult problem to address.

The benefits of addressing the over stressed stress response are clear from the papers presented in this issue of Alternative Therapies in Health and Medicine. Disparate conditions such as back pain, obesity, and dementia appear to be ameliorated through restoring balance to the autonomic nervous system and the HPA axis. These authors in this issue underscore the necessity of incorporating clinical tools to modulate and balance the stress response. In our culture, we are presumed to be immune to do lists, lack of time, and more importantly, a lack of livestock and the disintegration of our social fabric that historically provided a buffer for life’s stresses. As a result, finding our biologic pause button becomes more critical.

The mind-body connection has been well established, but perhaps a more critical and primary link to our ill health and stress-related disorders—the mind-body—community connection—has escaped the conventional and integrative medical world. The disintegration of communities, the erosion of popular culture into our lives, the migration of the population from region to region for work or leisure, the lack of rich social and family networks, all prevent the normal buffering from trauma and stress hormones received throughout evolution through the support of tribes and large family groups. The loss of “refrigerator rights” is a fundamental problem in our culture that has insidious and continuous effect on our health. How many people in your immediate social network can come over to your house, walk over to your fridge, and help themselves to leftovers? How many people in your circle, or in your town, afford you that right? The loss of close, intimate connections creates a broad echo of isolation and distress and underlies the difficulties we have in recovering from stress. Isolation plays a key role in the over expanding incidences of depression, anxiety, and post traumatic stress disorder we see in our practices. We hire therapists, trainers, advisors, and coaches to fill the void caused by the lack of people in our circle with refrigerator rights.

Maybe the lack of refrigerator rights is behind our obesity epidemic. The paper by Crisol et al highlights an unappreciated aspect of the obesity epidemic—the impact of stress on weight gain. How can yoga be associated with weight loss? It is simply the calories burned or perhaps something more lasting that occurs in yoga practice? Two techniques or tools are available to rebalance the autonomic nervous system. Yoga is one such tool, and its effect, perhaps, is mediated through meeting our bodies’ alarm systems, finding the pause button that extracts the practitioner, even for a moment, from the unrelenting effects of chronic stress. A wide body of literature on obesity and stress suggests that obesity, in part, the body’s way of protecting itself from danger. It is the alarm response unchecked.

A STATE OF ALARM

Ester was a dancer and lived life. She moved gracefully through it, always delicate and light. Her children were her greatest passion—all beautiful and good, smart and loving. Nearing seventy, Ester never struggled with her weight. Never much for formal exercise, she walked, gardened, and still danced. Then one of her daughters moved to Israel during the worst period of the uprising and escalating violence. Ester began to watch CNN day and night, waiting, anxious, and uncertain. Would her daughter be safe? Was the latest safe haven of a rubber bullet or would bullets hit in her neighborhood? This went on for months and months, despite attempts by Ester’s family to distract her. Her daughter would call and reassure her that she was happy and safe, but that did little to settle her anxiety. Ester’s stress multiplied by the day, and so did her dress size. She gained 15 pounds watching CNN.
A SYSTEMS APPROACH: Social and Biological Networks

- Shift Gene-Environment Interactions that drive disturbed metabolic and social networks
- THE SOCIAL CURE: GETTING HEALTHY TOGETHER
- Address the sociopolitical factors that promote a toxic food and chemical environment
- Address underlying causes: High GL, Low PI diet, EFA and nutrient deficient diet
- Address underling triggers: diet, microbes, toxins, allergens, stress
- Address mechanisms: core clinical imbalances
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