

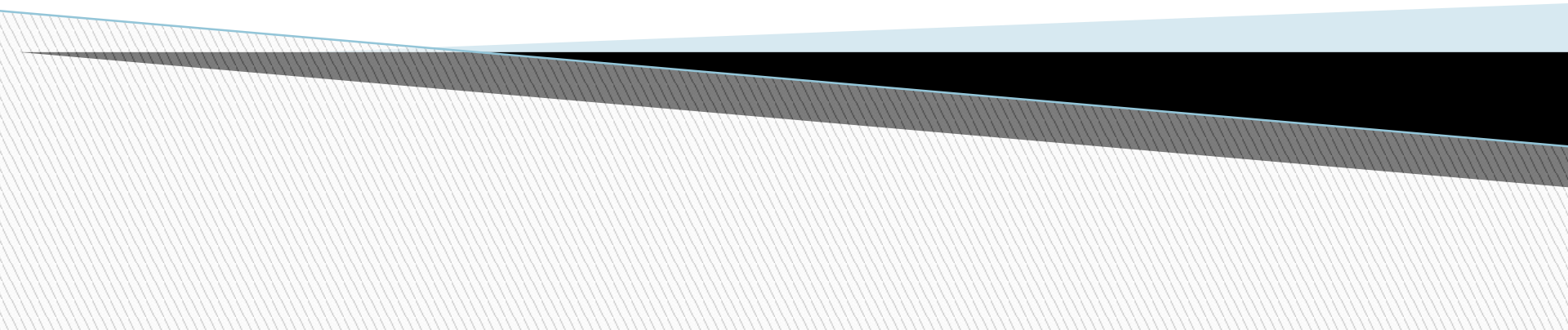
Principles and Practice Of Integrative Medicine

Treating the Whole Person By Targeting the Root Cause

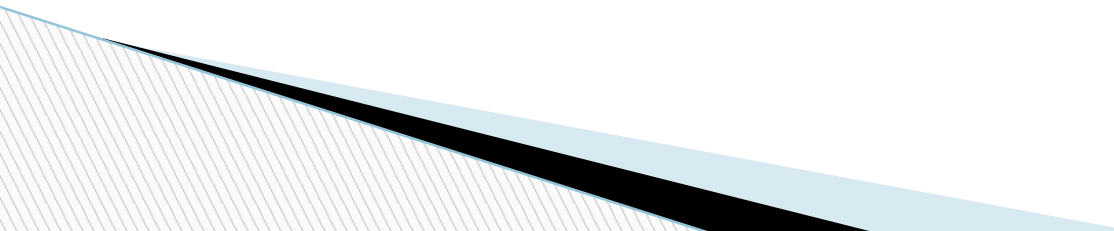
Presented by Joanne Pizzino, MD, MPH

Medical Director

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Objectives

- ? Introduction to the paradigm shift of Integrative Medicine
 - ? Review the science of Functional Medicine
 - ? Discuss how to apply Integrative Medicine principles to common disorders, such as fatigue and cognitive dysfunction
 - ? Describe the inflammatory process as one mechanistic model
 - ? Demonstrate how drilling down to the genetic level through epigenomics provides explanation and treatment for many different disorders.
- 

“If you are a hammer,
everything looks like a nail.”



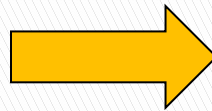
- The limits of allopathic medicine.

- Focus is on catastrophic care.
 - By the time that laboratory values are abnormal, there is serious end organ failure.
- Organ focus rather than cellular level, but if cells are not healthy, organ will not be.
- Doctor's bag has only what big pharmaceutical companies put in it.

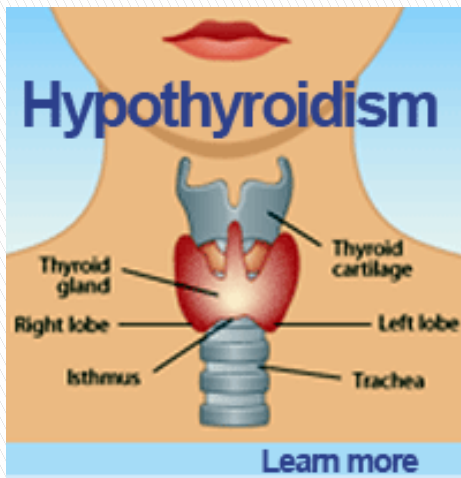
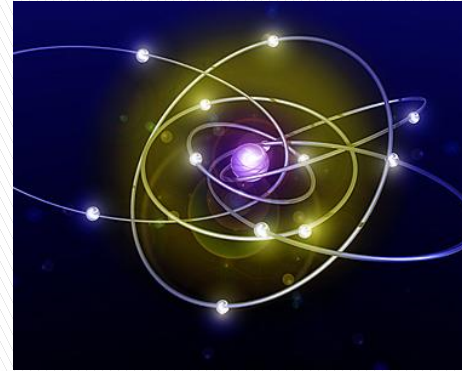


Consider a Change in Perspective

Newtonian Physics



Quantum Physics



Medicine at the *Functional* Level

? The minute:

- Organ dysfunction begins at the intracellular, or even intermolecular level

? The grand:

- The individual is intimately connected with its micro- and macro-environment

Terminology: *Integrative vs. Functional* Medicine???
Splitters vs. Lumpers...

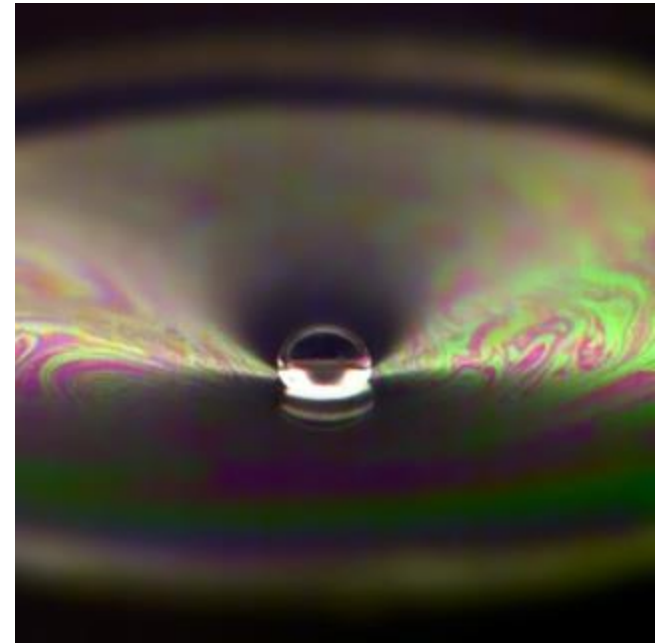
A New Paradigm

*Complexity Theory & the
Study of Chaotic Systems
Provides
A Scientific Framework for
Functional (Matrix) Medicine*

**CHAOS TRUMPS
REDUCTIONISM**

Complexity Theory: The study of chaotic systems

- Nonlinear, fluid dynamics: a weblike model
- *Analysis & prediction of trends (pattern recognition)* supersedes linear cause/effect:
- *The Butterfly effect*: small changes in initial conditions can lead to large changes in outcome. “Less is more.”



Source: <http://www.scientificamerican.com/article.cfm?id=chaos-theory-simplified-droplet>

“...the great gift of chaos theory to the practice of medicine has been the simple but profound negative statement: **traditional science cannot predict complex systems...** Chaos theory will provide us with a new vocabulary, equally “scientific” and respectable as that of scientific medicine, with which to do battle with our reductionist colleagues.”

James Goodwin, M.D.

“Chaos and the Limits of Modern Medicine”

JAMA, November 5, 1997,

Vol 278(17): pages 1399-1400

THE SYNDROME OF DIABETES MELLITUS AND ITS CAUSES*

H. P. HIMSWORTH, M.D. Lond., F.R.C.P.

PROFESSOR OF MEDICINE, UNIVERSITY OF LONDON; DIRECTOR OF THE MEDICAL UNIT, UNIVERSITY COLLEGE HOSPITAL, LONDON

The history of modern knowledge is concerned in no small degree with man's attempt to escape from his previous concepts. Within the present century we have seen physics liberated from the cramped philosophy of a rigid causality to the more fluid concept of probability. We are now witnessing a similar liberation of medical thought by the substitution of syndromes for "disease entities" as the units of illness. Implicit in the concept of a disease entity is the idea that any particular illness has a specific cause, which, though its action in the body may be modified by circumstances, is an essential and invariable prerequisite for the development of the illness in question. The syndrome, on the other hand, has its philosophical basis not in specific disease factors but in a chain of physiological processes, interference with which at any point produces the same impairment of bodily function. The same syndrome may thus arise from many different causes. This newer view inspires a far more catholic concept of etiology and renders pointless many existing controversies. But the revision of medical thought entailed by its application has hardly begun. It is my purpose to apply these considerations to the syndrome of diabetes mellitus.

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"The history of modern knowledge is concerned in no small degree with man's attempt to escape from his previous concepts. Within the present century we have seen physics liberated from the cramped philosophy of a rigid causality to the more fluid concept of probability. We are now witnessing a similar liberation of medical thought by the substitution of syndromes for 'disease entities' as the units of illness.....The syndrome, on the other hand, has its philosophical basis not in specific disease factors but in a chain of physiological processes, interference with which at any point produces the same impairment of bodily function. The same syndrome may thus arise from many different causes."

H.P. Himsworth, Lancet, 1949; V.1:465-473

It is evident that interference in this system of processes could occur at many points and lead, in each case, to the syndrome we recognise as diabetes mellitus. But before such possible interferences are discussed the hypothesis must be reconsidered in the light of recent knowledge.

Mode of Action of Insulin

In the path of intracellular carbohydrate metabolism there are certain obligatory stages through which the metabolic stream must pass without option of circumvention. One of the most important of these occurs at the very beginning in the reaction by which glucose, under the influence of adenosine triphosphate, is turned into glucose-6-phosphate. This reaction is catalysed by the enzyme hexokinase. Once glucose-6-phosphate has been formed, synthesis of glycogen and the whole chain of carbohydrate oxidation become possible even to diabetic animals. Cori and his school^{1,2,3,4} have now shown that, in vitro, the vital hexokinase reaction is inhibited by anterior pituitary extracts (A.P.E.); that tissue preparations made from animals previously injected with such extracts show similar inhibition; and, further, that this inhibition is counteracted by insulin. Muscle extracts made from alloxan-diabetic rats show the same impaired ability to use glucose as do extracts from normal rats injected with A.P.E.; but, if the animals are previously injected with insulin, the hexokinase activity is normal. Such inhibition is enhanced by adrenocortical extracts, and this also is removed by insulin. Insulin, however, does not directly facilitate the activity of hexokinase; it simply removes any A.P.E. inhibition that is present. These results have

who A.P.E. dogs vitro, such -vitro whole. s was and that, all of ed the erated ousay abetes iminals eneral level livers eprea-ucose. ed by erated with under A.P.E. whose berts.⁴ esthe- cluded ractly falling in an exclu- ously, occurs these A.P.E. ;;

* Oliver-Sharpay lectures to the Royal College of Physicians, March 15 and 17, 1949.

a striking difference was observed. The spontaneous fall of blood-sugar proceeded at practically the same

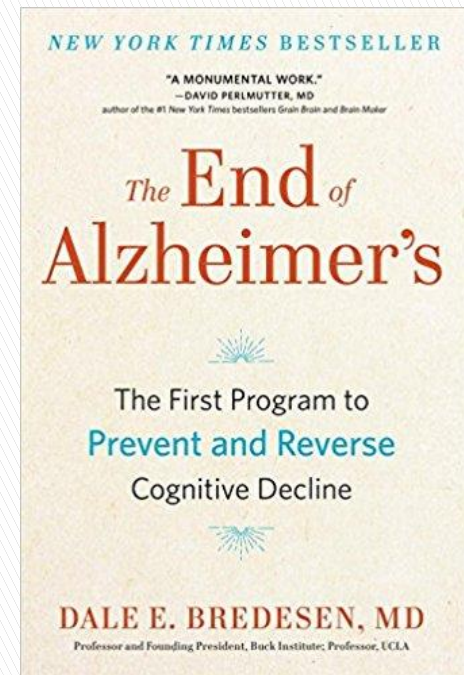
Applying Integrative Medicine

- ? ICD-10 “Diagnosis” vs. 7 Essential Functions
 - Effects vs. root causes:
 - A FEW ROOT CAUSES CAN CREATE MYRIAD SYMPTOMS
- ? Clues in “distant” organ systems
 - Immune & endocrine systems affects ALL body systems at the cellular level
- ? Gut-Brain Axis
 - Nutrition affects ALL body systems
 - Food is the *densest* chemical messenger input to direct the body
 - Produces greater amounts of neurotransmitters than the brain
 - 2/3 of the immune system is in the gut
 - More efferent nerve fibers than afferent
- ? Cell *membrane* IS the “brain” of the cell

Function Medicine Headliners

Multiple Sclerosis Patient
Terry Wahls, M.D.

Real Hope for Dementias

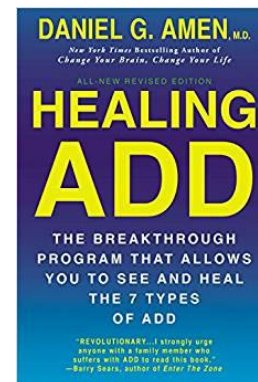


Alzheimer's Dementia (AD) Burden

- ? 5.4 MILLION AMERICANS/ 30 MILLION GLOBALLY
 - Projected to grow to 13 million Americans by 2050
- ? AD INCREASING WHILE CAD AND CA DECREASING
 - From 2000 to 2015, deaths associated with Alzheimer's disease increased by 123% while other major causes have declined.
- ? AD NOW THIRD LEADING CAUSE OF DEATH IN THE UNITED STATES
- ? WOMEN AT THE EPICENTER
 - Woman's chance of developing AD is now greater than her chance of developing breast cancer
 - 65% of patients and 60% of caregivers are women
- ? "EVERYONE KNOWS SOMEONE WHO IS A CANCER SURVIVOR; NO ONE KNOWS AN ALZHEIMER'S SURVIVOR, UNTIL NOW."

The New Science of Brain Dysfunction

- ? Applies to mood and cognitive disorders
 - The same factors which affect mood and concentration in younger persons, lead to dementia in older people.
 - ? Depression Increases Risk for Dementia:
 - ? 2x for females, 4x for males
- ? Multiple Causes >> 1 Diagnosis << Multiple Causes
 - Dale Bredeisen, MD > *The End of Alzheimer's*
 - Daniel Amen, MD > *Healing ADD*
 - Terry Wahl's, MD > *Wahl's Protocol*



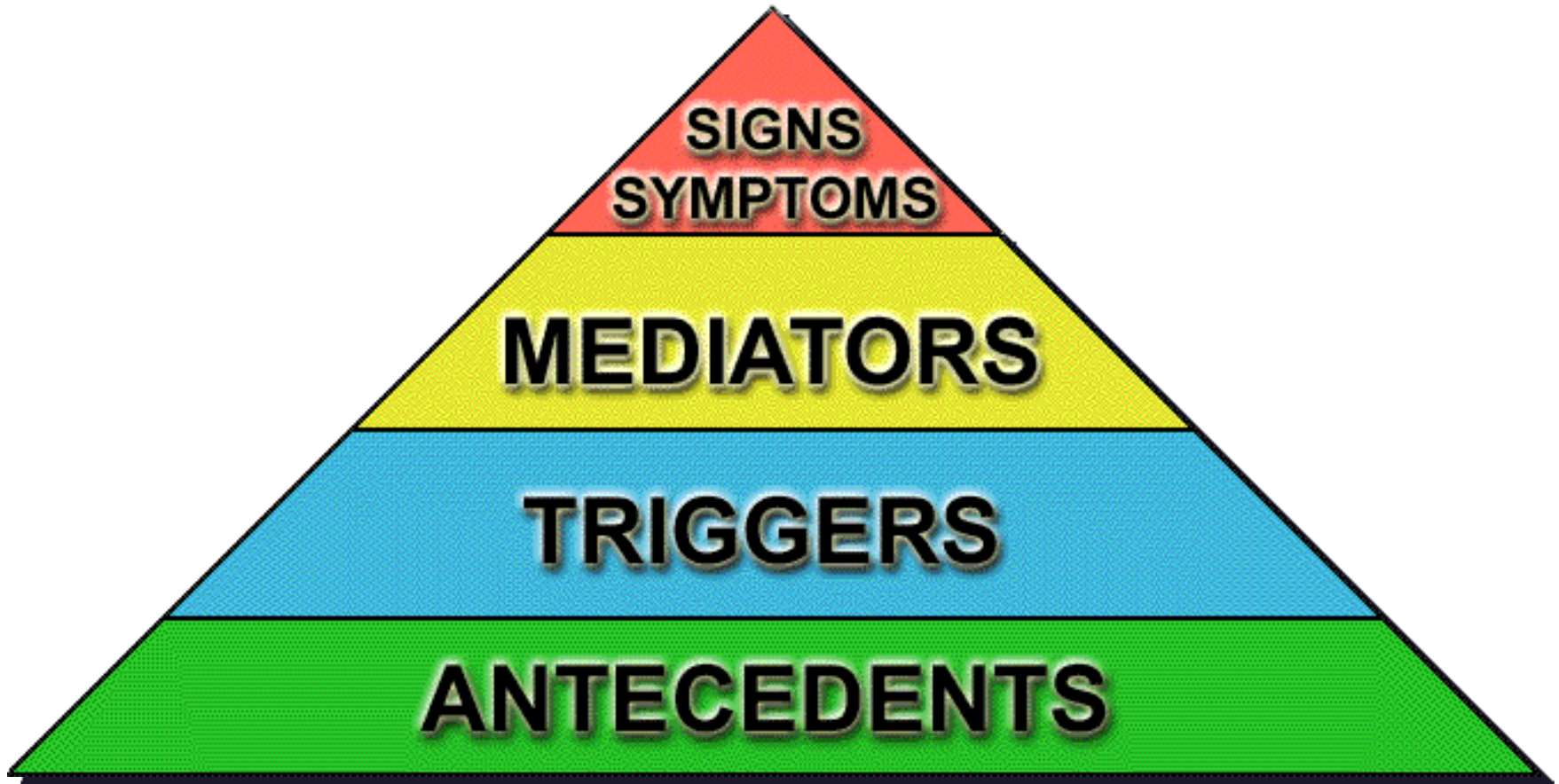
Fatigue and Brain Dysfunction

- ? Common denominator of most neurodegenerative diseases is mitochondrial dysfunction
- ? People complaining of fatigue are often really describing brain dysfunction exhausting them:
 - Concentration is taxing
 - Brain Fog
 - Mood (motivation)

Case History

- 36YO white male
- On disability.
- Fatigue and malaise
- More trouble falling asleep than staying asleep. Sleep wake cycle may be completely flipped.
- Feverishness. Temp not usually high.
- Neuro Sx. Memory poor. Forgets what he is saying. Can't read a book because of focus issues. Forgetfulness of where he is going or people's names. Has tonic-clonic mvts of whole body esp when having emotional breakthroughs.
 - Severely depressed about his condition.
 - Bipolar hospitalization on 3 occasions.
- Has put on 50 lbs since this started. Poor exercise tolerance: prolonged wheezy cough w/ exercise, such as walking.

Treating Root Causes



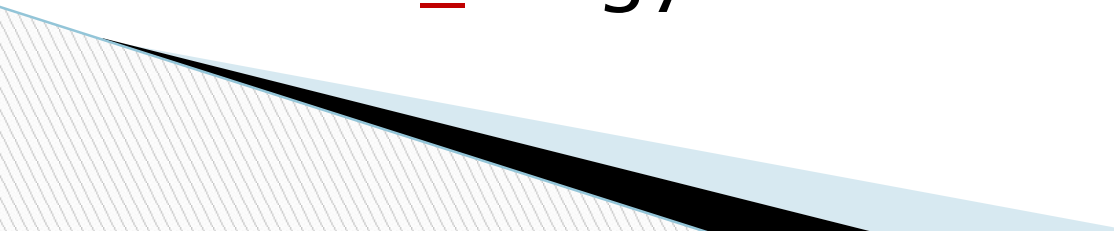
FUNDAMENTAL MECHANISMS AND PROCESSES



Think “**SHINES ON ME**”

- **Sleep**
 - **Hormonal deficiencies**
 - **Infections**
 - **Nutritional deficiencies**
 - **Exercise**
 - **Structure**

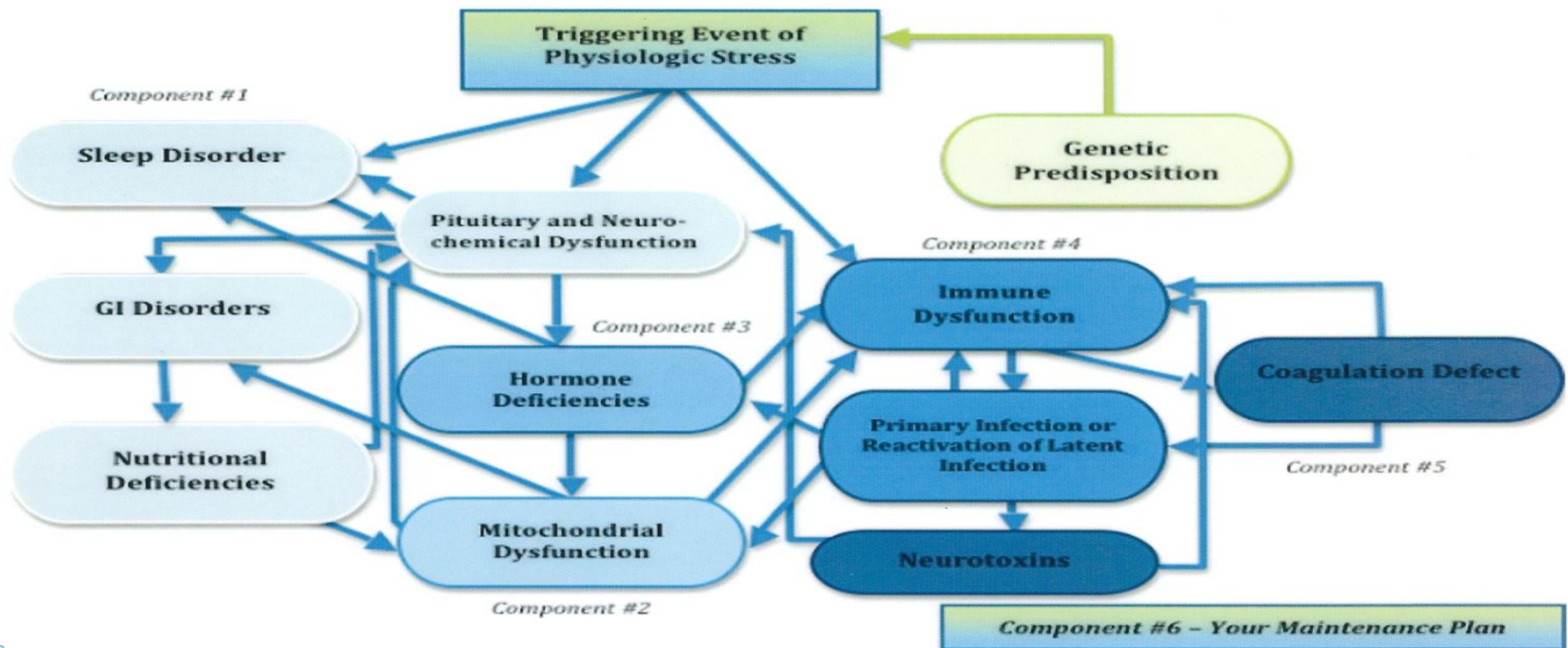
 - **One**
 - **Noxious**

 - **Mind-body-spirit**
 - **Energy**
- 

Multi-factorial Conditions Spectrum

Fatigue <> Malaise <> Pain

Cycle of Dysfunction in Fibromyalgia and Chronic Fatigue Syndrome



THE PRINCIPLES of FUNCTIONAL MATRIX MEDICINE: A *SCIENCE-BASED* FIELD OF HEALTHCARE

- *Biochemical individuality* based on genetic and environmental uniqueness
 - *Patient centered* versus disease centered
 - *Dynamic balance* of internal and external factors
 - *Web-like interconnections* of physiological factors
 - *Health as a positive vitality* – not merely the absence of disease
 - *Promotion of organ reserve – healthspan*
- “APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE”

<http://www.functionalmedicine.org/>

Functional Matrix Medicine: Basic Principles

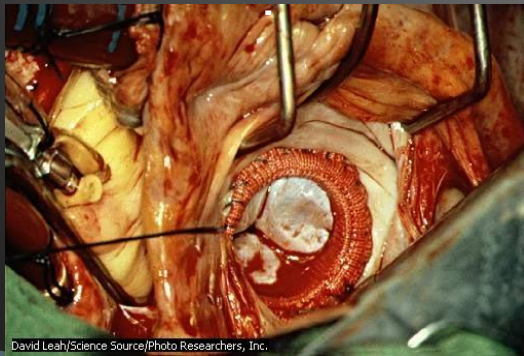


- Biochemical make-up is based upon genetic AND environmental factors unique to the individual.

Functional Matrix Medicine: Basic Principles



vs



David Leah/Science Source/Photo Researchers, Inc.

- Patient-centered versus disease-centered. We must know the person who has the disease, rather than just which disease a person has. (Osler)

Functional Matrix Medicine: Basic Principles



- Health is a dynamic balance of internal and external factors.
 - What is the individual environment that has provided a foothold for this disease?
 - How do we make that environment less able to support dysfunction, and better able to flourish harmoniously?

Functional Matrix Medicine: Establish a Health Foundation First



- Treat CAUSE, not EFFECT
- Healing from the cells on up
- More than just symptom-suppression and “band aid” therapeutics

Treating Root Causes Rather Than Disease Labels



? ROOT CAUSES

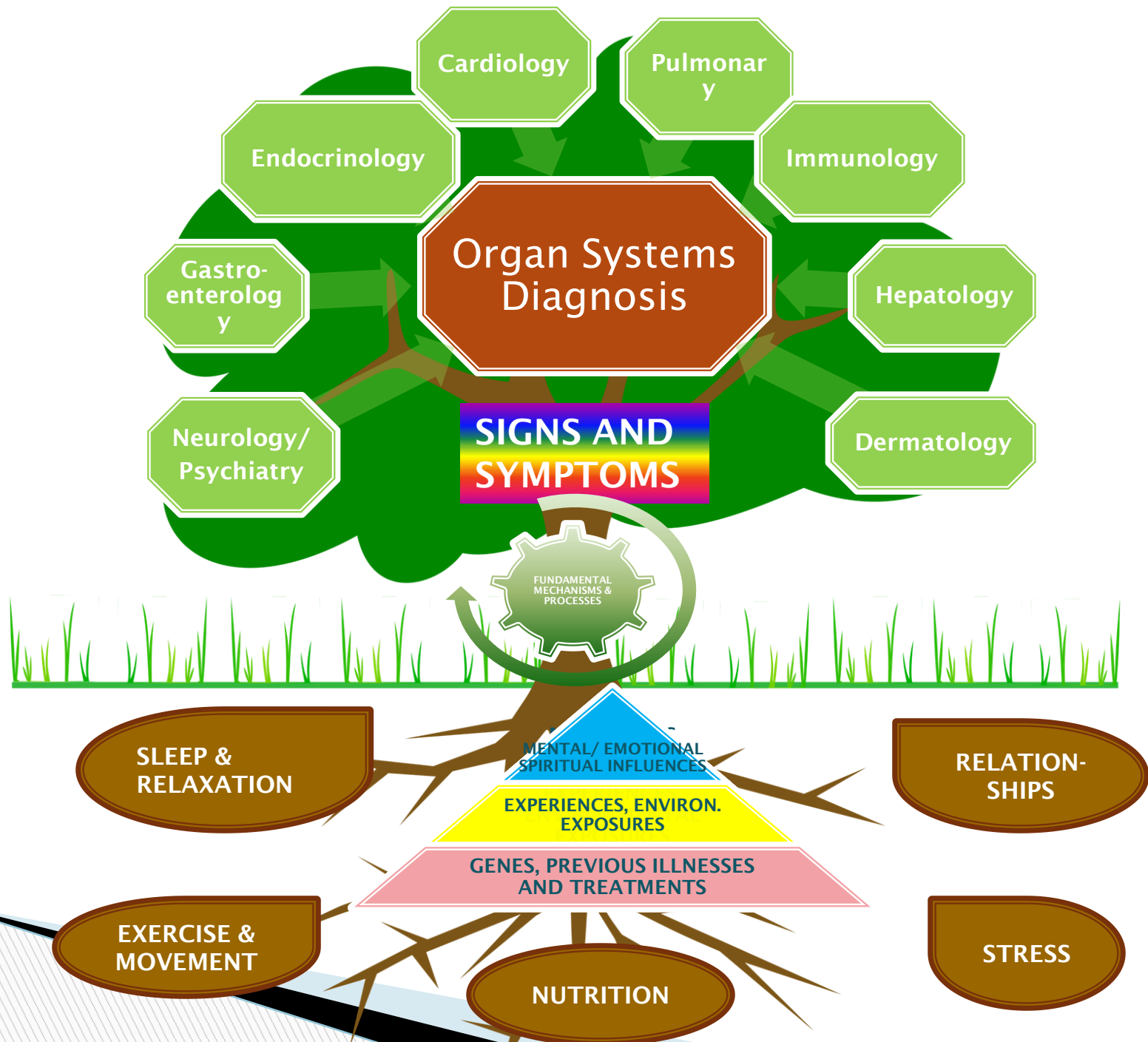
- DYSBIOSIS (MICROBIOME IMBALANCE)
- SYSTEMIC INFLAMMATION AND BRAIN INFLAMMATION
- MULTIPLE HORMONAL IMBALANCES
- IMPAIRED METABOLISM
- FOOD SENSITIVITIES
- HIDDEN INFECTIONS: LYME, EPSTEIN-BARR, CANDIDA SYNDROME, PARASITES, ETC.
- IMPAIRED DETOXIFICATION: OVEREXPOSURE, GENETIC, HEAVY METALS
- MOLD EXPOSURE

? DISEASE LABELS

- NEUROLOGIC: DEMENTIA, MOOD DISORDERS, PERIPHERAL NEUROPATHY
- CANCER
- OBESITY: HYPERTENSION, DIABETES, HIGH CHOLESTEROL, CARDIOVASCULAR DISEASE
- THYROID, MENOPAUSE/ANDROPAUSE
- GASTRO INTESTINAL: GERD, IBS, CONSTIPATION, DIARRHEA
- FIBROMYALGIA & CHRONIC FATIGUE SYNDROME
- AUTOIMMUNE DISEASES: RHEUMATOID ARTHRITIS, MULTIPLE SCLEROSIS

The Tree of Life





Michael Roizen, MD: Straight Talk About Chronic Disease

Lifestyle Changes Can Control Them and Bring Health Care Costs Down

● Four Factors that determine 75% of our health care costs.

- Tobacco
- Food choices and portion size
- Physical Inactivity
- Stress

? In 2007 these conditions were responsible for:

- 81% of our hospital admissions
- 91% of all prescriptions
- 76% of physician visits
- A cost of \$1.4 trillion dollars--about \$6000 a year per person

One definition of collective insanity:
*“Continuing old behaviors
and expecting new outcomes.”*

New drugs will not solve today’s healthcare problems...
...nor will new surgical procedures,
...nor will improving acute care,
...nor will managing costs.

**PERSONAL RESPONSIBILITY FOR
HEALTH BEHAVIORS IS THE KEY.**

Functional Medicine Therapies



- Nutritional imbalance:
 - Have improper diet, effects of previous medical treatments, alcohol or genetic susceptibility led to improper molecules being admitted to the body through disrupted gut ecology?
 - Are strengthening nutrients being passed out?

MANY MEDICATIONS BLOCK NUTRIENT UPTAKE OR FUNCTION

Do the Prescriptions You Take Deplete Your Nutritional Status?

SOURCE: DRUG-INDUCED NUTRIENT DEPLETION HANDBOOK, 2ND EDITION



DRUG	NUTRIENT DEFICIENCY	POTENTIAL HEALTH PROBLEMS
ANTACIDS/ULCER MEDICATIONS Pepcid, Tagamet, Zantac, Prevacid, Prilosec, Magnesium & Aluminum antacids	Vitamin B12 Folic Acid Vitamin D Calcium Iron Zinc	Anemia, depression, tiredness, weakness, increased cardiovascular risk Birth defects, cervical dysplasia, anemia, heart disease, cancer risk Osteoporosis, muscle weakness, hearing loss Osteoporosis, heart and blood pressure irregularities, tooth decay Anemia, weakness, fatigue, hair loss, brittle nails Weak immunity, wound healing, sense of smell/taste, sexual dysfunction
ANTIBIOTICS Gentamycin, neomycin, streptomycin, cephalosporins, penicillins	B Vitamins Vitamin K	Short term depletion effects are minimal, but failure to re-inoculate the GI tract with beneficial bacteria (probiotics) often results in dysbiosis which causes gas, bloating, decreases digestion & absorption of nutrients, and may also lead to a variety of other health problems.
Tetracyclines	Calcium Magnesium Iron Vitamin B6 Zinc	Osteoporosis, heart & blood pressure irregularities, tooth decay Cardiovascular problems, asthma, osteoporosis, cramps, PMS Slow wound healing, fatigue, anemia Depression, sleep disturbances, increased cardiovascular disease risk Weak immunity, wound healing, sense of smell/taste, sexual dysfunction
CHOLESTEROL DRUGS Lipitor, Crestor, Zocor and others	Coenzyme Q10	Various cardiovascular problems, weak immune system, low energy
ANTI-DEPRESSANTS Arapin, Avanti, Elavil, Pamelor, & others	Coenzyme Q10 Vitamin B2	Various cardiovascular problems, weak immune system, low energy Problems with skin, eyes, mucous membranes and nerves
Major Tranquilizers (Thorazine, Mellarin, Prolixin, Serenital & others)		
FEMALE HORMONES Estrogen/Hormone Replacement Oral Contraceptives	Vitamin B6 Folic Acid Vitamin B1 Vitamin B2 Vitamin B3 Vitamin B6 Vitamin B12 Vitamin C Magnesium Selenium Zinc	Depression, sleep disturbances, increased cardiovascular disease risk Birth defects, cervical dysplasia, anemia, cardiovascular disease Depression, irritability, memory loss, muscle weakness, edema Problems with skin, eyes, mucous membranes and nerves Cracked, scaly skin, swollen tongue, diarrhea Depression, sleep disturbances, increased cardiovascular disease risk Anemia, depression, tiredness, weakness, increased cardiovascular risk Lowered immune system, easy bruising, poor wound healing Cardiovascular problems, asthma, osteoporosis, cramps, PMS Lower immunity, reduced antioxidant protection Weak immunity, wound healing, sense of smell/taste, sexual dysfunction
ANTICONVULSANTS Phenobarbital & barbiturates	Vitamin D Calcium Folic Acid	Osteoporosis, muscle weakness, hearing loss Osteoporosis, heart & blood pressure irregularities, tooth decay Birth defects, cervical dysplasia, anemia, cardiovascular disease
Dilatril, Tegretol, Mysoline, Depakane/Depacon	Biotin Carnitine Vitamin B12 Vitamin B1 Vitamin K Copper Selenium Zinc	Hair loss, depression, cardiac irregularities, dermatitis Various cardiovascular problems, weak immune system, low energy Anemia, depression, tiredness, weakness, increased cardiovascular risk Depression, irritability, memory loss, muscle weakness, edema Blood coagulation, skeletal problems Anemia, fatigue, cardiovascular and connective tissue problems Lower immunity, reduced antioxidant protection Weak immunity, wound healing, sense of smell/taste, sexual dysfunction

Do the Prescriptions You Take Deplete Your Nutritional Status?

SOURCE: DRUG-INDUCED NUTRIENT DEPLETION HANDBOOK, 2ND EDITION



DRUG	NUTRIENT DEFICIENCY	POTENTIAL HEALTH PROBLEMS
ANTI-INFLAMMATORIES Steroids: Prednisone, Medrol, Aristocort, Decadron	Calcium Vitamin D Magnesium Zinc Vitamin C Vitamin B6 Vitamin B12 Folic Acid Selenium Chromium	Osteoporosis, heart and blood pressure irregularities, tooth decay Osteoporosis, muscle weakness, hearing loss Cardiovascular problems, asthma, osteoporosis, cramps, PMS Weak immunity, wound healing, sense of smell/taste, sexual dysfunction Lowered immunity, easy bruising, poor wound healing Depression, sleep disturbances, increased cardiovascular disease risk Anemia, depression, tiredness, weakness, increased cardiovascular risk Birth defects, cervical dysplasia, anemia, cardiovascular disease Lower immunity, reduced antioxidant protection Elevated blood sugar, cholesterol & triglycerides, diabetes risk
NSAIDS (Motrin, Aleve, Advil, Anaprox, Dolobid, Feldene, Naprosyn and others)	Folic Acid	Birth defects, cervical dysplasia, anemia, cardiovascular disease
Aspirin & Salicylates	Vitamin C Calcium Folic Acid Iron Vitamin B5	Lowered immune system, easy bruising, poor wound healing Osteoporosis, heart & blood pressure irregularities, tooth decay Birth defects, cervical dysplasia, anemia, cardiovascular disease Anemia, weakness, fatigue, hair loss, brittle nails Fatigue, listlessness, and possible problems with skin, liver and nerves
DIURETICS Loop Diuretics (Lasix, Bumex, Edecrin) Thiazide Diuretics (HCTZ, Enduron, Diuril, Lozol, Zaroxolyn, Hygroton and others)	Calcium Magnesium Vitamin B1 Vitamin B6 Vitamin C Zinc Coenzyme Q10 Potassium Sodium	Osteoporosis, heart and blood pressure irregularities, tooth decay Cardiovascular problems, asthma, osteoporosis, cramps, PMS Depression, irritability, memory loss, muscle weakness, edema Depression, sleep disturbances, increased heart disease risk Lowered immunity, easy bruising, poor wound healing Weak immunity, wound healing, sense of smell/taste, sexual dysfunction Various cardiovascular problems, weak immune system, low energy Irregular heart-beat, muscle weakness, fatigue, edema Muscle weakness, dehydration, memory problems, loss of appetite
Potassium Sparing Diuretics	Calcium Folic Acid Zinc	Osteoporosis, heart & blood pressure irregularities, tooth decay Birth defects, cervical dysplasia, anemia, cardiovascular disease Weak immunity, wound healing, sense of smell/taste, sexual dysfunction
CARDIOVASCULAR DRUGS Antihypertensives (Catapres, Aldomet)	Coenzyme Q10 Vitamin B6 Zinc Vitamin B1	Various cardiovascular problems, weak immune system, low energy Depression, sleep disturbances, increased cardiovascular disease risk Weak immunity, wound healing, sense of smell/taste, sexual dysfunction Depression, irritability, memory loss, muscle weakness, edema
ACE Inhibitors (Capoten, Vasotec, Monopril & others)	Zinc	Weak immunity, wound healing, sense of smell/taste, sexual dysfunction
Beta Blockers (Inderal, Corgard, Lopressor and others)	Coenzyme Q10	Various cardiovascular problems, weak immune system, low energy
DIABETIC DRUGS Metformin	Coenzyme Q10 Vitamin B12 Folic Acid	Various cardiovascular problems, weak immune system, low energy Anemia, depression, tiredness, weakness, increased cardiovascular risk Birth defects, cervical dysplasia, anemia, heart disease, cancer risk
Sulfonylureas (Tolinase, Micronase/Glyrase/Diabeta)	Coenzyme Q10	Various cardiovascular problems, weak immune system, low energy
ANTIVIRAL AGENTS Zidovudine (Retrovir, AZT & other related drugs)	Carnitine Copper Zinc Vitamin B12	Increased blood lipids, abnormal liver function and glucose control Anemia, fatigue, cardiovascular and connective tissue problems Weak immunity, wound healing, sense of smell/taste, sexual dysfunction Anemia, depression, tiredness, weakness, increased cardiovascular risk
Foscarnet	Calcium Magnesium Potassium	Osteoporosis, heart and blood pressure irregularities, tooth decay Cardiovascular problems, asthma, osteoporosis, cramps, PMS Irregular heart-beat, muscle weakness, fatigue, edema

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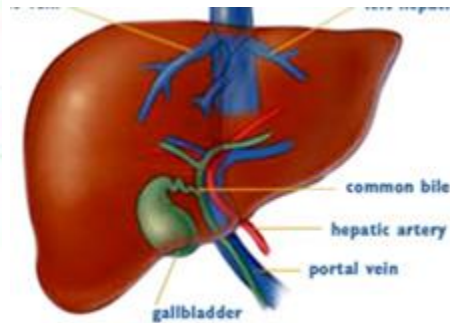
SPECTRACELL LABORATORIES
ADVANCED CLINICAL TESTING

Functional Medicine Therapies

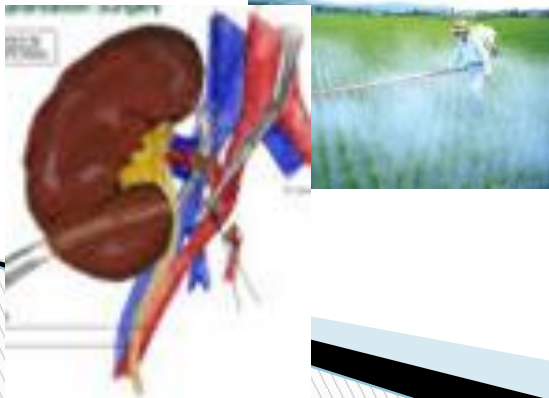
- Immunologic dysfunction and inflammatory response:
 - Have the basic systems which distinguish “self” from “other” gone awry?
 - the body attacking itself (i.e. arthritis)
 - under-activity (i.e. immunodeficiency)



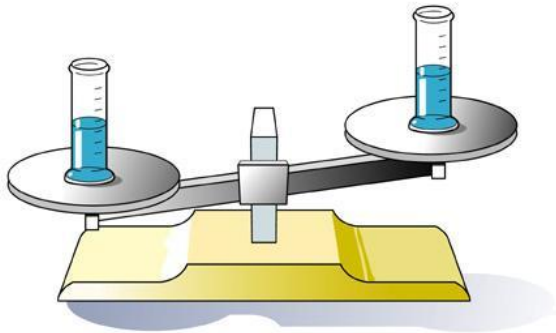
Functional Medicine Therapies



- Impaired detoxification:
 - Primary detoxifying organs= liver & kidney
 - oxidative stress= accumulation of internal wastes
 - external toxins?
- Impaired elimination
 - Constipation is a major risk factor for AD, PD, FM, CFS, CA, and more

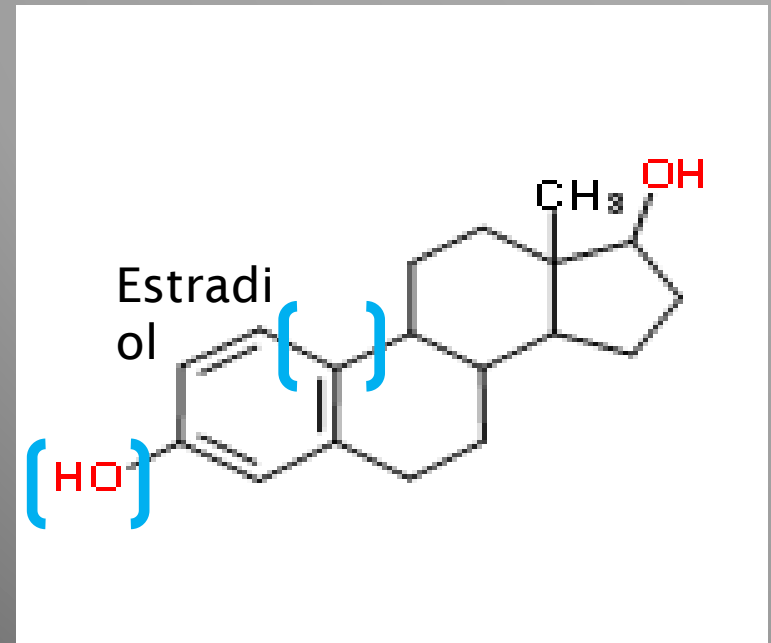
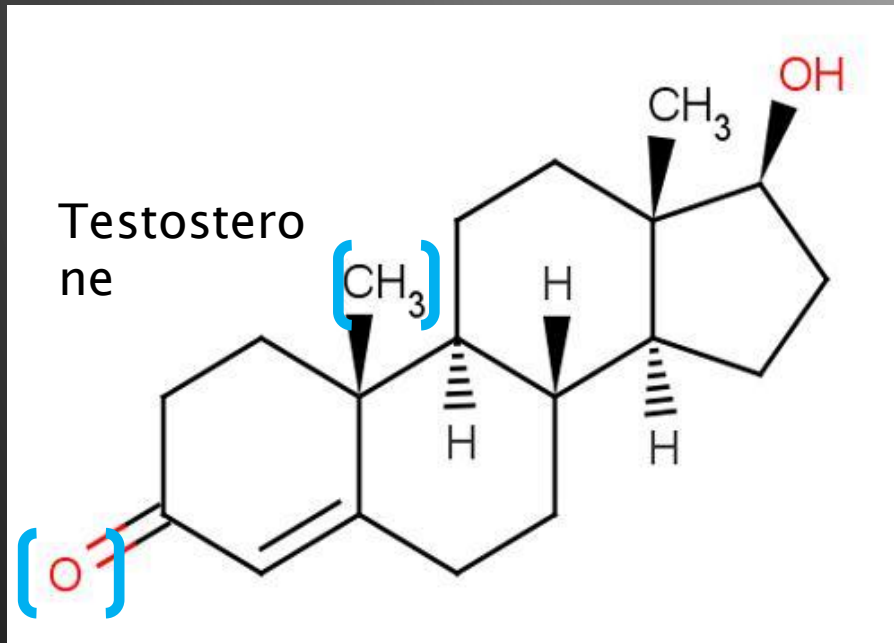


Functional Medicine Therapies

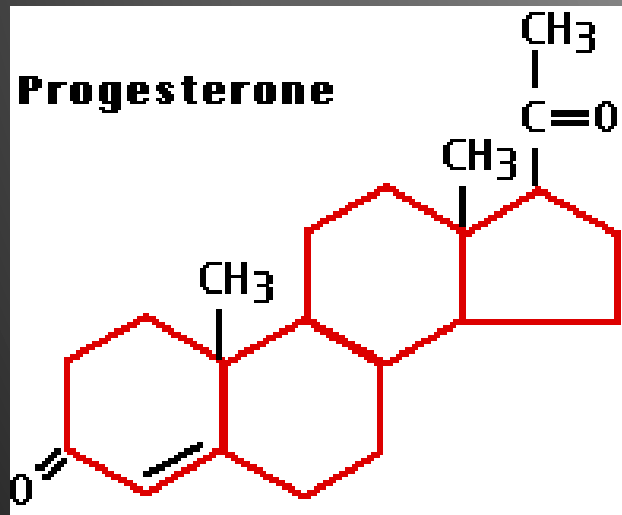


- Endocrine imbalances
 - Hormones
 - Over-production
 - Under-production
- Bio-Identical Hormone Therapies vs. Synthetic HRT

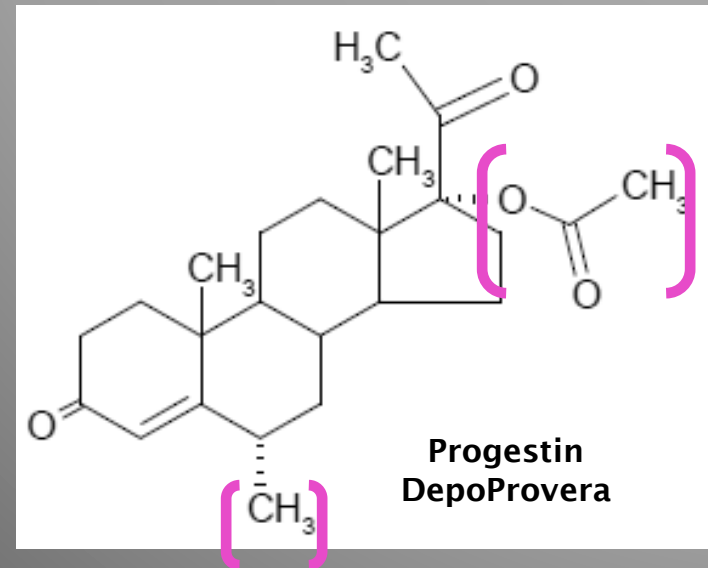
Small Changes With Big Effects



Chemical Changes Influence Side Effects



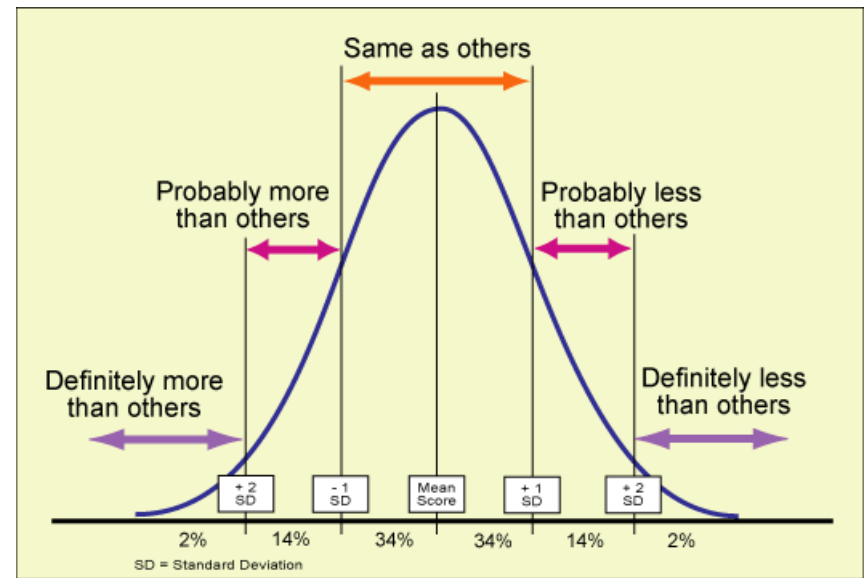
RARE: headache,
depression



COMMON: menstrual irregularities,
abdominal pain or discomfort,
weight changes, headache, fatigue,
depression, hair loss and
nervousness, skin breakouts.

“The Doctor says there is nothing wrong.”

- Normal values do not measure or predict good health. They are simply average levels, based upon statistical definitions, found in other patients tested in that laboratory. Values vary from lab to lab.
- Bell curve determined by who shows up to have the test.



Specialized Laboratory Testing

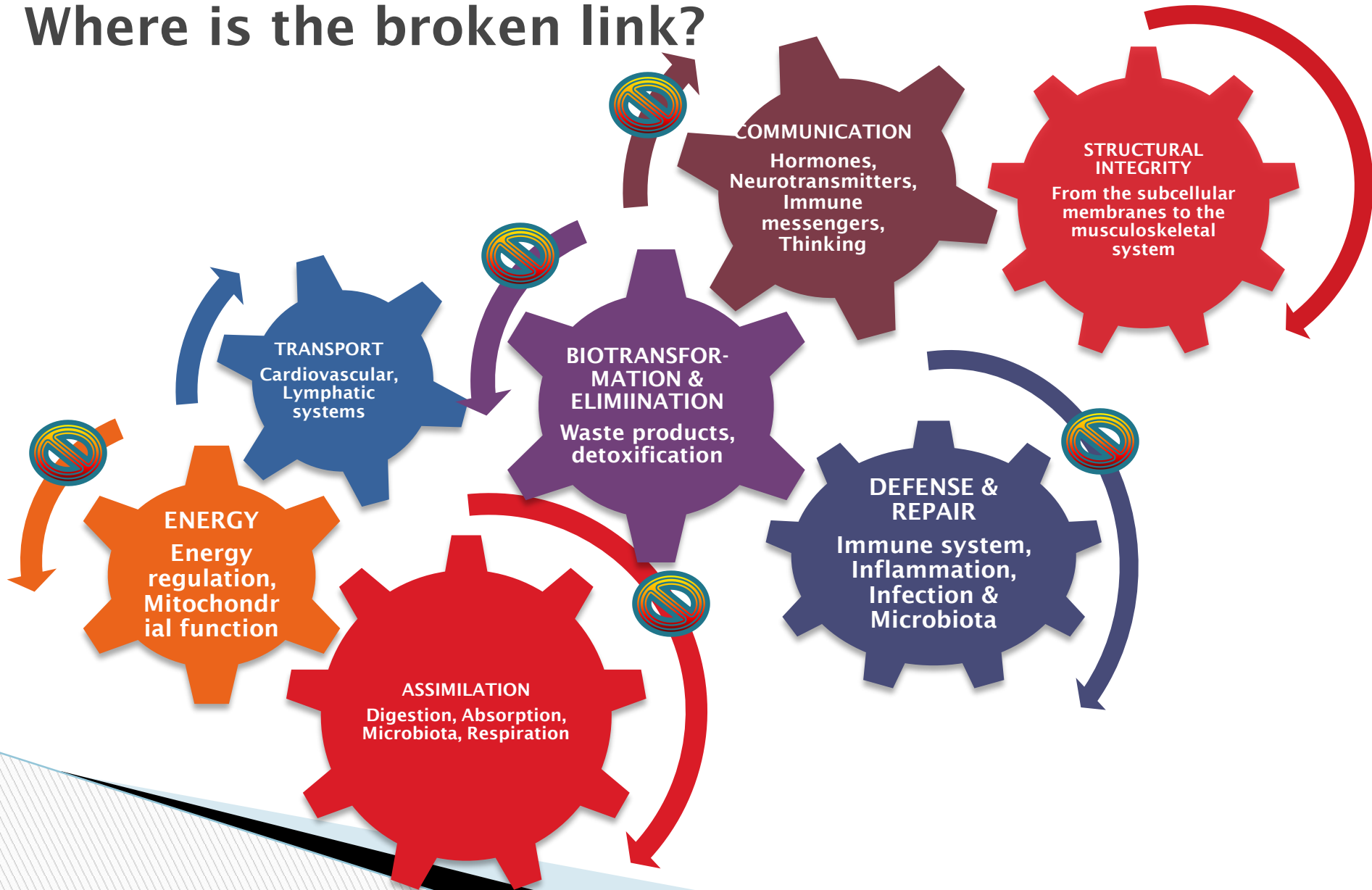


- Genetic and Epigenetic Markers for Weight Management and Mental Health
- Complete Digestive Stool Analysis (CDSA)
- Intestinal Permeability (Leaky gut)
- Specialty Parasite testing
- Food Sensitivities
- Thyroid Function Specialty Testing
- Adrenocortical Stress Index
- Bio-Impedance Analysis (BIA)
- Igenex Lyme/Tick-borne Diseases
- Autoimmune Antibodies
- Heavy Metal Challenge testing
- Mold sensitivity testing



ORGANIC ACIDS TESTING

Where is the broken link?



EPIGENETICS

? “Above the genes”

- More important than individual genes
 - Around 20,000 genes control >100,000 chemical processes
- How groups of genes function as a whole
- Determines which genes are turned on or off

? Many factors affecting epigenetics are under our control (nature vs. nurture)

- Nutrition, exercise, environment (ie. mold, chemicals)
- Many inherited diseases (cardiovascular, cancer, diabetes, Alzheimer's) more affected by lifestyle/environment (>50%) than DNA (12-20%)

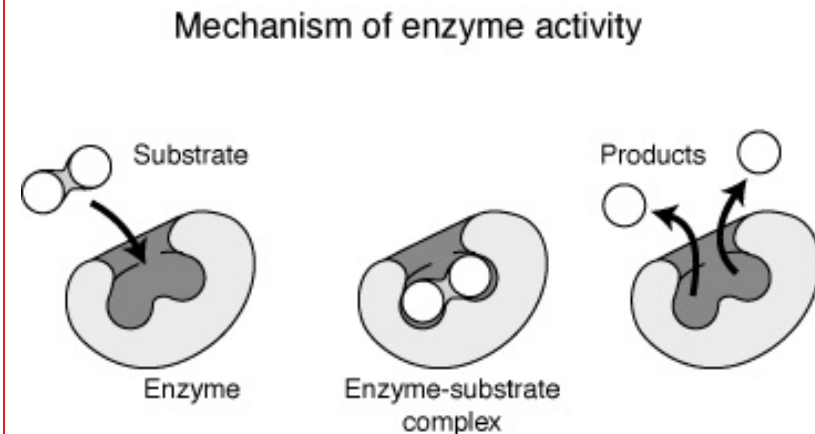
Your Genes Do Not Determine Your Destiny. Your Behavior Does.

- ❖ Nature vs. Nurture
- ❖ The Science of **Epigenomics**
 - Epigenomics is the study of the effects of environmental factors and constituents on gene expression.
 - DNA is turned on or off by the Epigenome
 - The Epigenome is most strongly influenced by food and exercise.



Single Nucleotide Polymorphisms ("SNP's")

- Occur in at least 1% of the population
- Can cause the enzymes to work faster or slower than "normal"
- An individual may have more than one SNP
- Newest pharmaceutical science has discovered over 30 variations in the detoxifying enzymes
- Often signaled by inability to tolerate many medications, bizarre side effects, etc.



Cytochrome P450 Isoforms

CYP1A2:

Clozapine
Imipramine
Caffeine
Paracetamol
Phenacetin

CYP3A4/-3A5:

Amitriptyline
Carbamazepine
Clarithromycin
Cyclosporine
Lignocaine
Midazolam
Nifedipine
Paroxetine
Terfenadine

CYP2E1:

Chlorzoxazone
Enfluran
Halothan

CYP2C19:

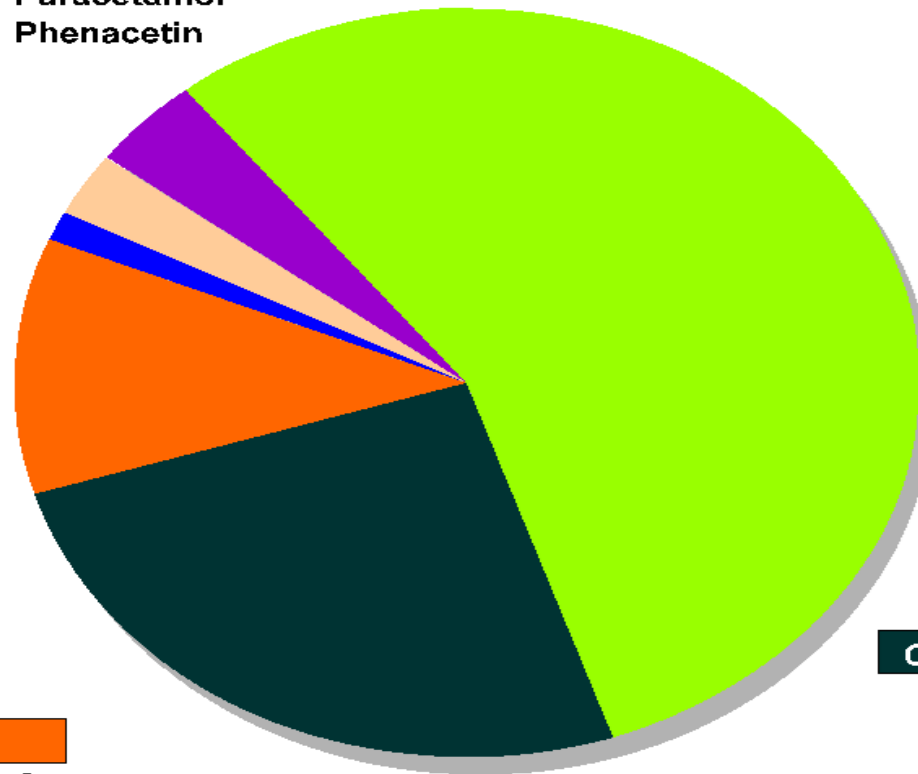
Diazepam
Citalopram
Omeprazole
Proguanil

CYP2C9:

Diclofenac
Ibuprofen
Losartan
Phenytoin
Tolbutamide

CYP2D6:

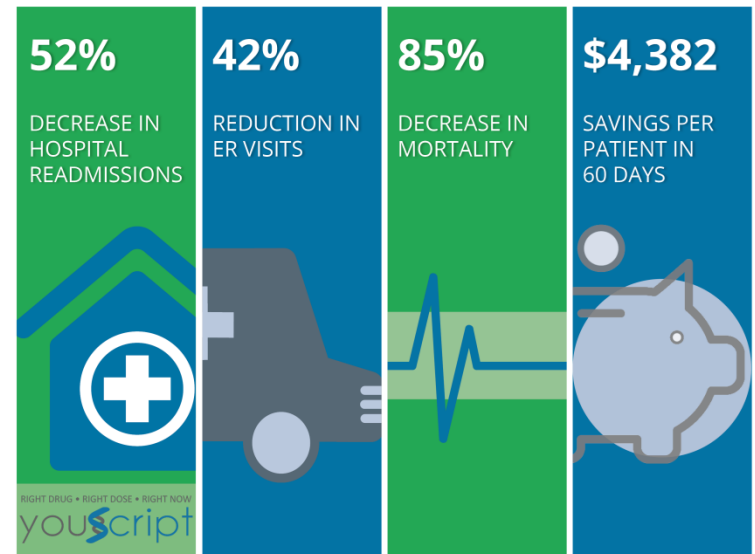
Amitriptyline
Codeine
Haloperidol
Imipramine
Metoprolol
Nortriptyline
Ondansetron
Propafenone



Impact of Epigenetics on Polypharmacy

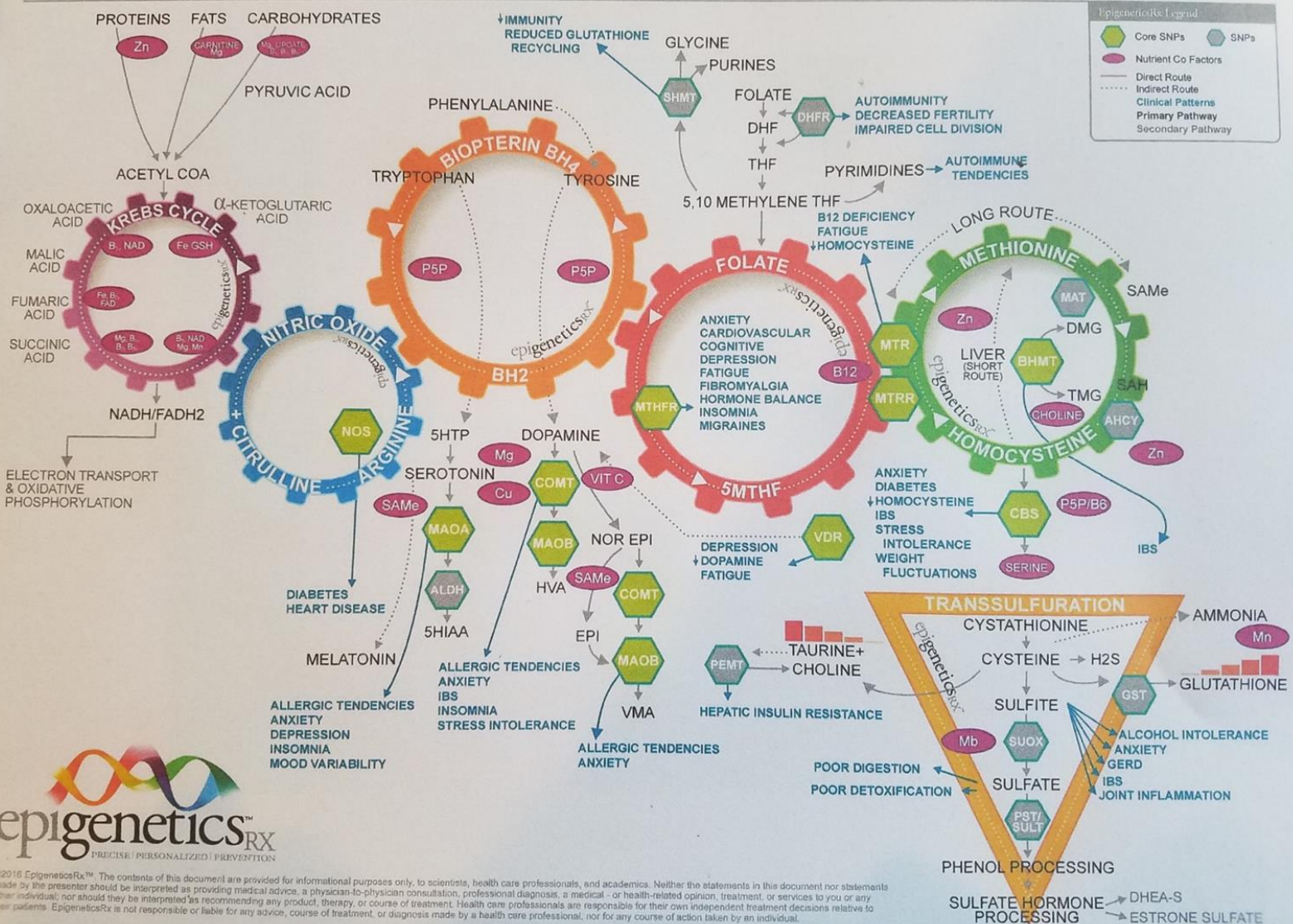
? **PLOS ONE**: Clinical impact of pharmacogenetic profiling with a clinical decision support tool in polypharmacy home health patients: A prospective pilot randomized controlled trial

- Lindsay S. Elliott , et al
- Published: February 2, 2017
- <http://dx.doi.org/10.1371/journal.pone.0170905>



FUNDAMENTAL PHYSIOLOGIC CYCLES IMPACTED BY EPIGENETICS

Metabolic Pathways



Microbiome/Microbiota

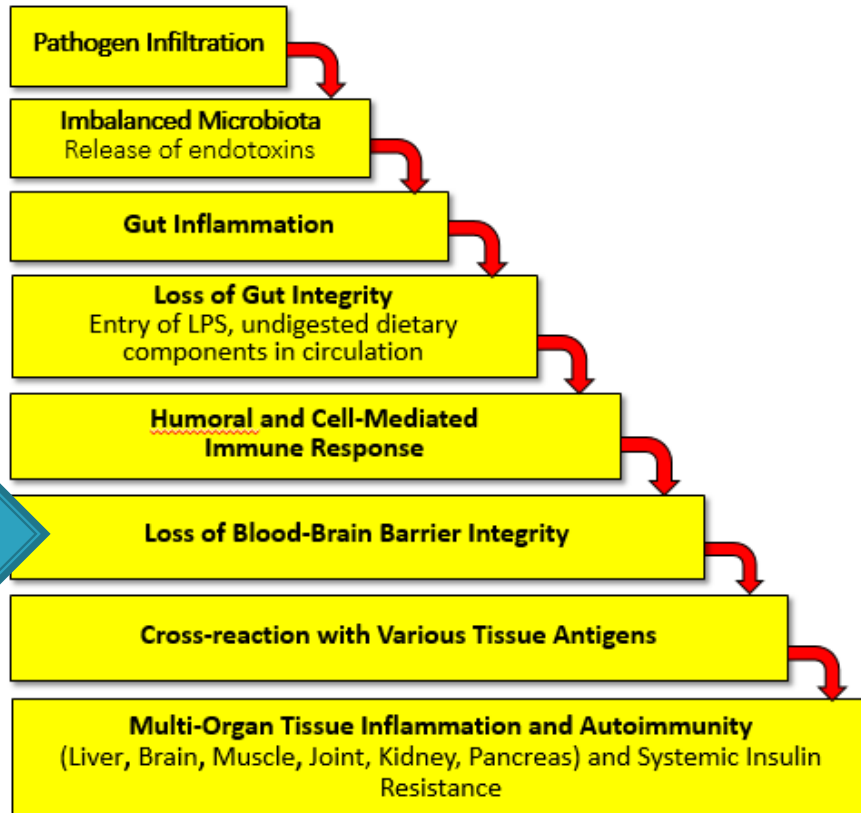
- ? The **microbiome** is “the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space.”
 - Term coined by Joshua Lederberg in 2001
 - Constitutes 90% of the DNA traveling with us but weighs less than 3 lbs.
- ? “may contribute to the regulation of multiple neuro-chemical, immunologic, and neuro-metabolic pathways through a complex series of highly interactive and symbiotic host-microbiome signaling systems that mechanistically interconnect the gastrointestinal (GI) tract, skin, liver, and other organs with the central nervous system (CNS).”
 - *Front Cell Neurosci* 2013; 7: 153

Diseases now associated with an altered microbiome:

- ? Acne
- ? Antibiotic-associated diarrhea
 - ? Asthma/allergies
 - ? Autism
- ? Autoimmune diseases
 - ? Cancer
 - ? Dental cavities
- ? Depression and anxiety
 - ? Diabetes
 - ? Eczema
 - ? Gastric ulcers
- ? Hardening of the arteries
- ? Inflammatory bowel diseases
 - ? Obesity
- ? **RHEUMATOID ARTHRITIS**

Pathogen Invasion Cascade

Pathogens include: micro-organisms, toxins, food/drink components, stress



HLA B-27 & AS (Ankylosing Spondylosis)

- ? Susceptibility involves multiple genes (HLA-B27 only contributes between 16-50% of genetic risk for AS)
- ? Gut flora play major role as trigger (transgenic HLA-B27 rats raised in germ-free environment do not develop gut & joint inflammation)
- ? Association between AS & Klebsiella (high % of antibodies to Klebsiella found in AS)
- ? Increased small bowel permeability found in patients with AS & also in their first degree relatives

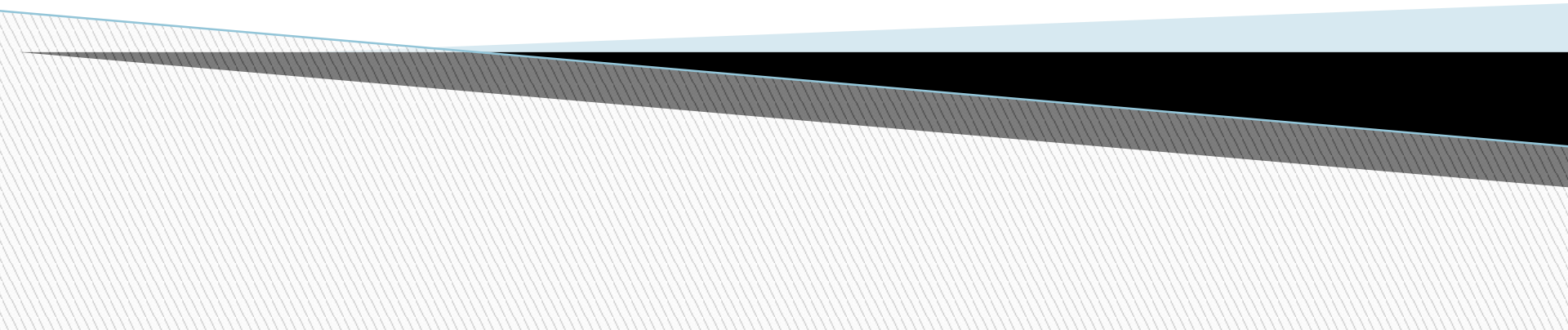
Oxidative Stress

- **A condition of free radical excess**
- **A result of increased exposure to free radicals from exogenous and endogenous sources, in combination with insufficient antioxidant defenses**
- **Oxidative damage to DNA in humans estimated as 104 hits per cell per day.**
- **Severe oxidative stress leads to cell death (necrosis or apoptosis).**
- **Mild but chronic oxidative stress is both a causative factor and a result of chronic inflammatory disease.**

“Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition.

Khaw, K-T, et al, BMJ, 2001, Vol 322: 1-6

“The predictive value of HbA1C for total mortality was **stronger** than that documented for cholesterol concentration, body mass index and blood pressure.”

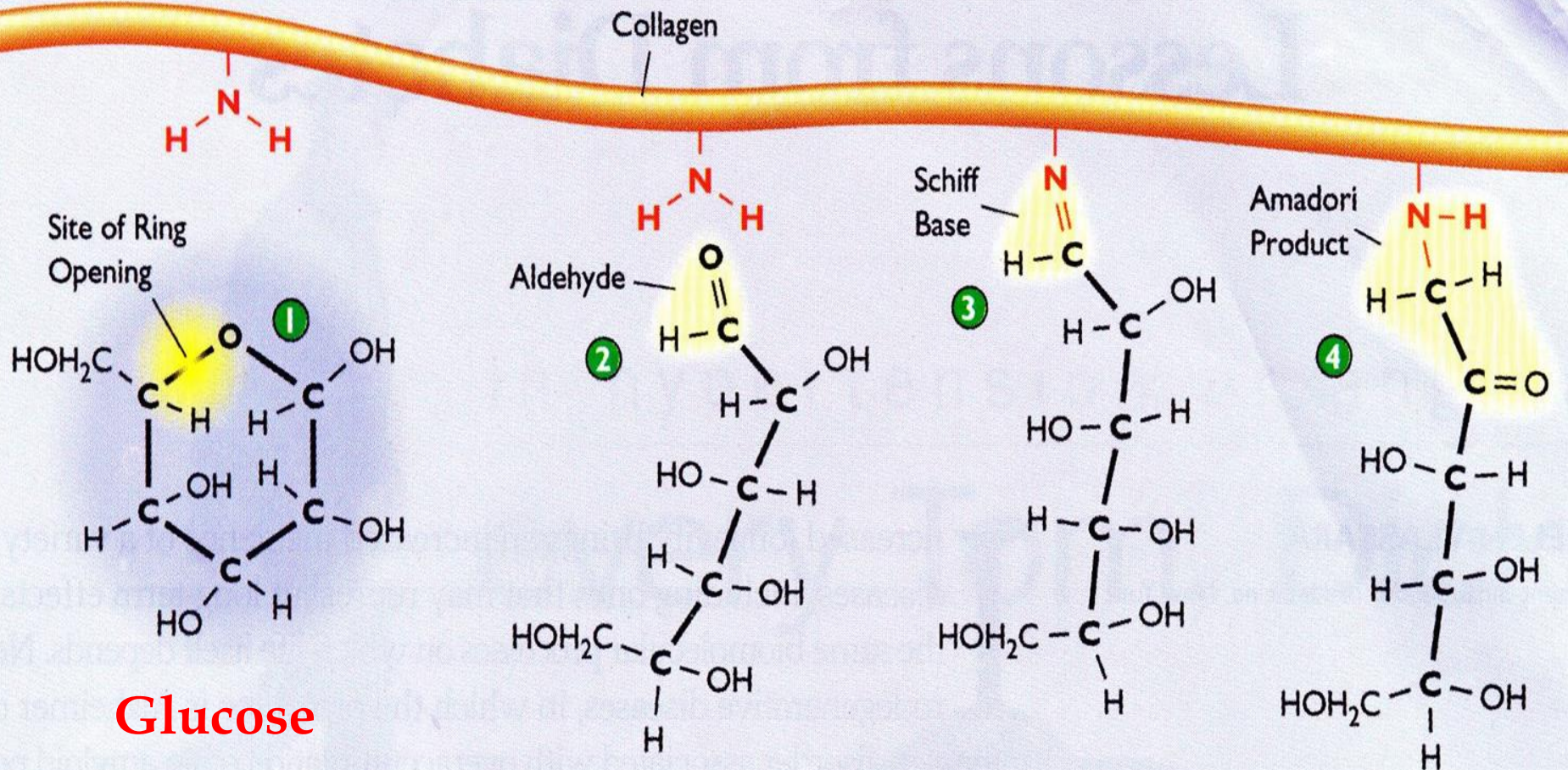


Why Sugar is Bad for You

New Scientist - Sept. 23 1989, pages 44-47

- ? Protein + glucose → Schiff's base (hours) (reversible process, but brief exposure sufficient).
- ? Schiff's base converts to highly reactive Amadori product over several days (irreversible and long lived).
- ? Amadori products crosslink into clumps called **AGEs**, Advanced Glycosylation Endproducts (weeks).
- ? AGEs scavenged by macrophages and microglia, generating oxidative stress.

AGE Formation



DIABETES IS A TOXIN DISORDER

- Persistent Organic Pollutants (POPs)
 - Low-level exposure
- **Diabetes prevalence is strongly positively associated with lipid-adjusted serum concentrations of all six POPs.**
 - After adjustment for age, sex, race and ethnicity, poverty income ratio, BMI, and waist circumference, and classified according to the sum of category numbers of the six POPs,
- **Higher #'s of POPs increased DM risk up to 38x's**
 - **Adjusted odds ratios were 1.0, 14.0, 14.7, 38.3, and 37.7 (P for trend < 0.001).**
 - Striking dose-response relations between serum concentrations of six selected POPs and the prevalence of diabetes.
- **Stronger association than cigarettes and lung cancer**

Diabetes Care. 2006 Jul;29(7):1638-44.

A strong dose-response relation between serum concentrations of persistent organic pollutants and diabetes: results from the National Health and Examination Survey 1999-2002.

Lee DH1, Lee IK, Song K, Steffes M, Toscano W, Baker BA, Jacobs DR Jr.

The “In’s and Out’s” of Life

- “Systems”, both living and non-living, require a source of energy input (fuel), and a method to release waste products



Life in a Chemical Soup

- Sources of toxins

- Body's naturally occurring waste-products

- Carbon dioxide, urea, decomposed remains of cell renewal

- Food

- Undigested parts of food, pesticides, food additives

- Environment

- Air/water pollution, outgassing of building materials, clothing treatments, DEET, etc.

- Alcohol, recreational drugs, OTC and RX medications

- Medications are just toxins we use for their beneficial side effects



Typical Symptoms of “Intoxication”: Known Acute and Chronic Effects of Alcohol

- ? Headache
- ? Cognitive dysfunction
- ? Body aches
- ? Tingling and “nerve pain” in extremities
- ? Nausea
- ? Balance disturbances
- ? Irregular heart beats



Sources of “Toxins”

- ? Mostly our own waste products
- ? OTC medications, ie Tylenol/acetaminophen
- ? Rx medications
- ? Herxheimer reactions
- ? Inflammation



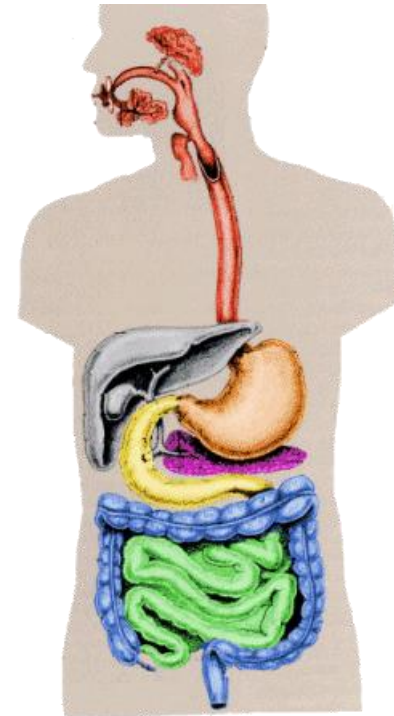
Conditions Associated With Detoxification Challenges

- ? Cancer
 - pre- and post-treatment
- ? Fatigue
- ? Migraines
- ? Allergies
- ? “Brain Fog”
 - declining cognitive function
- ? Fibromyalgia
- ? Autoimmune disorders
 - Rheumatoid Arthritis, Lupus, psoriasis, MS
- ? Inflammatory states
 - **DIABETES**, hypertension, heart disease, osteoporosis, ? Long COVID
- ? Frequent or chronic infections
- ? Chronic pain



Pathways to Remove Toxins From The Body

- Gut: vomitus, feces
- Skin: sweat
- Kidneys: urine
- Liver: neutralizes toxins at the cellular level
 - makes them water-soluble to be processed by the organs listed above.



Treatment Course

- Initial CD57 = 24 in 2-2012.
- Treatment
 - Stopped all ABX and medications other than neuropsychiatric Rx
 - Stopped approximately ½ of long list of supplements he was taking (everything from every book/website on Lyme)
 - Ondamed: 6 treatments
 - NET: >1 Tx/wk for 2 months
 - Nutritional/detox IV x 4
- Results
 - CD 57 = 117 in 6-2012
 - Felt well enough to move to California and pursue life long dreams for a new life.

Integrative Medicine

Advantages

- M.D. = Medical Doctor
 - Extensive scientific training
 - Knowledge certified by comprehensive examination procedures
 - Able to prescribe what works best, and know how to stop meds: allopathic, complementary, alternative
- Additional training in other healing arts and sciences
 - Informs patient of treatment options, ways to avoid side effects
 - Able to scientifically evaluate clinical application of complementary and alternative (CAM) therapies
 - Reviews interactions of allopathic medications and complementary treatments
- Integrates the Healing Team
 - Knows the *whole* person, not just specialized areas
 - Coordinates other specialty doctors
 - Collaborates with complementary and alternative healers

Establishing an Integrative Medicine Practice

- Must express compassion, open-mindedness, tolerance
 - Leave your “M.D. Diet” at the door
- Over-achievement in scientific competency
- Differentiate yourself in the marketplace
 - Have a “door-opener” skill, ie. acupuncture, homeopathy, condition-specific nutrition, anti-aging
- Schedule management
 - Adequate time per patient = or > 30 minutes
 - How to handle acute cases
- Understanding E&M coding issues
 - Documentation of allopathic SOAP components

Self Empowered Healing

Joanne Pizzino, MD, MPH, FACOEM

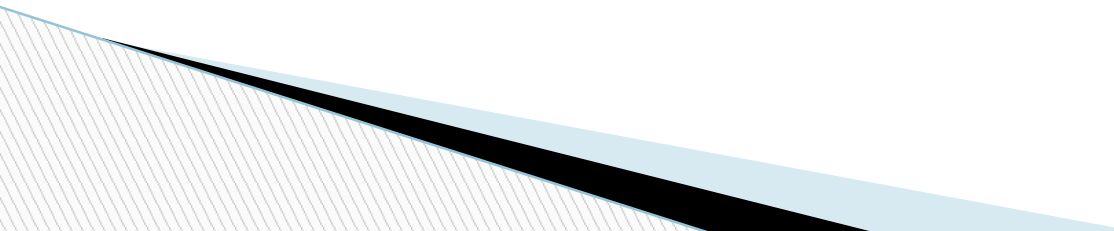
WWW.SelfEmpoweredHealing.net
DR.JP@SelfEmpoweredHealing.net



SELF EMPOWERED HEALING

TUNING INTO YOU UNLIMITED!

Questions



82YO Female with Mild Dementia

• BEFORE

- Unaware of problem
- Unable to pay attention during exam
- Pre-diabetes
- HTN controlled with 2 drugs but hypo K+
- Positive nasal swab for MARCONS (mold exposure association)



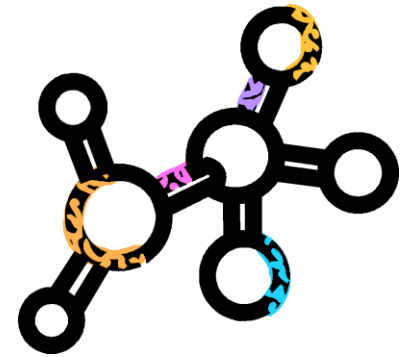
Remove gluten
Stop statin
Replace Vitamin D
Treat dysbiosis
Treat Marcons

• AFTER

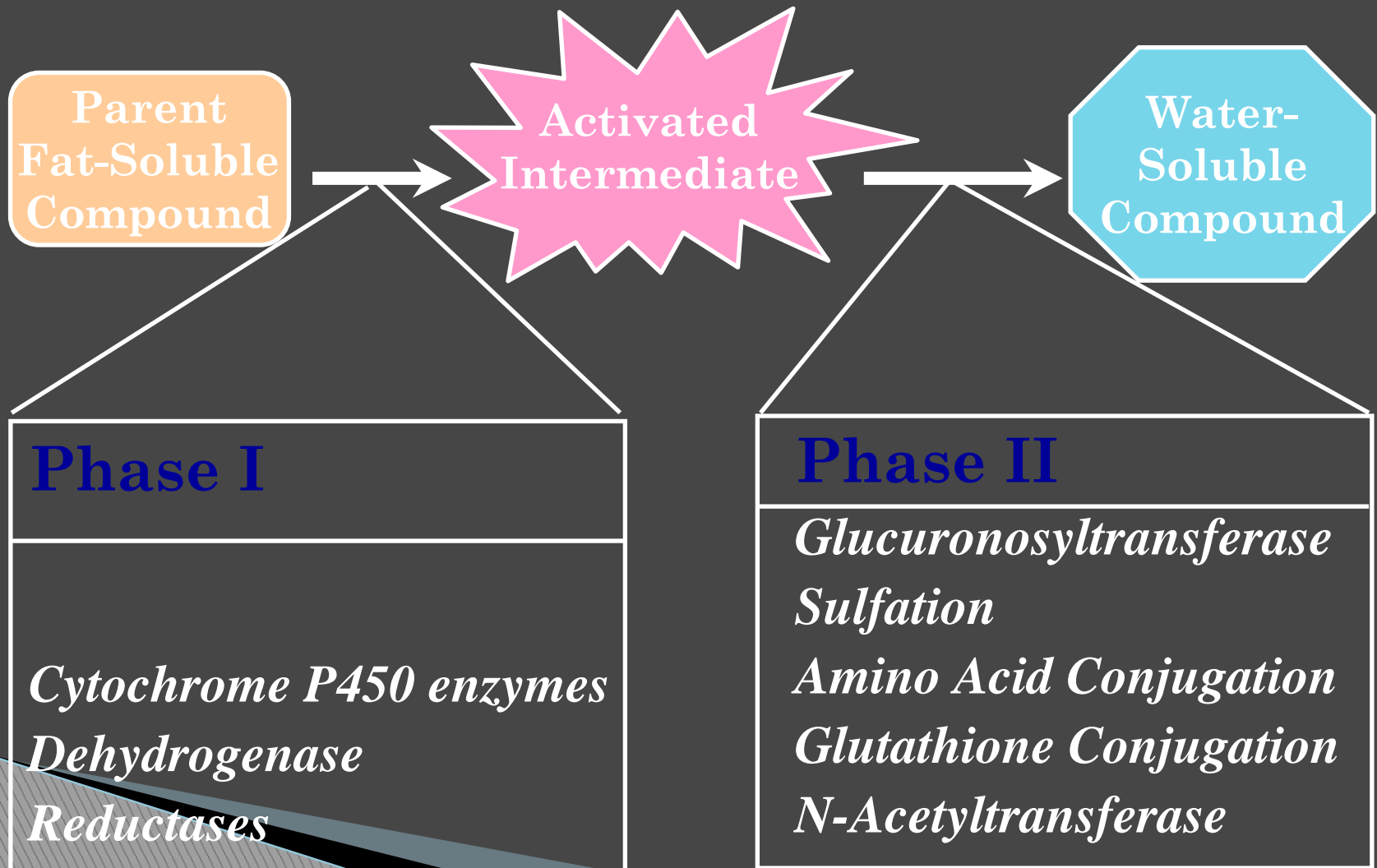
- MoCA improved 2 points
- Taking notes during consultation
- Correcting husband's spelling
- Husband notes improvement has stalled
- Has not remediated mold
- HgA1c still 6.2

Detoxification Biochemistry 101

- Three phases necessary to remove toxins from the body.
 - Phase 1: enzymes mobilize the toxins from the tissues, creating reactive free radicals.
 - Phase 2: Molecules from the liver, ie. glutathione, attach to the reactive toxins and make them water-soluble
 - Phase 3: to be flushed out of the body via urine and feces



Types of Reactions



Detoxification Biochemistry 101

(continued)

- Both **Phase 1** and **Phase 2** must happen.
 - Enzymes need vitamins and minerals to make them work.
- **Phase 1** minus **Phase 2** = More Free Radicals
 - May feel sicker
- **Phase 2** minus **Phase 1** = Toxins still in tissues
 - No improvement in condition

Top 10 medications by number of monthly prescriptions (2015)

- ? Synthroid (levothyroxine), 21.5 million
- ? Crestor (rosuvastatin), 21.4 million
- ? Ventolin HFA (albuterol), 18.2 million
- ? Nexium (esomeprazole), 15.2 million
- ? Advair Diskus (fluticasone), 13.7 million
- ? Lantus Solostar (insulin glargine), 10.9 million
- ? Vyvanse (lisdexamfetamine), 10.4 million
- ? Lyrica (pregabalin), 10.0 million
- ? Spiriva Handihaler (tiotropium), 9.6 million
- ? Januvia (sitagliptin), 9.1 million

(notice # related to inflammation conditions)

6 Types of Alzheimer's Disease

? **INFLAMMATION**

- Chronic inflammation, whether due to infections or poor diet or other factors, is the key contributor to Type 1 Alzheimer's disease.

? **TROPHIC LOSS**

- Reduction in hormonal, vitamin, nutrient, or growth factor support drives Type 2 Alzheimer's disease.

? **TOXINS**

- Some toxins are "dementogens" - in other words, they cause dementia. Examples are some metals such as mercury, and mycotoxins (toxins produced by specific molds).

? **GLYCOTOXICITY**

- Sugar toxicity causes both inflammation and insulin resistance, and therefore contributes to both type 1 and type 2 Alzheimer's disease.

? **VASCULAR**

- Chronic vascular disease (which may be associated with high homocysteine or vascular amyloid or breach of the blood-brain barrier, among other contributors) is associated with the development of Alzheimer's disease.

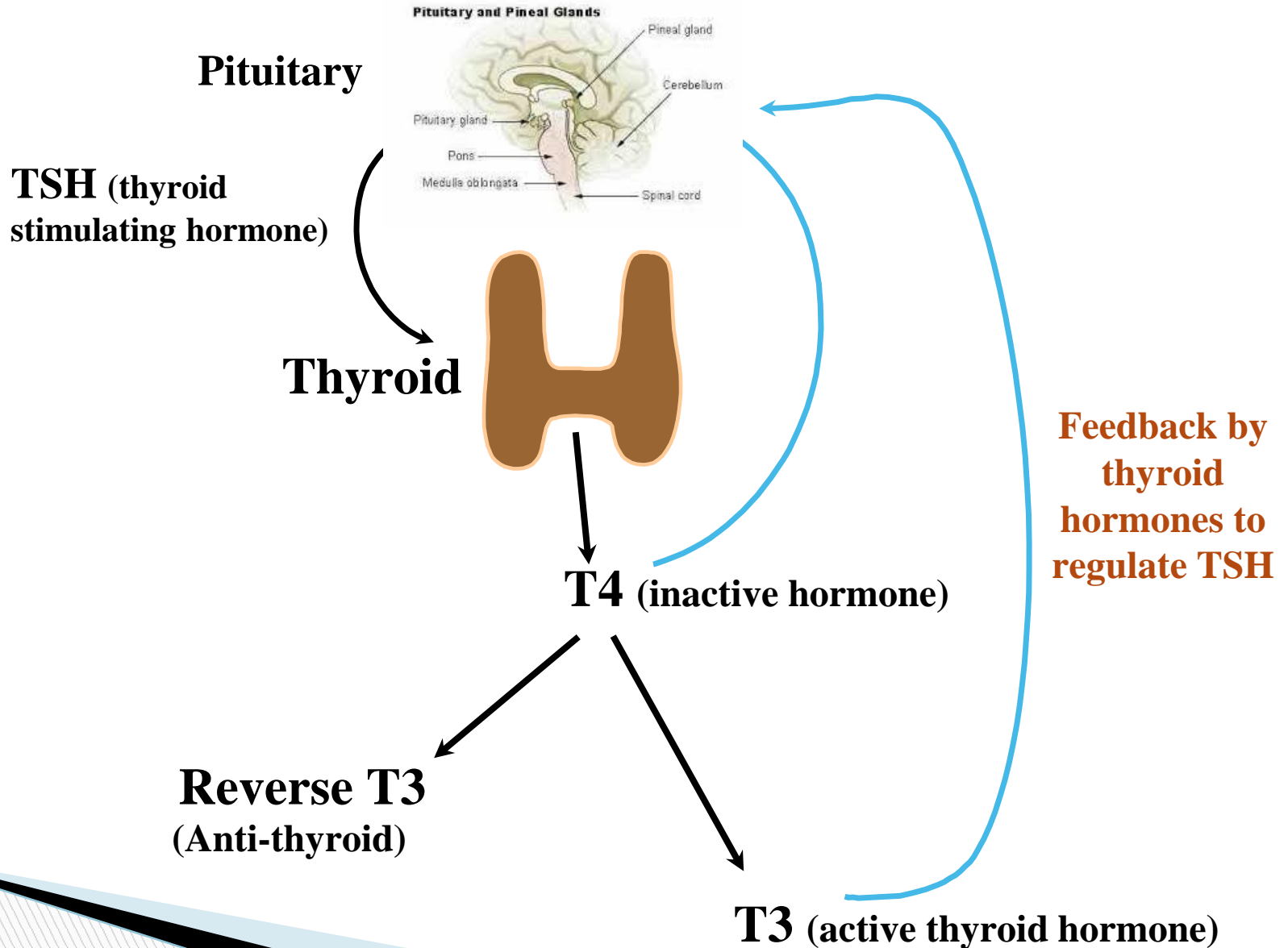
? **TRAUMATIC**

- When the brain is traumatized, for example due to an auto accident, the amyloid associated with Alzheimer's disease is produced as a response.

Uncovering Thyroid Root Causes

- ? Increased or decreased production
- ? Conversion issues
- ? Receptor malfunction
- ? Target “organelle” dysfunction
 - ie. mitochondria
- ? **Autoimmune**
 - ?Is this really the body attacking itself?
 - Food sensitivities, suspect gluten and dairy first!
 - Hidden infections
 - Toxins

Thyroid Physiology

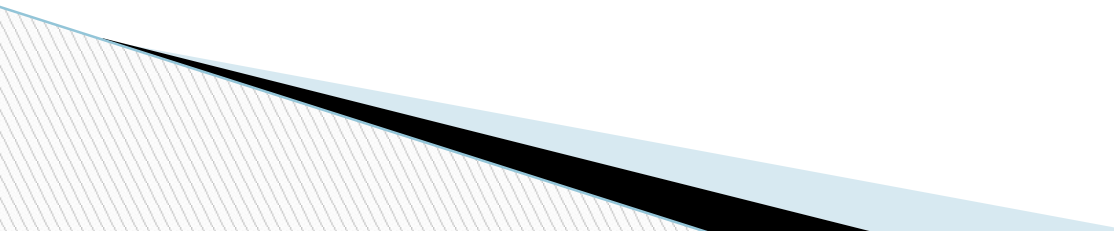


Hypothyroidism and Hashimoto's Thyroiditis

- ? Up to 80% of hypothyroidism may have anti-thyroid antibodies
- ? 97% of Hashimoto's have gluten sensitivity
- ? Recommended: all new hypothyroidism Dx should be screened with TPO Ab and TGB Ab

Is Fibromyalgia the body-wide manifestation of autoimmune thyroiditis?

Thyroid Resistance

- ? Thyroid in blood has less effect
 - ? Thyroid receptor block secondary to toxin, genetics or infection
 - ? Inhibition of active transport of thyroid into the cell due to infection, toxin or fibrin deposition
 - ? This is a *clinical diagnosis*
 - No blood tests will detect resistance, but can give clues
- 

Reverse-T3 (RT3) and Cellular Metabolism

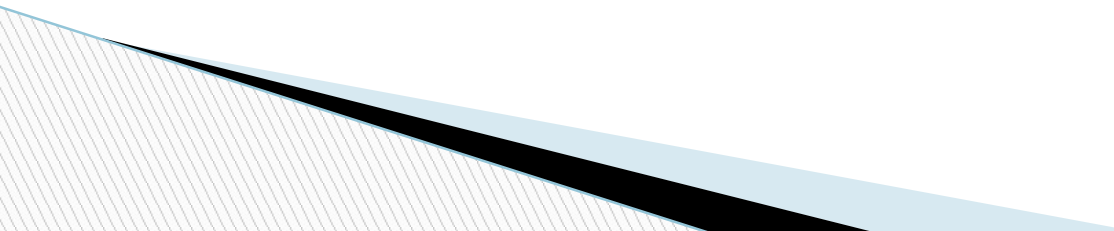
- ? Reverse T3 decreases cellular energy production
- ? Blocks T3 effect at the receptor

Res Exp Med (Berl) 1997;197(4):211-7

Endocrinolgy, 2005

Metabolism. 1960 Mar;9:293-5.

EFFECTIVE DETOXIFICATION SHOULD

- Reduce Toxic Load (*external*)
 - Increase Mobilization (*hepatic*)
 - Maximize Excretion (*hepatic, renal & 5R's*)
 - Minimize Redistribution (*5R's*)
- 

5 R's to Heal Gut/Immune/Brain...

1. Remove

Remove stressors: get rid of things that negatively affect the environment of the GI tract including allergic foods, parasites and potential problematic bacteria or yeast.

2. Replace

Replace digestive secretions: add back things like digestive enzymes, hydrochloric acid, and bile acids that are required for proper digestion and that may be compromised by diet, medications, diseases, aging, or other factors.

3. Reinoculate

Help beneficial bacteria flourish by ingesting probiotic foods or supplements that contain the “good” GI bacteria such as bifidobacteria and lactobacillus species, and by consuming the high soluble fiber foods that good bugs like to eat, called prebiotics.

Probiotics are beneficial microorganisms found in the gut that are also called “friendly bacteria.” Use of antibiotics kills both good and bad bacteria. Probiotics in the form of supplements or food are often needed to help reestablish a balanced gut flora. Fermented foods, such as yogurt, miso, and tempeh are food sources of probiotics.

Prebiotics are food ingredients that selectively stimulate the growth of beneficial microorganisms already in the colon. In other words, prebiotics feed probiotics. Prebiotics are available in many foods that contain a fiber called inulin, including artichokes, garlic, leeks, onion, chicory, tofu, and other soy products. Grains such as barley, flax, oats, and wheat are also good sources of prebiotics. Another good prebiotic source is a supplement called “fructo-oligosaccharide” or FOS.

4. Repair

Help the lining of the GI tract repair itself by supplying key nutrients that can often be in short supply in a compromised gut, such as zinc, antioxidants (e.g. vitamins A, C, and E), fish oil, and the amino acid glutamine.

5. Rebalance

It is important to pay attention to lifestyle choices. Sleep, exercise, and stress can all affect the GI tract. Balancing those activities is important to an optimal digestive tract.

High Tech Detoxification

- Consult knowledgeable physician for Condition-specific detoxification tailored to each individual
- **IM and IV THERAPIES**
 - Useful when gut is dysfunctional
 - High doses of vitamins and minerals needed by Phase 1 enzymes
 - Glutathione is poorly absorbed orally
 - Chelation may be necessary for heavy metals
- Vibrational therapies
 - Homeopathic detox formulas
 - EMF
 - Rife
 - ONDAMED
- Infrared sauna
 - Promotes skin detoxification mechanisms
- Hydrocolonic therapy
 - Useful with steps to repair gut dysfunction



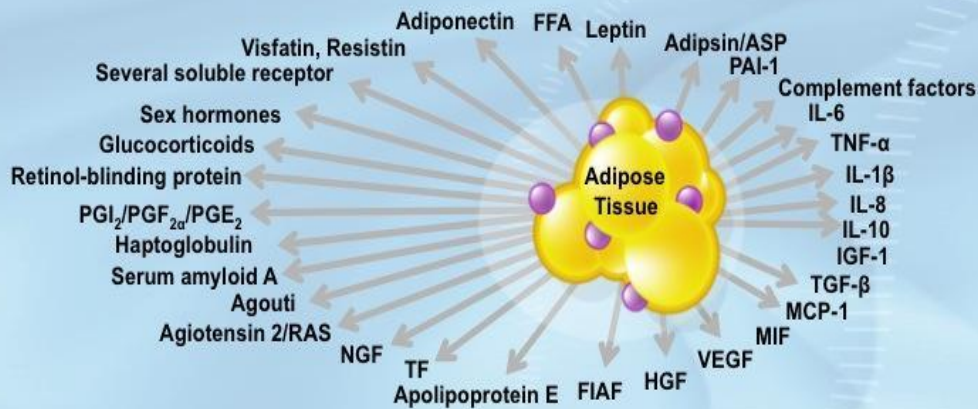
Root Cause Analysis:

Consider the case for INFLAMMATION

- ? Inflammation has been shown to be antecedent, trigger and perpetuator for many common but diverse conditions not usually treated as “inflammatory”:
 - Cardiovascular disease
 - Alzheimer’s Disease
 - Cancer
 - Osteoporosis
 - Depression (30-50% will go on to have dementia)

Actions of Fat:

ADIPOSE TISSUE AS AN ENDOCRINE ORGAN



Legend

ASP= Acylation-stimulating protein
 FFA= Free fatty acid
 FIAF= Fasting-induced adipose factor
 HGF= Hepatocyte growth factor
 IGF-1= Insulin-like growth factor-1
 IL= Interleukin
 MCP-1= Monocyte chemoattractant protein-1
 MIF= Macrophage migration inhibitory factor
 NGF= Nerve growth factor
 PAI-1= Plasminogen activator inhibitor-1
 PGE₂= Prostaglandin E₂
 PGF_{2α}= 8-iso-prostaglandin F_{2α}
 PGI₂= Prostaglandin I₂
 RAS= Renin-angiotensin system
 TF= Tissue factor
 TGF-β= Transforming growth factor-β
 TNF-α= Tumor necrosis factor-α
 VEGF= Vascular endothelial growth factor

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

- Inflammatory
 - (via adipocytokines)
 - Increases risk for
 - ✓ Heart disease
 - ✓ Hypertension
 - ✓ Insulin insensitivity
 - ✓ Diabetes
- Makes estrogen
 - (via aromatase)
 - Increases risk for
 - ✓ High CRP, T2DM
 - ✓ PCOS, PMS, endometriosis, fibroids in women
 - ✓ Low libido, BPH, depression in men
- Stores Toxins
 - Increases risk for cancer and other toxicity syndromes

Smoldering Arteries?

Low-grade Inflammation and Coronary Heart Disease

John Danesh, MBChB, MSc, DPhil

C-REACTIVE PROTEIN (CRP) IS THE CLASSIC "acute-phase reactant," the plasma levels of which can increase as much as 10 000-fold in response to tissue injury and infection.¹ C-reactive protein was discovered in the plasma of patients with acute pneumococcal pneumonia 70 years ago and was named for its capacity to bind

"C-reactive protein is the classic acute phase reactant, the plasma levels of which can increase as much as 10,000-fold in response to tissue injury and infection."

serum samples; and, despite sharp increases that occur during the acute-phase response, longer-term plasma CRP levels show about the same degree of year-to-year consistency within individuals as some more extensively studied risk factors (such as blood cholesterol levels and blood pressure).² Moreover, highly sensitive assays for CRP are now available that can precisely measure values within the range less than 1.0 mg/dL and thereby detect low-grade inflammation that would not previously have been noticed.

In this issue of THE JOURNAL, the study by Visser and colleagues³ illustrates several advantages of studying CRP in large-scale epidemiological samples. Previous reports suggested an association between plasma CRP levels and obesity, but these studies were relatively small and unable to exclude some possible biases. By contrast, Visser et al studied 16 000 American adults in a cross-sectional community-based national survey. This sample included large numbers of nonsmokers and

younger individuals, groups in whom some potential biases, such as confounding by cigarette smoking or preexisting inflammatory diseases, should be minimized. The study convincingly demonstrates that plasma CRP levels are substantially higher in obese and overweight people than in leaner people. As the authors point out, future studies of obesity should attempt to measure other inflammatory factors, par-

...ine pro-
the liver
out low-
) by sug-
liate the
umber of
redictive
onary re-
for acute
ded lim-
ited information because increased CRP levels in such patients might be partly attributable to the severity of the dis-

"The study [by Visser et al] convincingly demonstrates that plasma CRP levels are substantially higher in obese and overweight people than in leaner people."

Author: John Danesh, Clinical Service Unit and Epidemiological Studies Unit, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, England. Corresponding Author and Reprints: John Danesh, MBChB, MSc, DPhil, Clinical Trial Service Unit, Radcliffe Infirmary, Oxford OX2 6HE, England.

See also p 2131.

C-Reactive Protein, Interleukin 6, and Risk of Developing Type 2 Diabetes Mellitus

Aruna D. Pradhan, MD, MPH

JoAnn E. Manson, MD, DrPH

Nader Rifai, PhD

Julie E. Buring, ScD

Paul M Ridker, MD, MPH

TYPE 2 DIABETES MELLITUS (DM) is estimated to affect 15 million people in the United States, especially in middle-aged and older individuals. The microvascular injury typical of this disease, the economic and functional burdens are greatest during mid-to-late adulthood. Compounding these issues, as many as one third of individuals with type 2 DM are undiagnosed, and approximately 20% have diabetic retinopathy or evidence of systemic vasculopathy at clinical presentation.⁴

Although the main physiological abnormalities are insulin resistance and impaired insulin secretion,⁵⁻⁷ the specific underlying determinants of these metabolic defects remain uncertain. An accumulating body of evidence suggests that inflammation may play a crucial intermediary role in pathogenesis, thereby linking diabetes with a number of commonly coexisting conditions thought to originate through inflammatory mechanisms. In this regard, substantial experimental evidence and more recent cross-sectional data suggest that interleukin 6 (IL-6) and C-reactive protein (CRP), 2 sensitive physiological markers of subclinical systemic inflammation, are associated with hyperglycemia, insulin resistance, and overt type 2 DM.⁸⁻¹⁵ Indeed, it recently has been postulated that type

Context Inflammation is hypothesized to play a role in development of type 2 diabetes mellitus (DM); however, clinical data addressing this issue are limited.

Objective To determine whether elevated levels of the inflammatory markers interleukin 6 (IL-6) and C-reactive protein (CRP) are associated with development of type 2 DM in healthy middle-aged women.

Design Prospective, nested case-control study.

Setting The Women's Health Study, an ongoing US primary prevention, randomized clinical trial initiated in 1992.

Participants From a nationwide cohort of 27 628 women free of diagnosed DM, cardiovascular disease, and cancer at baseline, 188 women who developed diagnosed DM over a 4-year follow-up period were defined as cases and matched by age and fasting status with 362 disease-free controls.

Main Outcome Measures Incidence of confirmed clinically diagnosed type 2 DM by baseline levels of IL-6 and CRP.

Results Baseline levels of IL-6 ($P < .001$) and CRP ($P < .001$) were significantly higher among cases than among controls. The relative risks of future DM for women in the highest vs lowest quartile of these inflammatory markers were 7.5 for IL-6 (95% confidence interval [CI], 3.7-15.4) and 15.7 for CRP (95% CI, 6.5-37.9). Positive associations persisted after adjustment for body mass index, family history of diabetes, smoking, exercise, use of alcohol, and hormone replacement therapy; multivariate relative risks for the highest vs lowest quartiles were 2.3 for IL-6 (95% CI, 0.9-5.6; P for trend = .07) and 4.2 for CRP (95% CI, 1.5-12.0; P for trend = .001). Similar results were observed in analyses limited to women with a baseline hemoglobin A_{1c} of 6.0% or less and after adjustment for fasting insulin level.

Conclusions Elevated levels of CRP and IL-6 predict the development of type 2 DM.

“Elevated levels of CRP and IL-6 predict the development of type 2 DM. These data support a possible role for inflammation in diabetogenesis.”

2 inflammatory cytokine, is produced in a variety of tissues, including activated leukocytes, adipocytes, and endothelial cells. C-Reactive protein is the principal downstream mediator of the acute phase response and is primarily derived via IL-6–dependent hepatic biosynthesis. In rodent models of glucose metabolism,

investigations further support a role for inflammation in the etiology of diabetes;

Author Affiliations and Financial Disclosures are listed at the end of this article.

Corresponding Author and Reprints: Paul M Ridker, MD, MPH, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital, 900 Commonwealth Ave E, Boston, MA 02215-1204 (e-mail: pridker@partners.org).

Chronic Inflammatory Disorders: Potential Antecedents

- ? Family history;
 - chronic inflammatory or autoimmune disease
 - celiac disease
 - thyroid disease (80% of hypothyroidism is autoimmune)
- ? Genetic markers
 - Class 1 and 2 MHC (eg.HLA B27; HLA DR4)
 - Delta-6 desaturase deficiency
(Sx of EFA deficiency, atopic syndrome)
 - SNPs: TNFalpha, IL-4, 6, 13
- ? Neonatal or childhood problems (esp GI)
 - Cesarean section, Colic, reflux, developmental issues
- ? Chronic nutrient deficiencies (minerals, antioxidants)
 - ie. SAD diet

The Inflammatory Process

(A Model)

Environment

Allergens, Toxins, Stress, Infection, Trauma, Lowered oxygen, Drugs, Alcohol



Genes

Polymorphisms which render individuals with different susceptibilities



Diet

Macronutrients, micronutrients, accessory nutrients, phytonutrients



Function

Shifts physiologic state into "alarm" reaction characterized by inflammatory process



Symptoms of Inflammation

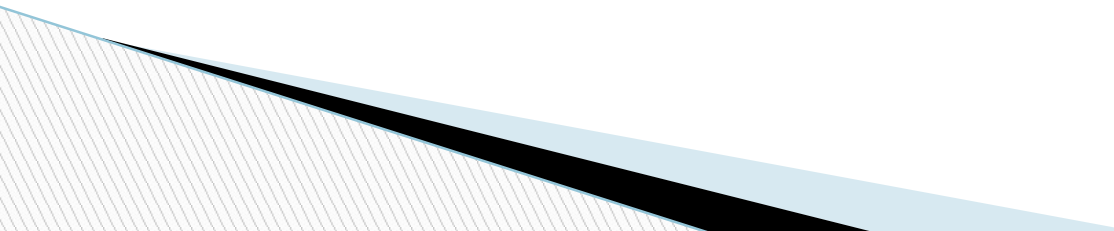
-osis becomes -itis with increasing severity

Inflammation

Acute vs. Chronic

- ? **Acute: rejection of stressor**
 - **Usually localized**
 - **Usually adaptive (allergy is exception)**
- ? **Chronic: self-perpetuating/recursive**
 - **Disrupted homeostasis**
 - **Altered cellular physiology**
 - **Destruction of tissue**
 - **Maladaptive**

Inflammatory Triggers

- ? Trauma
 - ? Toxins
 - ? Infection
 - ? Allergens
 - ? Dysglycemia
 - ? Homocysteine
 - ? Oxidative Stress
- 

**Caveat:
The
trigger
is NOT
the
disease.**



Acute lead
poisoning?

Chronic Inflammation: Basic Principles

- ? Focus on pattern instead of diagnosis
- ? Identify potential antecedents (genetic markers, family history)
- ? Remove ongoing triggers (both identified and potential), ↓ total toxic load
- ? Modify mediators:
 - correct nutritional deficiencies & oxidative stress
 - balance neuroendocrine axis
 - modulate regulatory enzymes
 - anti-inflammatory nutrients and botanicals

Inflammatory Disorders: Basic Principles

- ? *Primum Non Nocere* (First, do no harm.)
- ? *Vis Medicatrix Naturae* (Utilize the healing power of nature.)

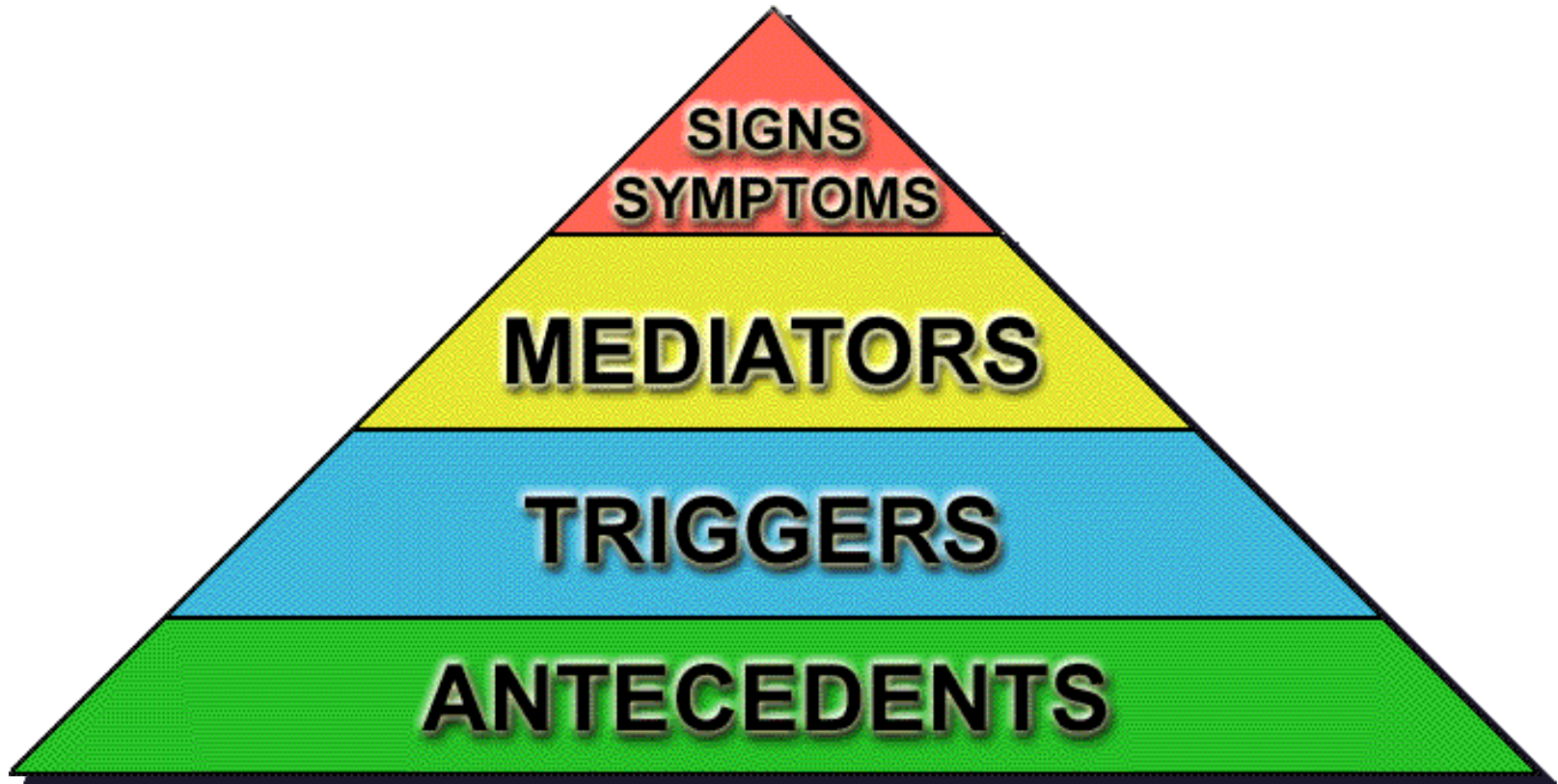
Chronic Inflammatory Disorders: Functional Medicine Diagnostics

- ? Assessment of environment/lifestyle for potential toxic exposures (e.g., pesticide use)
- ? Dietary analysis (macro & micronutrient)
- ? Elimination diet and/or allergy testing
- ? Stool analysis for maldigestion, dysbiosis
- ? Intestinal permeability testing
- ? Blood, urine, & hair analysis for heavy metals

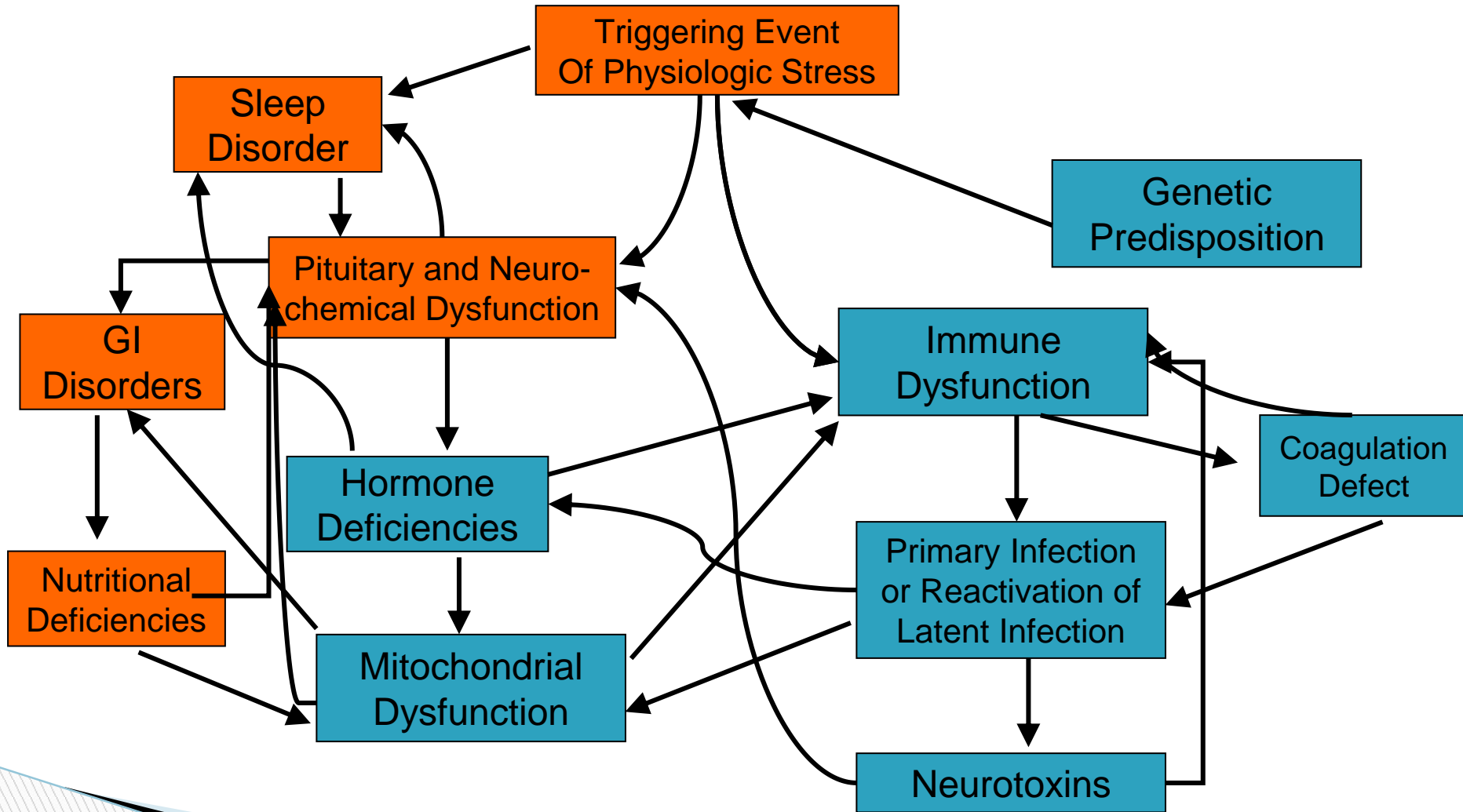
Chronic Inflammatory Disorders: Functional Medicine Diagnostics

- ? Essential fatty acid profile
- ? Cortisol and/ or DHEA (blood, urine, salivary)
- ? Homocysteine
- ? Hemoglobin A1C
- ? Hepatic detoxification profiles
- ? Serum antioxidants (extra and intra-cellular)
 - Reduced/oxidized glutathione
 - Carotenoids (lycopene, β -carotene)
 - Coenzyme Q10
 - Tocopherols (α and γ), tocotrienols

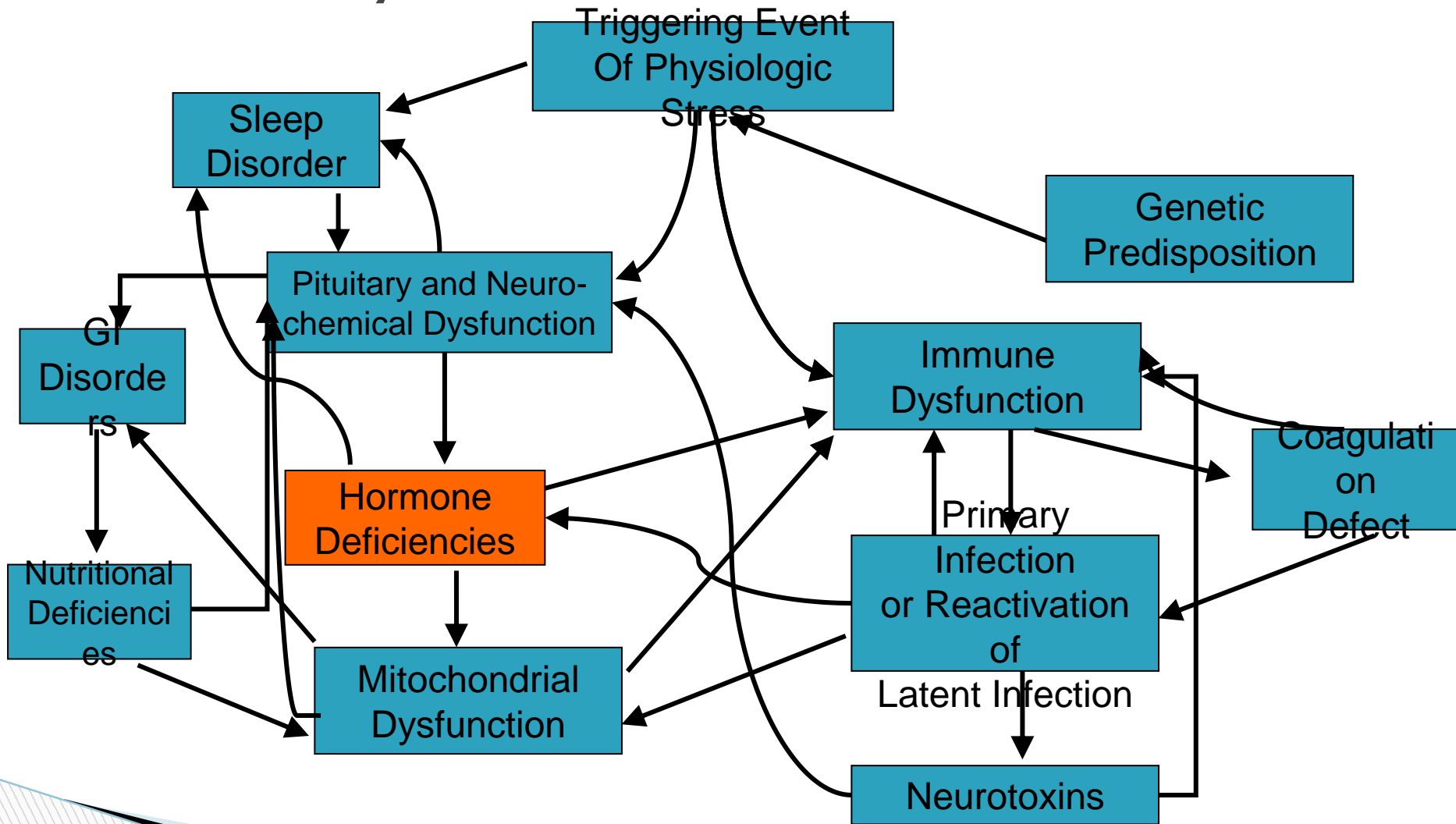
Back to Root Causes



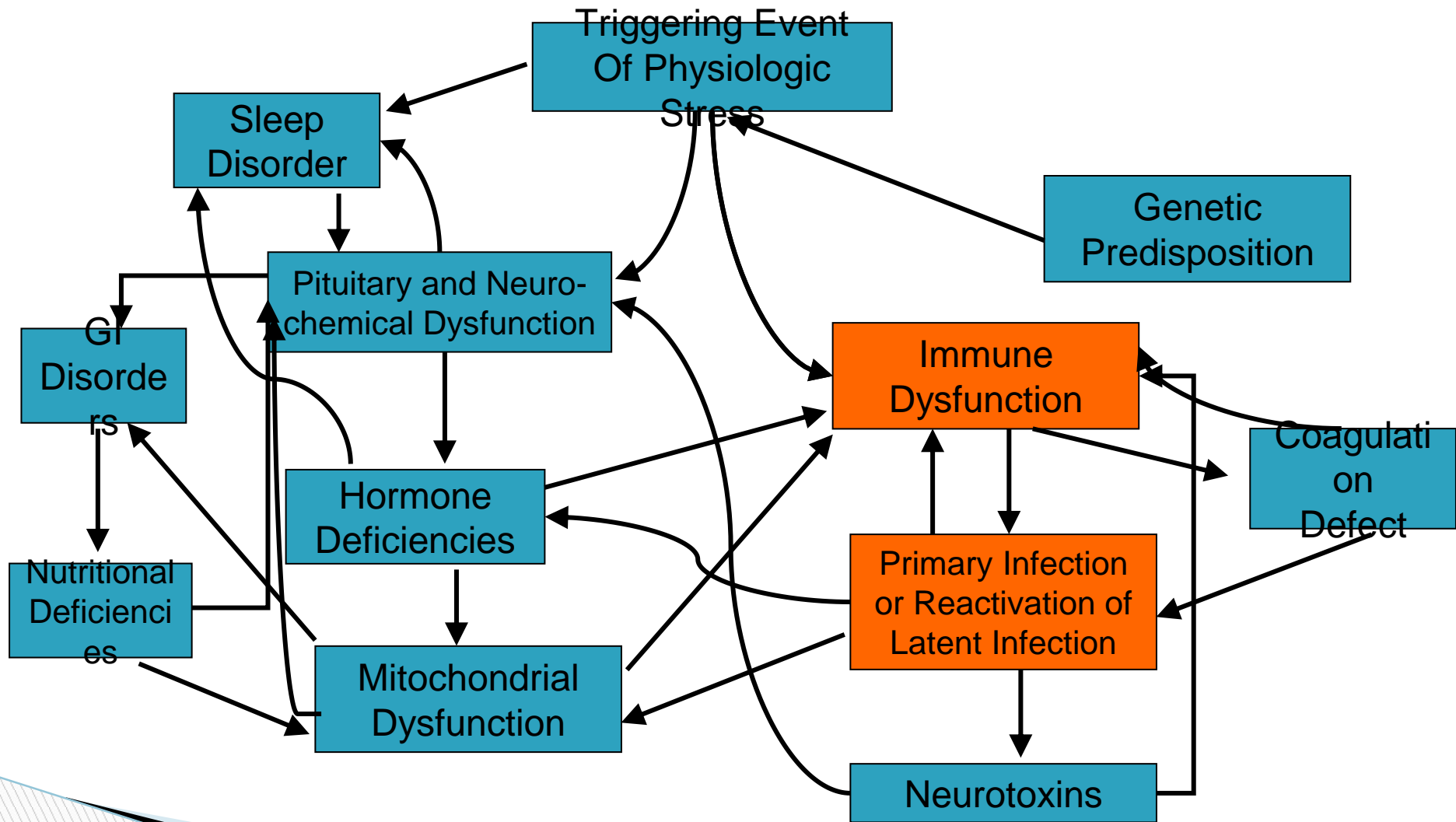
The Multiple Contributors to Dysfunction



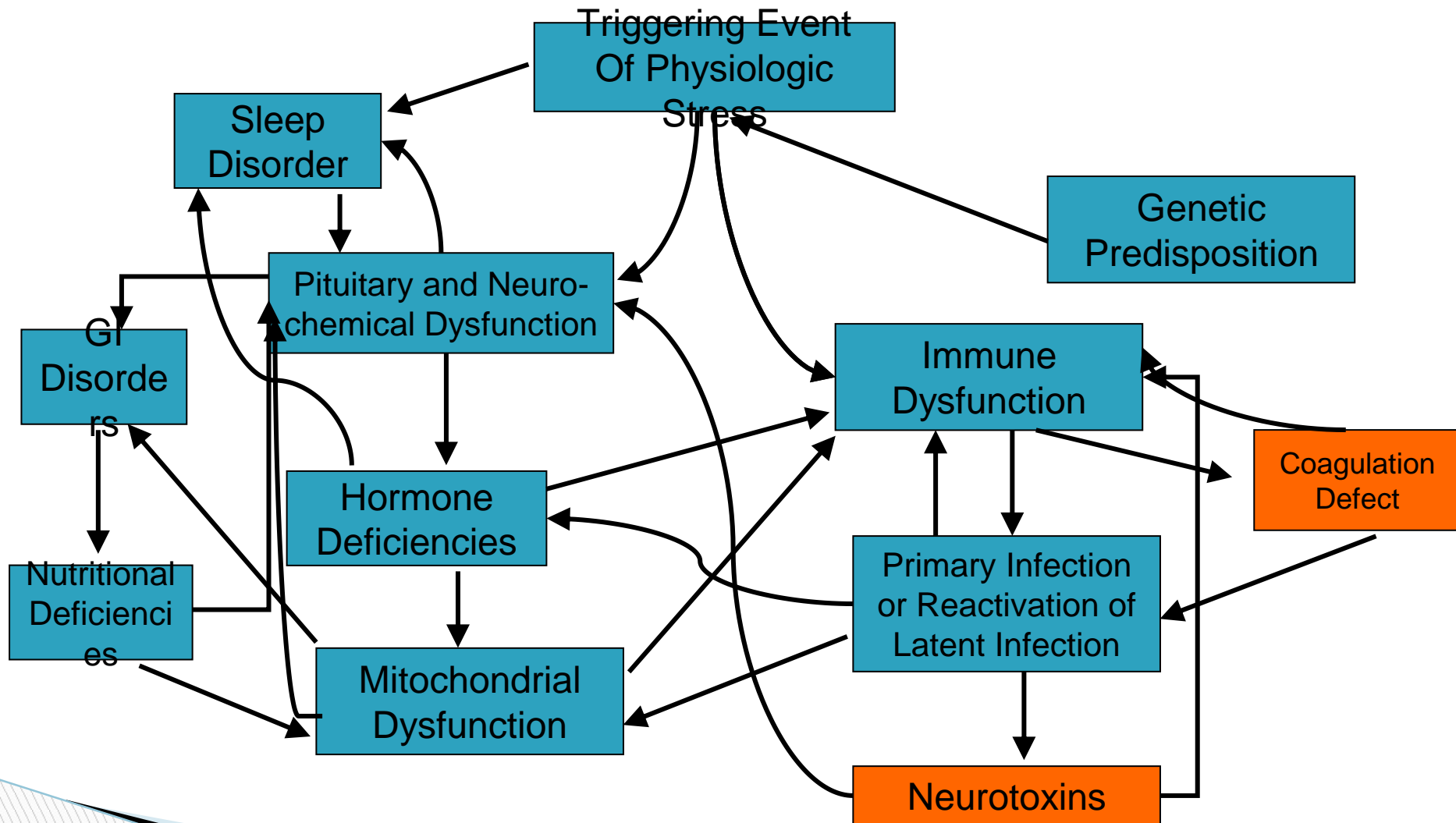
The Multiple Contributors to Dysfunction



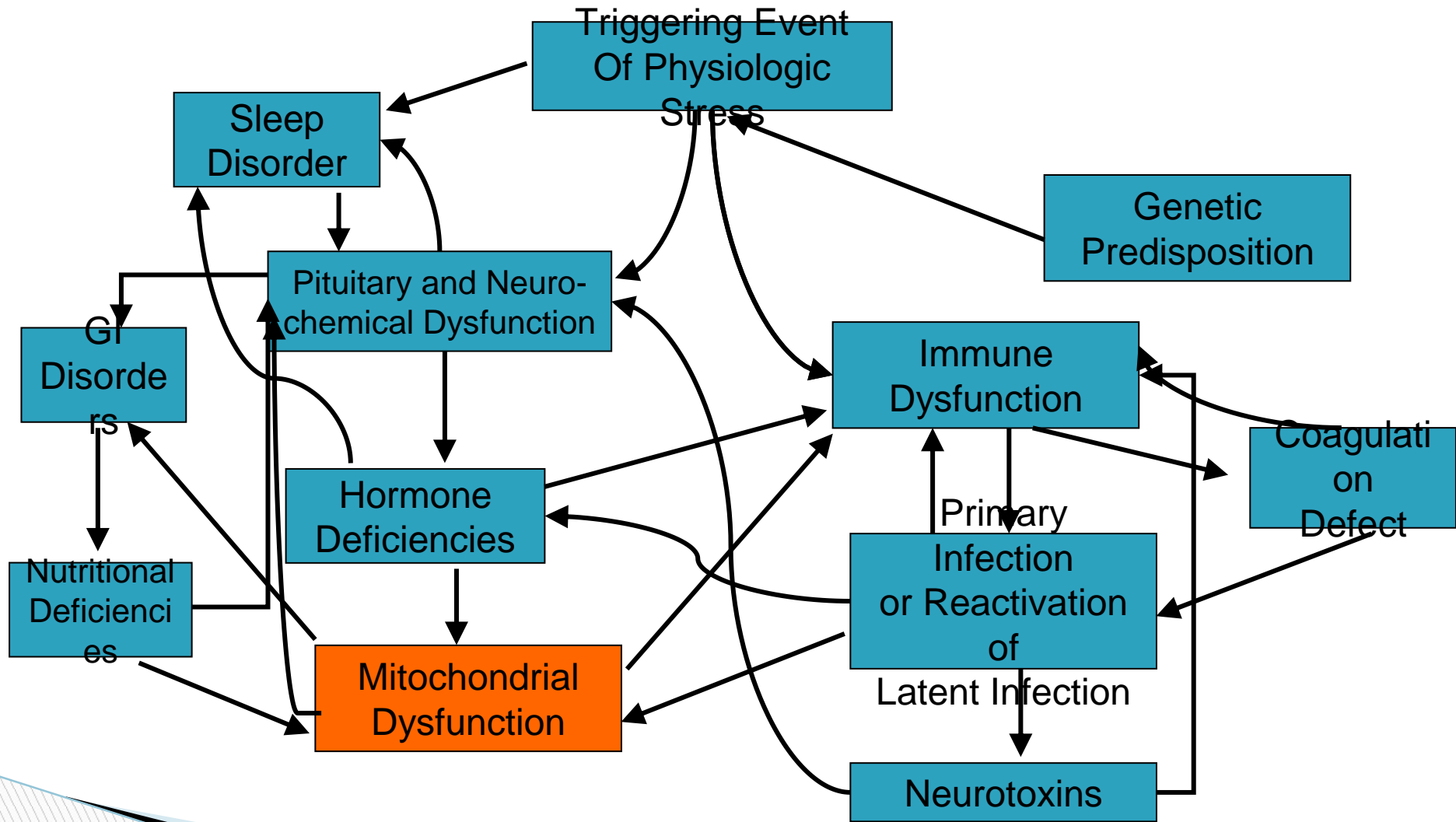
The Multiple Contributors to Dysfunction



The Multiple Contributors to Dysfunction



The Multiple Contributors to Dysfunction



Mitochondrial Functions

Energy Production

(phosphorylating respiration)

Synthesis of
useful compounds



Regulation of
cytosolic calcium

Control of apoptosis

Removal of unwanted
compounds

More on the Case History

- Tick bite in 2007 in Rhode Is. Tested positive for Lyme, bartonella, babesia, and possible mycoplasma
- Seen by Dr's in Connecticut, and NY. could not tolerate doxy b/o sun. Got hypothyroid on minocycline. Also on amoxicillin, Mepron, Rifampin, Zithromax, nystatin. Never on IV ABX.
- Put on Lamictal
- 2-page list of current supplements and nutraceuticals used for Lyme disease by “Dr. Google”.
- Using Welchol to absorb toxins.

Think “SHINES ON ME”

Sleep

Hormonal deficiencies

Infections/Immunity

Nutritional deficiencies

Exercise

Structure

Oslers

Noxious

Mind-body-spirit

Energy

FOCUS:

What function is out of balance, not what diagnostic label fits which drugs.

Image Acknowledgement

- From Princeton U. care of *Szymon Rusinkiewicz, Doug DeCarlo, Adam Finkelstein, and Anothony Santella*
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