STRESS — A MULTI-SYSTEM DISORDER

Presented by Dr Andrew Heyman, MD, MHSA

The HPA Axis

August 2015 Seminar Presentations
Objectives

- Review physiologic stress response
- Evaluate impact of cortisol on nervous and immune system
- Examine common illnesses in the context of hypocortisol states that mediated disease progression and prognosis
- Review treatment strategies and clinical cases

The following potential conflict of interest relationships are germane to my presentation.

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N/A

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N/A

“Stress and the Immune-Brain Connection”

Stress and the Immune-Brain Connection
Andrew Heyman, MD MHSA
A human being is much more than the sum of blood, bone, and viscera. In the same way, each fragment of truth in itself is a lie; therefore, the accumulation of unintegrated scientific facts does not protect us against ignorance.

In the measure that we interrelate a greater number of fragments, the closer we can come to truth, although truth as an absolute is unattainable.

Fuad Lechin
Bertha van der Dijs

Integrative Physiology

- Examine multiple organ systems simultaneously
- Seeks primary causative factors driving complex biochemical abnormalities
- Utilizes treatment strategies aimed at restoring allostasis and reducing allostatic load
- Emphasizes treatments that improves physiologic function while avoiding risk or harm
- Ecological model of medicine
Stress

- **Allostasis** - the ability to achieve stability through change — is critical to survival.
- Stress system - protect the body by responding to internal and external stress.
  - Autonomic nervous system
  - Hypothalamic–pituitary–adrenal (HPA) axis
  - Cardiovascular and metabolic systems
  - Immune systems
- **Allostatic load** - the price of accommodation to stress, (wear and tear) that results from chronic overactivity or underactivity of allostatic systems.


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Environmental stressors

- work, home, neighborhood

Major life events

- Trauma, abuse

Individual differences

- genetics, development, experiences

Perceived stress

- distress, vigilance, vigilance

Behavioral responses

- flight or fight;
  - personal behavior — diet, smoking, drinking, sexuality

Physiologic responses

- Allostasis

Adaptation

Allostatic load


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Neural

- Normal

Adaptation

- Progressive

Recovery

- Protracted

Lack of adaptation

- Progressive

• Reduced biosynthesis or release of (CRF/AVP/ACTH/Cort)
• Hypersecretion of secretagogue with down-regulation of target receptors
• Enhanced sensitivity to the negative feedback of cortisol
• Decreased availability of free cortisol
• Reduced effects of cortisol on the target tissue

The HPA Axis

• Neuroexcitation
• Neurodegeneration
• Structural Plasticity

• Th1/Th2/Th17 balance
• Innate immunity
• Microglial activation
Cortisol and the Hippocampus

- Repeated stress affects brain function, especially hippocampus.
- High concentrations of cortisol and NMDA receptors.
- Participates in verbal memory and memory context.
- Impairment decreases the reliability and accuracy of contextual memories.
- Damage may exacerbate stress by preventing access to the information needed to decide that a situation is not a threat.
- Regulates the stress response and acts to inhibit the response of the HPA axis to stress.


Hippocampal Changes in Chronic Stress

- Hippocampus alterations in both structure and function have been identified in long term stress.
- Volume loss demonstrated in PTSD, depression, Cushing's syndrome.
- Functional changes include reduction in hippocampal excitability, long-term potentiation and memory.

Dendritic Retraction of Hippocampus

- Induce shrinkage of the apical dendrites of the CA3 and CA1 pyramidal cells and dentate granule cells.
- Changes of neuronal morphology likely to contribute to cognitive deficits.
- A functional outcome of dendritic retraction is a disturbance of HPA axis regulation, leading to unregulated glucocorticoid release.
- Increased oxidative stress, neuroexcitation, loss of counter-regulatory control.
NMDA Receptors

*Neurons need to protect themselves from the excitotoxic effect of glutamate by reducing their input surface area.*

Adult Neurogenesis

- Adult neurogenesis refers to the production of new neurons in an adult brain
- Follows a similar complex multi-step process that starts with the proliferation of progenitor cells, followed by their morphological and physiological maturation.
- Ends with a fully functional neuron that is integrated into the pre-existing hippocampal network
Adult Neurogenesis

Mediators of Adult Neurogenesis

- Stress and sleep disruption suppress adult neurogenesis.
- Stress interferes with all stages of neuronal renewal, and inhibits both proliferation and survival.
- Glucocorticoid and NMDA receptors have been identified on progenitor cells.
- Lasting inhibition of AN occurs after an initial stressor, despite later normalization of cortisol.

Neurodegeneration

- Hippocampal atrophy
- Hippocampal regulation of HPA axis
- Memory and cognitive deficits
- PFC, amygdala, locus coeruleus involved
The HPA Axis

Brain-Immune Interface

Brain
- Hypothalamus, Hippocampus
- Locus Coeruleus, amygdala
- Vagal afferents
- Spinal cord and brain stem

Stress

Immune
- Thymus
- Immune cells
- Microglia
- Bone Marrow
Stress, Immune System and Acquired Immunity

- **IBS**
  - Stress increases HPA axis, and both branches of the ANS
  - Cortisol, NE, Ach inhibit the mucosal immune system, especially Th1-type responses.
  - Shift toward Th2 cytokine responses (IL-4) that can further inhibit Th1 responses.

- **IBD**
  - CRF response blunted, leading to diminished Cortisol and NE release.
  - Favor production of Th1 cytokines and proliferation of macrophages, natural killer (NK) cells, and cytotoxic T cells (Tc).
  - TNF stimulates IL-1 (Th1 pathway) and IL-6 (by lymphoid and nonlymphoid tissues).

- **Chronic stress**
  - Both types shift to Th1 response.
  - TNF-, IL-1, and IL-6 increase to concentrations that stimulate CRF production
  - Both IFN (Th1 cytokine), produced by NK cells in response to TNF, and IL-4 (Th2 cytokine)
HPA dysregulation and Cancer

Flattened cortisol rhythms in metastatic breast cancer patients
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Hypocortisolism, IL-6, and Breast Cancer

Inflammatory responses to psychological stress in fatigued breast cancer survivors: Relationship to glucocorticoids
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Neuroinflammation: Microglial Cells

![Image of Neuroinflammation and Microglial Cells]

Abstract
Fatigue is a common problem following cancer treatment and recent studies suggest that a chronic inflammatory process might contribute to cancer-related fatigue. However, immune responses to challenge have not yet been examined among individuals with cancer.
Neurodegeneration Hypothesis of Depression

**Psychological Stress**
- Serotonin
- Serotonin Receptors
- Tryptophan
- IDO
- Kynurenine
- Kynurenate
- Neuronal degeneration
- Major depression

**Physical Stress**
- Proinflammatory cytokines
- Antinflammatory cytokines

- Flattened cortisol slope
- Immune response
- Microglial activation
- Serotonin degradation
- Non-specific symptoms of sickness

**Systemic Inflammation**

Progression of Stages of Adrenal Exhaustion

- Hypothalamus
- Adrenal Cortex
- Systemic Inflammation

A new view on hypocortisolism

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**Key Words**

Hypocortisolism; Germany; adolescent and adult

Summary. Low cortisol levels have been observed in patients with different stress-related disorders such as chronic fatigue syndrome, fibromyalgia, and post-traumatic stress disorder. Data suggest that these disorders are characterized by a symptom trail of enhanced stress sensitivity, pain, and fatigue. This overview will

Raison and Miller (2003) assume that prolonged or repeated exposure to immune stimuli might predispose an individual to reduced glucocorticoid signaling as a means of freeing bodily defenses from inhibitory control in the face of an ongoing infectious threat. Thus, an enhanced release of
Key Points

- Models of Hypocortisolism
  - Developmental Model
  - Immune mediated
- Prolonged cortisol production is neurotoxic
- Reciprocal relationship between immune system and HPA axis

Hypocortisolism may be an adaptive mechanism to liberate the immune system or protect the nervous system
Multiple Factors: Stress Immune Brain Connection

• Cortisol
• NMDA excitation
• Reduced neuroplasticity
• SNS/PNS imbalance
• Th1/Th2 imbalance
• Microglial activation
• IL-6, TNFα
• Gut permeability
• IDO elevation

Phellodendron/Magnolia

• Combination of magnolia and phellodendron
  • Anti-anxiety and anti-stress properties similar to benzodiazepines, yet non-sedating
  • Anti-depressant properties
  • Has been shown to normalize high cortisol and DHEA levels
  • Low side-effect profile
  • Dosage: 1 capsule TID

L-theanine

• Green tea contains 1% to 3% theanine
• Theanine has historically been used for its relaxing and anti-anxiety effects
**L-theanine**

- Analog of glutamate
- Demonstrates a protective effect on neuroexcitotoxicity by decreasing ischemic neuronal death in the forebrains of animal models.
- Antagonistic effects on glutamate and N-methyl-D-aspartate (NMDA) receptors
- Reduces norepinephrine levels and decreases systolic and diastolic blood pressure
- Suppresses the stimulatory effects of caffeine

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**L-Theanine**

- An amino acid found in green tea - acts antagonistically against the stimulatory effects of caffeine in the tea on the nervous system.
- Increases GABA (gamma-aminobutyric acid), and reduces restlessness, insomnia, and other disruptive conditions.
- Increases levels of dopamine and improves mental awareness.
- Increases alpha waves (meditative state)

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**L-Theanine**

- Non-sedating
- Dosage - 50-200 mg 2-4 times/day
- No toxicity or reported side effects
- There are no dietary limits on L-theanine intake by the Japan Food Additive Association.
- Maximum daily dose – 1200 mg daily
Aged Garlic Extract

Organically Grown Garlic in Stainless Steel Tanks

Extraction (up to 20 months)

Natural Enzymatic Reactions

Increase in Water-Soluble Compounds, such as SAC

Harsh and irritating compounds converted into safe and beneficial compounds

### Safety of Aged Garlic Extract

- Acute toxicity test
- Chronic toxicity test
- Mutagenicity test
- Teratogenicity test (Segments I, II, III)
- Toxicity test conducted by USFDA
- Clinical studies on more than 1,000 subjects

### Seven Features of Aged Garlic Extract

- Organic
- Natural and Standardized with SAC
- Safe (No contra-indication with drugs)
- Odorless
- Quality Control under ISO 9002 & GMP
- Many Health Benefits
- Scientific Support (400+ papers)
Aged Garlic Extract

- Cardiovascular System
  - Reduce plaque formation
  - Cholesterol, LDL, Triglycerides, Homocysteine
  - Anti-LDL oxidation
  - Microcirculation
  - Blood Pressure
  - Platelets
  - Flexibility of Red Blood Cells
- Immune System
- Healthy Liver Function
- Reduction of Cancer Risk
- Additional Functions
  - Antioxidative Effects
  - Detoxification
  - UV Protection
- Anti-Aging/Cognitive

Key areas of clinical value:
- Detoxification of heavy metals
- Altering insulin resistance
- Altering stress hormone output
- Restoring gut flora integrity
- Managing chronic inflammation

A.G.E. : Detoxification

- Protects Red Blood Cells from Oxidative Damage caused by heavy metals
- Increases Mercury excretion
- Enhances detoxification liver enzymes
- Significant Acetaldehyde detox
- May protect against mutagenic changes in liver cells
- Increase glutathione, glucuronide
A.G.E.: Stress and Insulin Resistance

- Improved Recovery from Athletic performance
- Reduced Physiologic stress
- Improved recovery from oscillation stress (dizziness)
- Reduces stress induced Hypertrophy of Adrenal Gland and Hyperglycemia
- Reduce Stress induced Activation of the peripheral Sympathetic nervous system

A.G.E. Immune Function

- Helps NK Cell activity
- Helps improve TH1/TH2 ratios
- Indirect anti-tumor effects
- Anti-viral effects against Influenza
- Inhibits histamine release
- Improves age related deterioration of Immune response

A.G.E. Intestine Health

- Anti-fungal activity against Candida
- Enhances gastrointestinal motility
- Enhances mucosal barrier integrity
- Enhances growth of beneficial flora
### A.G.E. Inflammation/CVD
- Anti Alzheimer’s reduce plaque formation
- Decreases inflammatory cytokines PGE-2 & PGF-2
- Reduces homocysteine
- Reduces LDL, triglycerides, improves HDL
- Reduces plaque formation
- Helps reduce blood pressure
- Reduces platelet “stickiness”
- Helps with NO production

### A.G.E. Antioxidant effect
- Scavenges reactive oxygen species
- Reduces DNA damage & mutations
- Reduces oxidative damage in smokers
- Protection from lipid peroxidation ox-LDL
- Enhances antioxidant system in the body
- Protects vascular system and RBC from oxidative damage
- Attenuates ischemic brain damage (↑ROS)

### Aged Garlic
- Numerous other references available at www.kyolic.com
**IMMUNE MODULATORS VS IMMUNE BOOSTERS.**

- **Immune modulator:** restores the balance.
- **Immune booster:** increases or boosts the abnormality of an already dysfunctional immune response.

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**Plant Sterols**

- Patented blend of plant sterols and sterolins in a clinically proven ratio of 100:1
- Natural pine source
- Used in Germany for over 30 years

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**Plant Sterols**

- Immune modulating activity
- Moducare targets the regulatory CD4 helper cells which tell the immune system when to be more active or when to switch off to prevent damage to healthy tissues
- Moducare enhances Natural Killer (NK) cell activity
- Moducare balances TH1 and TH2 cells
- Has anti-inflammatory properties (decreases IL6 and TNF-a)

Plant Sterols

- Clinical studies conducted with Moducare have had positive effects on several infectious diseases, chronic inflammatory conditions and in models of immune stress.
- Moducare® has the ability to restore, strengthen and balance the immune system.

Plant Sterols

- Strenuous exercise can suppress the immune system due to increased cortisol
- Athletes using Moducare®:
  - decreased cortisol levels
  - improved DHEA
  - no immune alteration post-event


Plant Sterols: Rheumatoid Arthritis

- Six-month study of patients with active RA
- Patients on Moducare® show
  - 85% improvement in tender joint counts
  - reduced inflammation (decrease in ESR by 56%)
- The placebo group had no significant improvement

Plant Sterols: Allergies

- 24 patients (mainly pollen sensitive)
- Results:
  - significant reduction in allergy symptoms
  - lower IgE levels (IgE triggers histamine)
  - improved TH1/TH2 balance


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Plant Sterols and HIV

- The longest clinical usage of Moducare® (in use since 1992)
- HIV-infected patients in South Africa not on anti-retroviral drug therapy
- Results:
  - stable CD4 cell counts
  - decrease in plasma viral loads


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Plant Sterols

Suggested Use:
- Adults:
  - one three times daily or two upon rising and one before bed
- Children:
  - (under 5 years) one per day
  - (5 to 12 years) two per day

Available in vegetarian capsules and natural grape chewable tablets.
23 patients (mainly pollen sensitive)

Results:
- Significant reduction in allergy symptoms
- Lower IgE levels (IgE triggers histamine)
- Improved TH1/TH2 balance


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Rg3

- Supports healthy neurotransmitter function in the brain
- Decrease excitotoxic and oxidative stress-induced neuronal cell damage, leading to enhanced memory effects.
- Decrease both microglial activated inflammation and neuronal cell apoptosis in neurodegenerative conditions, like Parkinson’s and Alzheimer’s diseases.


- Decrease oxidative iNOS, increase macrophage scavenger receptor type A
- Reduce inflammatory cytokine expression and significantly reduce the expression of TNF-alpha in activated microglia.
- Increases survival rate of neurons exposed to TNF-alpha.
- Attenuates NMDA receptor-mediated currents and NMDA-induced neurotoxicity


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- Dose – 5 mg BID, on empty stomach
- Nasal spray 1-2 mg/B12 1-2 mg/ml BID
- Use product for 4 weeks before beneficial effects can be expected
- Slight anticoagulant properties
Rhodiola Rosea (Rhodiola)

- Plant in the Crassulaceae family that grows in cold regions of the world
- Also known as golden or ‘arctic’ root, has been used for centuries to cope with the cold Siberian climate.

Rhodiola: Traditional Uses

- Energy
- Stamina
- Mood
- Sexual function
- Arrhythmias
- Hyperlipidemia
- Cancer
- Diabetes
- Cold and flu

Rhodiola: Mechanism of Action

- Contains over 30 compounds including phenylethanoids, phenylpropanoids, flavonoids, cyanoglycosides, monoterpenes, and triterpenes.
- Salidroside and rosavin is thought to be responsible for many of the stimulant or “adaptogenic” effects of roseroot.
Rhodiola rosea

- “Second generation” plant adaptogen-similar to the effects of ginseng
- Studied and used in Russia for over 30 years to combat stress
- Used to enhance physical and mental performance of athletes and cosmonauts

Rhodiola rosea

- Initial studies revealed cardioprotective benefits due to antiarrhythmia effect and protection against reperfusion injury
- Limits adrenergic effects on heart during stress
- Reduces catecholamines during alarm phase of stress and after intense exercise
- May influence levels of monoamines and beta-endorphins

Rhodiola rosea

- RCT, cross over trial
- 56 male and female night shift physicians treated for (3) two week periods
- 20% improvement in Fatigue Index (mental performance, short-term memory, calculation, concentration
  - Darbinyan, 2000
Case

- 15 year old female with 3 year history of Postural Orthostatic Tachycardia Syndrome (POTS)
- Complained of pre-syncope with standing, generalized fatigue and muscle aches
- Failed conventional medication
- No other significant medical history
- No medications, surgeries or allergies
- Competitive swimmer, unremarkable social history

Laboratory Values

- HS-CRP – 10
- CBC and Comprehensive Metabolic Panel Normal
- WBC differential > 7
- Pregnenolone - 25
Follow Up Laboratory Values

- Mycoplasma pneumonia IgM – 2250 (nl<760)
- EBV IgM – 1.1 (nl<1.0)

Treatment plan
- Valtrix and azithromycin
- Probiotic
- Tryptophan
- Rg3
- Moducare
- L-theanine
- Thymus protein extract

Post-treatment

Conclusion

- Hypocortisolism has diagnostic and prognostic value
- Stress system tightly integrated with nervous system (CNS and PNS) and immune system
- Flattened cortisol curve may be adaptive mechanism
- Clinical strategy to address low cortisol should include:
  - Seek primary or causative factors
  - Address nervous system and immune system in treatment plan
  - Avoid over-emphasis on supportive adrenal treatments only
Thank You
Triad 1: Adrenals | Thyroid | Pancreas

Adrenals-Thyroid-Pancreas
- Energy production and circulation
- Stress-metabolism-sugar
- Central regulator of physiology
- Normal: Vitality and Wellbeing
- Imbalanced: Fatigue and Obesity

Triad 1: Characteristics
- Balance
- Movement
- Energy
- Rhythmicity
- Vitality
- Spirituality
Thyroid

- Increases metabolism (ATP)
- Protein synthesis
- Growth & activity of nervous system
- Regulation of protein, carbohydrate, lipid, and nucleic acid metabolism
- Anti-inflammatory
- Energy production

Pancreas
- Converts glucose to glycogen
- Limits fat and protein to glucose
- Facilitates cell uptake of glucose

Adrenals
- Regulation of protein, carbohydrate, lipid, and nucleic acid metabolism
- Anti-inflammatory
- Energy production
Thyroid Adrenals Pancreas Triad 1

- Lowers TSH
- Limits T4 to T3 conversion
- Tyrosine, selenium, zinc
- Reverse T3

- Insulin sensitivity
- Carbohydrate cravings
- Serotonin
- Weight gain, central obesity

Pathologic Disturbances: Elevated Cortisol

- Hippocampal atrophy (Brain)
- Altered immunity (Immune)
- Increased IL-6, TNFα (Immune)
- Lowered DHEA (Hormones)

Pathologic Disturbances: Depressed Thyroid

- Insulin sensitivity
- Oxidative stress
- Lactic acid production

- Cholesterol to pregnenolone

Other

- Depressed cognition, mood, and memory (Brain)
- Reduced cardiac function (Cardiovascular)
- Slowed gastric motility (Gut)
- Loss of mitochondrial numbers and productivity.

Primary Disturbance: Elevated Insulin

- Insulin sensitivity

Other

- Reduced cardiac function (Cardiovascular)
- Slowed gastric motility (Gut)
- Loss of mitochondrial numbers and productivity.
Primary Disturbance: Elevated Cortisol

Thyroid

Adrenals

Pancreas

Primary Disturbance: Depressed Thyroid

Thyroid

Adrenals

Pancreas

Secondary Disturbance: Insulin Dominant

Thyroid

Adrenals

Pancreas

- Weight gain (evenly distributed)
- Post-prandial fatigue
- Cold cravings
- Irritability and shakiness
- Recurrent infections
- Achiness

- Cold intolerance
- Diminished cognition and mood
- Body heavy and slow
- Difficult start to the day

- Wired and tired
- Poor sleep
- Central obesity
- Mind racing

Weight gain (evenly distributed)
Post-prandial fatigue
Cold cravings
Irritability and shakiness
Recurrent infections
Achiness

Cold intolerance
Diminished cognition and mood
Body heavy and slow
Difficult start to the day

Wired and tired
Poor sleep
Central obesity
Mind racing
Secondary Disturbance: Insulin Dominant

- Normal to slightly elevated TSH
- Depressed T4 and/or T3
- No TPO, thyroglobulin antibodies

Sue B: Insulin Dominant

- 36 year old IT specialist who travels weekly
- 'Loves to eat,' mostly at restaurants due to work
- Requires frequent snacking on protein and candy bars for energy
- Complains of foggy thinking and recurrent yeast infections
- Notices weight gain, low energy but still complete tasks
- Complains of achy joints and can’t work out as a result
- ‘I feel like I have highs and lows, and my brain is like soup. Just don’t tell me to stop eating sugar’

Secondary Disturbance: Cortisol Dominant

- Cold intolerance
- Diminished cognition and mood
- Feels heavy and slow

Sue B: Cortisol Dominant

- Exhusted
- Poor sleep
- Inflammation and achy
- Low mood and memory
Secondary Disturbance: Cortisol Dominant

- Flattened cortisol curve
- Low morning cortisol
- Loss of rhythmicity
- High/Low DHEA

Other
- Elevated IL-6, TNF
- High normal CPK

Triad 1

Adrenals
- Slightly elevated TSH
- Depressed T4 and/or T3
- No TPO, thyroglobulin antibodies

Frank J: Cortisol Dominant

- 48 year old executive who works 70-80 hours per week for 'as long as he can remember'
- His wife complains that he does not sleep well at night
- He has lost interest in activities, due to weight gain, a pesky ankle injury, and lack of energy.
- He grudgingly notes that his mind is not as sharp as it used to be, and, 'neither is his body.'
- Frank feels tired and soft, inside and out.
- He reports decreased libido

Secondary Disturbance: Thyroid Dominant

- Cold intolerance
- Diminished cognition and mood
- Feels heavy and slow

Other
- Weight gain (evenly distributed)
- Post-prandial fatigue
- Cravings

Triad 1

Adrenals
- Exhausted
- Poor sleep
- Inflammation and self
- Low mood and memory
Secondary Disturbance: Thyroid Dominant

- Elevated TSH
- Depressed T4 and T3
- Elevated TPO antibodies

Betty R: Thyroid Dominant

- 52 year old housewife who loves to cook.
- Follows the food pyramid closely, utilizing plenty of grains, pasta, dairy and meat, with only occasional snacks as treats.
- Prides herself on feeding her children healthy balanced meals, and ensures that they are on a low fat diet.
- She noticed recently some ‘spread around the middle’ but can’t seem to lose weight despite effort.
- She is having trouble getting started in the morning and feels creaky.
- Since her energy levels were low, and she can ‘never get warm’, and was diagnosed hypothyroidism.
- Armour Thyroid was started but she feels just as sluggish as ever even though her TSH is now normal.

Symptom Scale Review
Laboratory Values

Dietary Recommendations

Thyroid
- Low allergy diet

Triad 1

Pancreas
- Caveman Diet
- Low Glycemic Index diet

Adrenals

Dietary Guidelines

- Caveman Diet
- Modified Caveman Diet with evening carbs
- Low glycemic index diet
- Low glycemic index diet with lower carbohydrate
- Gluten free diet
- Handouts
- Challenges
Supplement Recommendations

**Thyroid**
- Selenium
- Iodine
- Chromium
- Thyroid glandular
- Tyrosine
- Ferritin

**Triad 1**
- Adaptogen
- Neemseed glandular
- DHEA
- Tryptophan

**Pancreas**
- Bitter Mekon
- Cinnamon
- Sterols
- Arginine

**Adrenals**
- Adrenal glandular
- Adrenal Cortex Extract
- Holy Basil
- Magnolia/Phellodendron
- L-theanine
- Selenomethionine
- Iodine
- Chromium
- Thyroid glandular
- Tyrosine
- Ferritin

Sue B: Insulin Dominant

- Sugar addict
- Energetic highs and lows
- Progressive weight gain evenly distributed

**Fasting insulin 50**
- Glucose 95

**Thyroid**
- TSH 4.1
- Free T4 1.0
- Free T3 2.0
- TPO
- Ferritin 75

**Pancreas**
- Adrenals

Cortisol 19

Sue B: Clinical Strategy

- Break Insulin Resistance
- Manage Stress Response
- Enhance Thyroid Function
**Sue B: Nutrition**

**Dietary Advice**

**Caveman Diet**
- No grain/dairy/gluten
- 1-2 servings low GI carbs
- Low carbohydrate

**Evening carb cravings?**
- Yes
- No

**Caveman Diet**
- No grain/dairy/gluten
- Low carbohydrate

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**Sue B: Insulin Management**

**Trace Minerals and Vitamins**
- Mag (bowel tolerance) 300-500 mg BID
- Chromium GTF 1000 mcg po qam and 500 mcg qpm x 60 days then 500 mcg po BID
- Vitamin D3 to serum 60-80

**Trace Minerals and Vitamins (see above)**
- Chromium GTF 1000 mcg po BID x 60 days then 500 mcg po BID
- ALA 1 Tab (600 mg) po BID

**If no improvement in 60 days add:**
- Bitter Melon 3 tablets po qd x 60 days, then 1 Tab BID
- Cinnamon 125-250 mg po TID and Resveratrol 200 mg qd

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**Key Concept**

If patient not losing weight after 60 days, add Fish oil 1-2 grams po BID and Sterols 2 tabs po BID to decrease inflammation.
**Sue B: Thyroid Support**

**Subclinical Hypothyroidism**
(Borderline high TSH/low T4 and T3)

- Yes
- Symptoms?
- No

Selenomethionine 200 mcg/Iodine 1 mg*
Selenomethionine 200 mcg/Iodine 1 mg
Thyroid glandular OTC or Rx

*Consider Iodine up to 3 mg for 2 months then 1 mg qd

---

**Key Concept**

Ferritin

80-100
Ferritin 5 mg 2-4 tabs daily

<80
Ferritin 5 mg 6 tabs daily × 60 days then 3 tabs daily

---

**Key Concept**

*Chromium is required for conversion of T4 to T3*
Sue B: Stress Management

Elevated Cortisol

Yes

Anxiety and mind racing at night?

No

Add L-theanine 1-2 caps po 2-3x daily ➔ Magnolia/Phellodendron Holy Basil (or if IBS sx)

Phenyl-GABA GABA

Key Concept

If insulin resistance, cravings and stress then add L-tryptophan 500 mg po TID-QID

Sue B: Summary

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Supplements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>Caveman diet Trace minerals</td>
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<tr>
<td></td>
<td>ALA</td>
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<tr>
<td></td>
<td>Bitter Melon</td>
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<tr>
<td>Thyroid</td>
<td>Selenomethionine/Iodine</td>
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<tr>
<td></td>
<td>Ferritin</td>
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<tr>
<td>Adrenals</td>
<td>Magnolia/Phellodendron</td>
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<tr>
<td></td>
<td>Holy Basil</td>
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<td></td>
<td>L-tryptophan</td>
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</tbody>
</table>
Frank J: Cortisol dominant

- Lacking vitality, libido, and intellectual drive
- Burned out, stressed out, checked out...
- Weight gain, poor sleep and beginning to struggle

Thyroid
- TSH 1.5
- T4 0.9 and T3 1.2
- No TPO antibodies
- Ferritin > 100

Adrenals
- Flattened cortisol curve
- Low morning cortisol
- DHEA=35

Pancreas
- Fasting insulin 21
- Fasting glucose 97

Frank J: Clinical Strategy

- Support Central Stress Response
- Manage Growing Insulin Resistance
- Limit Stress On Thyroid

Frank J: Nutrition

**Dietary Advice**

Caveman Diet
- No grain/dairy/gluten
- 1-2 servings low GI carbs

Evening carb cravings?

- yes
- no
**Frank J: Stress Support**

- **Hypocortisolism**
  - Yes
  - On going stress?
    - Yes: Adrenal Cortex Extract 2 caps po BID
    - No: Hypocortisolism
  - No: Anxiety?
    - Yes: Adrenal glandular 2 caps po BID (flat and/or brain fog)
    - No: Hypocortisolism

- **DHEA-s**
  - 50-100 mg daily
  - 100-250 mg daily
  - 25 mg daily

- **On going stress?**
  - Yes: Adaptogen 1 cap BID
  - No: Hypocortisolism

---

**Key Concept**

*If patient reports difficulty sleeping, add Neuromedulla glandular 2 caps at night to reanimate hypothalamus*

---

**Key Concept**

*If patient reports depression and fatigue, add tryptophan to restore serotonin levels*
Frank J: Insulin Management

**FBS > 90/IR/Cortisol**
- Trace Minerals and Vitamins
  - Mag (bowel tolerance) 300-500 mg BID
  - Chromium GTF 1000 mg po qam and 500 mg qpm x 60 days then 500 mg po BID
  - Vitamin D3 to serum 60-80

**IR (>22)/Cortisol**
- Trace Minerals and Vitamins (see above)
  - Chromium GTF 1000 mcg po BID
  - ALA 1 Tab (600 mg) po BID

**Diabetes Mellitus**
- See above
- Bitter Melon 3 tablets po qd x 60 days, then 1 Tab BID
- Cinnamon 125-250 mg po TID and Resveratrol 200 mg qd

Frank J: Thyroid Support

**Subclinical Hypothyroidism**
(Borderline high TSH/low T4 and T3)

1. **Yes**
   - Selenomethionine 400 mcg/Iodine 1 mg*
   - Tyrosine 500 – 1000 mg BID
   - Thyroid glandular or Rx

2. **No**
   - Selenomethionine 400 mcg/Iodine 1 mg
   - Tyrosine 500 – 1000 mg BID

*Consider Iodine up to 3 mg for 2 months then 1 mg qd

Key Concept

Add tyrosine when adrenals and thyroid are low due to preferential consumption under times of stress
**Frank J: Summary**

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<tr>
<td></td>
<td>Tyrosine</td>
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<tr>
<td></td>
<td>Thyroid USP 15-30 mg</td>
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<tr>
<td>Adrenals</td>
<td>Adrenal glandular</td>
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<tr>
<td></td>
<td>Adaptogen</td>
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<td>Relora</td>
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<td>Tryptophan</td>
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<td>DHEA</td>
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**Betty R: Thyroid dominant**

- Loves to cook, follows food pyramid
- Treated with Armour Thyroid
- Weight gain and cold extremities

- **Thyroid**
  - TPO antibodies
  - TSH 3
  - T4 2.3 and T3 1.3
  - Ferritin > 100

- **Pancreas**
  - Fasting insulin 23
  - Fasting glucose 97

- **Adrenals**
  - Low morning cortisol 7
  - DHEA 110

**Betty R: Clinical Strategy**

- **Treat All Thyroid Abnormalities**
- Manage Growing Insulin Resistance
- Support Stress Response
Betty R: Nutrition

Dietary Advice

Low Allergy emphasis
Caveman Diet
No grain/dairy/gluten
1-2 servings low GI carbs

Evening carb cravings?
yes  no

Betty R: Thyroid Support

Hypothyroidism

Yes  +TPO?  No

Selenomethionine 400 mcg/Iodine 1 mg
Tyrosine 500 – 750 mg BID

Compounded T3/T4 only or...
Synthroid and/or Cytomel

*Selenomethionine 400 mcg/Iodine 1 mg
Tyrosine 500 – 750 mg BID
Thyroid gland or Armour Thyroid

*Consider Iodine up to 3 mg for 2 months then 1 mg qd

Key Concept

Presence of TPO antibodies indicate autoimmune process, seek causative factors:
food allergies, heavy metals, chronic infections, stress
Betty R: Thyroid Support

Hypothyroidism

Yes +TPO?

No

Selenomethionine 400 mcg/Iodine 1 mg*
Magnesium 200 mg BID
Sterols 20 mg 3 caps BID x 60 days, then 3 caps qam or...
Astragalus 250-500 mg TID

*Consider Iodine up to 3 mg for 2 months then ↓ 1 mg qd

Selenomethionine 400 mcg/Iodine 1 mg
Tyrosine 500 – 750 mg BID
Thyroid glandular OTC or Rx

Key Concept

If presence of TPO antibodies, do not use prescribed or over the counter glandulars

Betty R: Stress Support

Adaptogen 1 cap BID

Yes

Hypocortisolism

50-100

50 mg daily

DHEA-s

100-250

25 mg daily

Yes

Adrenal Cortex Extract 2 caps po BID

50 mg daily

On going stress?

No

Anxiety?

No

Adrenal gland 2 caps po BID (or brain fog)
**Betty R: Insulin Management**

FBS >90/

IR

Trace Minerals and Vitamins
- Mag (bowel tolerance) 300-500 mg BID
- Chromium GTF 1000 mcg po qam and 500 mcg qpm
- x 60 days then 500 mcg po BID
- Vitamin D3 to serum 60-80

IR (>22)/ Cortisol

Trace Minerals and Vitamins (see above)
- Chromium GTF 1000 mcg po BID
- x 60 days then 500 mcg po BID
- ALA 1 Tab (600 mg) po BID

If no improvement
in 60 days
add:

Cortisol

Trace Minerals and Vitamins (see above)
- Chromium GTF 1000 mcg po BID
- x 60 days then 500 mcg po BID
- ALA 1 Tab (600 mg) po BID

**Key Concept**

*Add tyrosine when adrenals and thyroid are low due to preferential consumption under times of stress*

**Betty R: Summary**

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