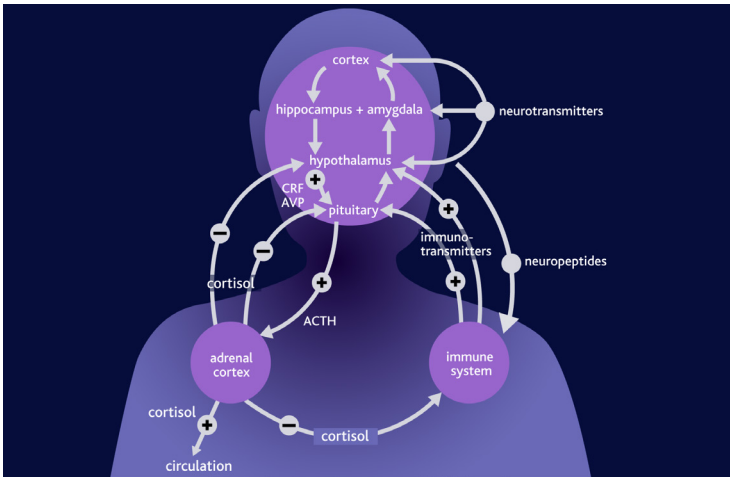
THE AUSTRALASIAN ACADEMY OF ANTI-AGEING MEDICINE

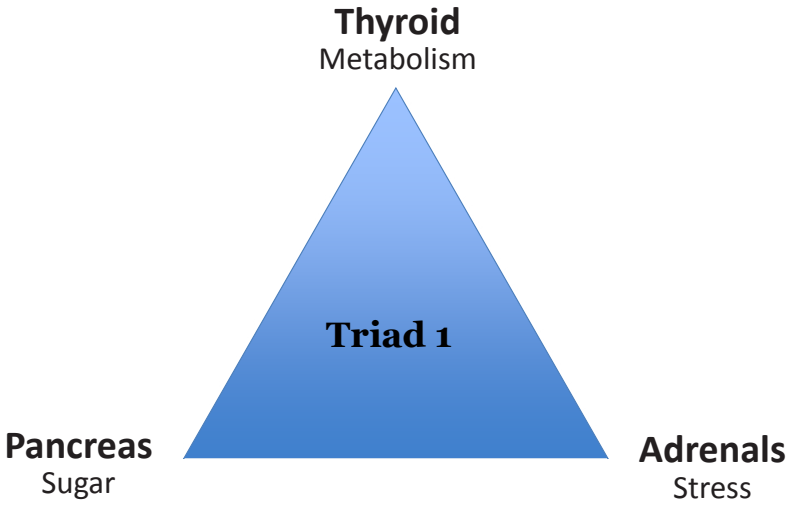
fxMED
First in Nutritional and Environmental Medicine

STRESS — A MULTI-SYSTEM DISORDER

Presented by Dr Andrew Heyman, MD, MHSA

The HPA Axis





August 2015 Seminar Presentations

"Stress and the Immune-Brain Connection"

Stress and the Immune-Brain Connection

ANDREW HEYMAN, MD MHSA

Stress and the Immune-Brain Connection
Andrew Heyman, MD MHSA

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

Equipment: None
Speakers Bureau: None
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Consultant: None

Status of FDA devices used for the material being presented
N/A

Status of off-label use of devices, drugs or other materials that constitute the subject of this presentation
N/A

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

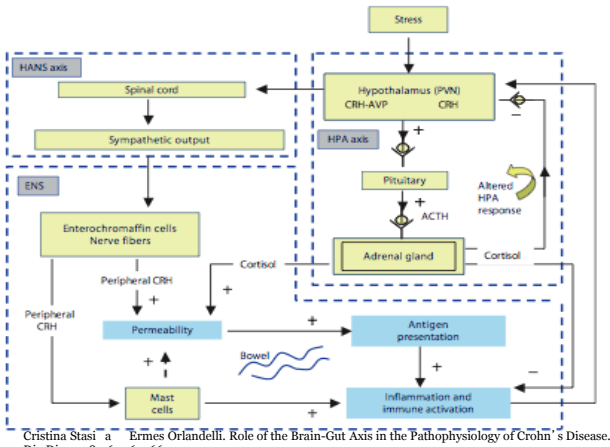
A human being is much more than the sum of blood, bone, and viscera.
In the same way, each fragment of truth in itself is a lie; therefore, the accumulation
Of unintegrated scientific facts does not protect us against ignorance.

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

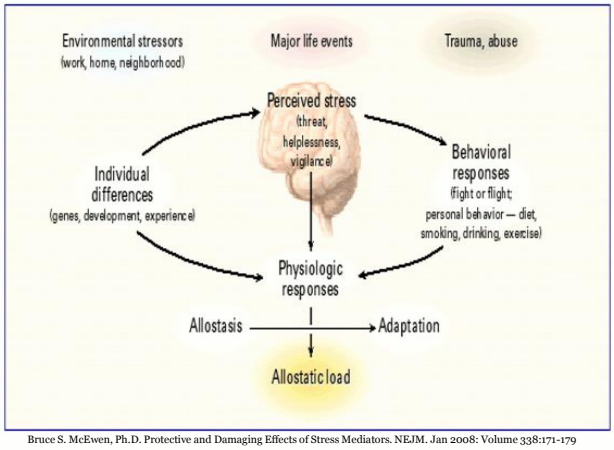


Cristina Stasi a Ermes Orlandelli. Role of the Brain-Gut Axis in the Pathophysiology of Crohn s Disease. Dig Dis 2008;26:156–166

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.

Bruce S. McEwen, Ph.D. Protective and Damaging Effects of Stress Mediators. NEJM. Jan 2008: Volume 338:171-179



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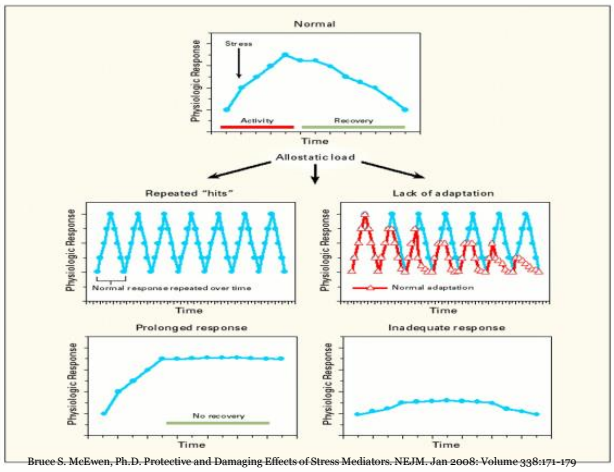

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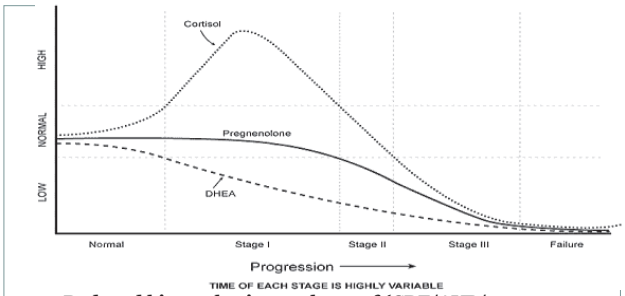
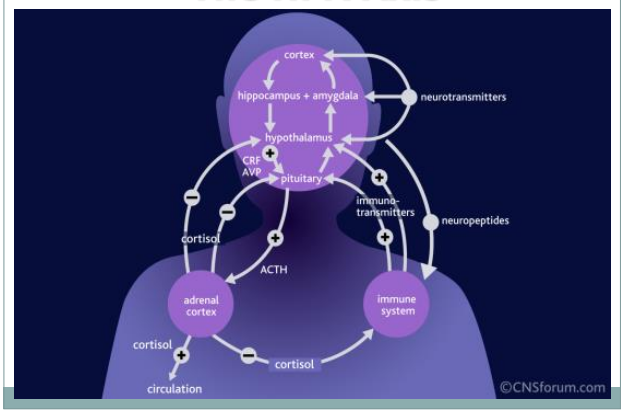
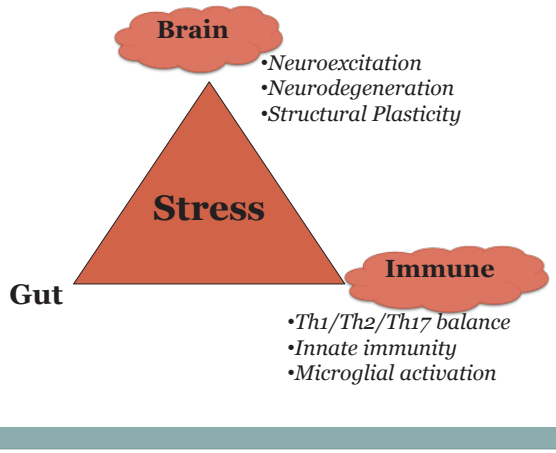


- **Reduced biosynthesis or release of (CRF/AVP/ ACTH/Cort)**
- **Hypersecretion of secretagogue with down-regulation of target receptors**
- **Enhanced sensitivity to the negative feedback of cortisol**
- **Decreased availability of free cortisol**
- **Reduced effects of cortisol on the target tissue**

The HPA Axis





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

Bruce S. McEwen, Ph.D. Protective and Damaging Effects of Stress Mediators. NEJM. Jan 2008: Volume 338:171-179

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.

European Neuropsychopharmacology (2010) 20, 1–17

ELSEVIER www.elsevier.com/locate/euroneuro

REVIEW

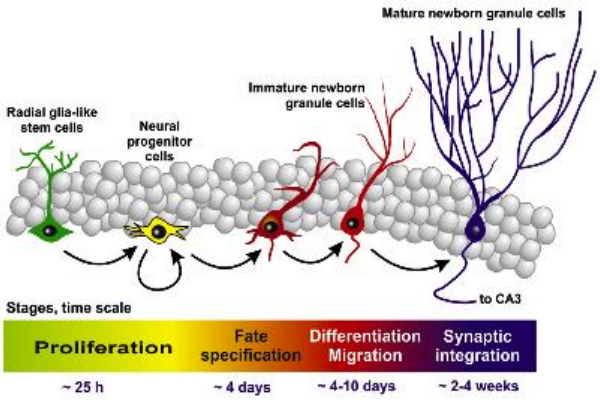
Regulation of adult neurogenesis by stress, sleep disruption, exercise and inflammation: Implications for depression and antidepressant action☆

P.J. Lucassen [a,*], P. Meerlo [b], A.S. Naylor [c,d], A.M. van Dam [e], A.G. Dayer [f], E. Fuchs [g,h], C.A. Oomen [a], B. Czéh [g,f]

Adult Neurogenesis

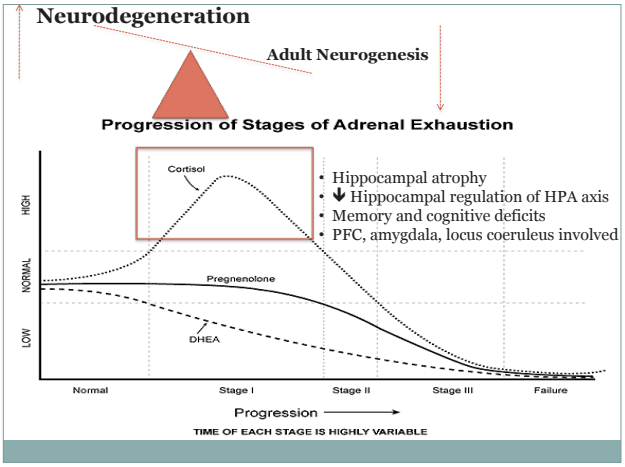
- Adult neurogenesis refers to the production of new neurons in an adult brain
- Follows a similar complex multi-step process that starts with the proliferation of progenitor cells, followed by their morphological and physiological maturation.
- Ends with a fully functional neuron that is integrated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

Adult Neurogenesis

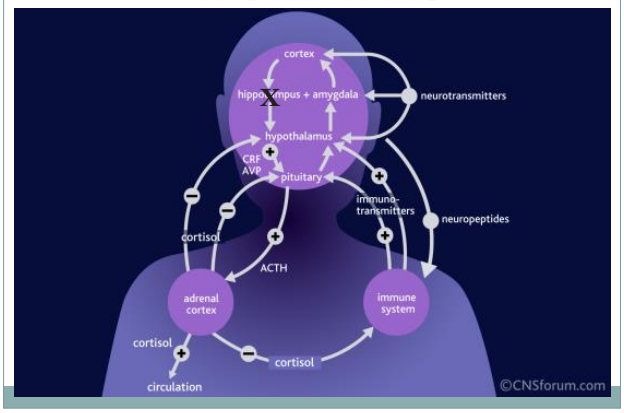


Mediators of Adult Neurogenesis

- 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.



The HPA Axis



Brain-Immune Interface

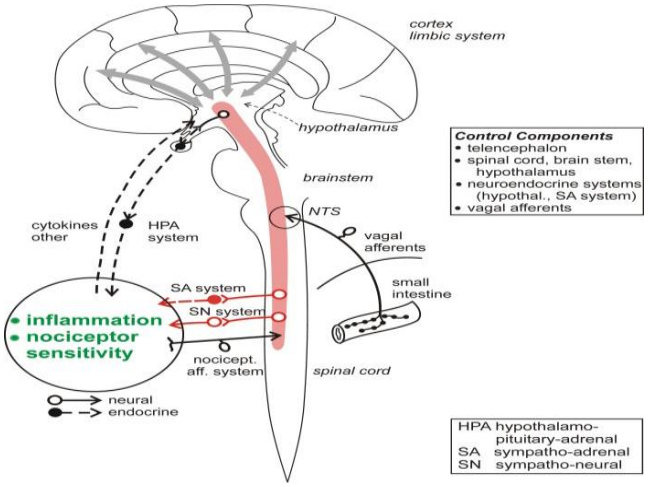
Brain

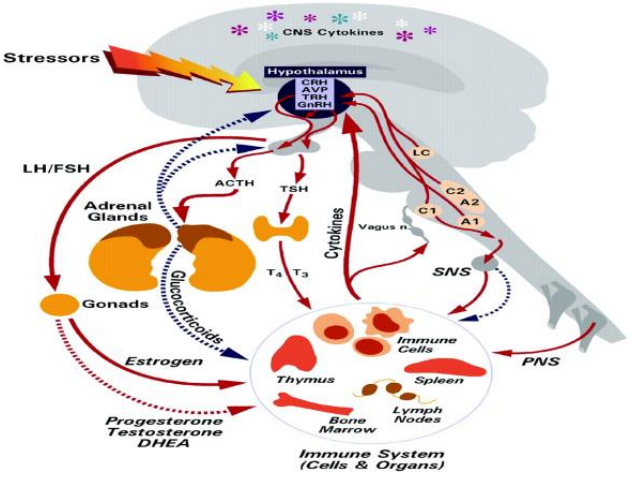
- Hypothalamus, Hippocampus
- Locus Coeruleus, amydala
- Vagal afferents
- Spinal cord and brain stem

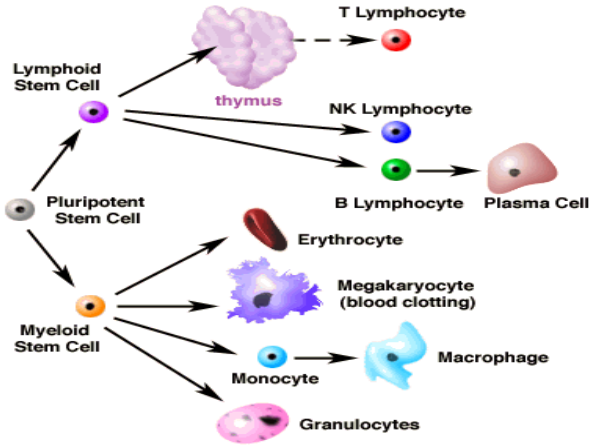
Stress

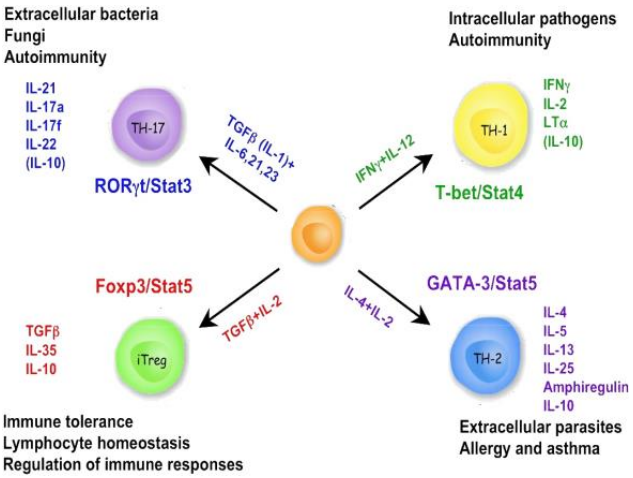
Immune

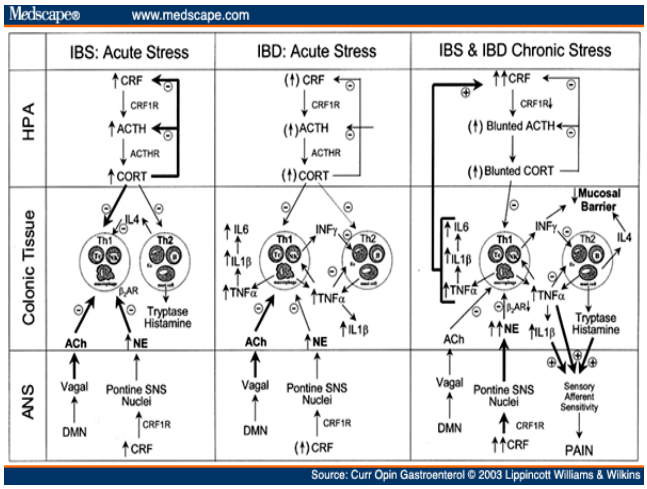
- Thymus
- Immune cells
- Microglia
- Bone Marrow




Stressors
CNS Cytokines
Hypothalamus
CRH
AVP
TRH
GnRH
LH/FSH
ACTH
TSH
LC
C2
A2
C1
A1
Vagus n.
Adrenal Glands
Cytokines
T4 T3
SNS
Gonads
Glucocorticoids
Immune Cells
Estrogen
Thymus
Spleen
PNS
Lymph Nodes
Progesterone
Testosterone
DHEA
Bone Marrow
Immune System
(Cells & Organs)

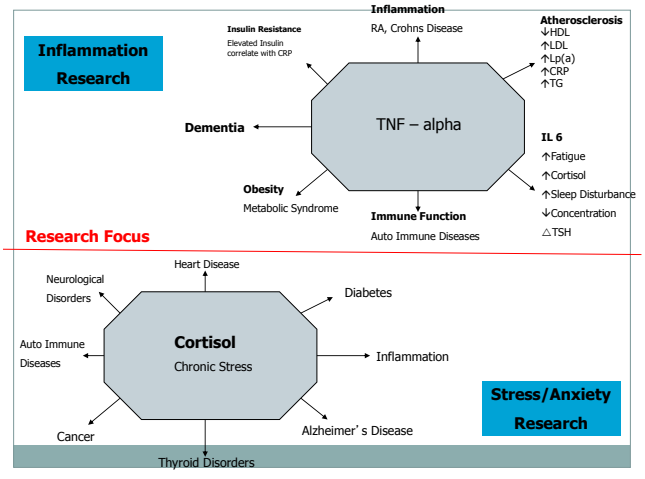

T Lymphocyte
Lymphoid Stem Cell
thymus
NK Lymphocyte
B Lymphocyte
Plasma Cell
Pluripotent Stem Cell
Erythrocyte
Megakaryocyte (blood clotting)
Myeloid Stem Cell
Monocyte
Macrophage
Granulocytes


Extracellular bacteria
Fungi
Autoimmunity
IL-21
IL-17a
IL-17f
IL-22
(IL-10)
TH-17
RORγt/Stat3
TGFβ (IL-1)+ IL-6,21,23
IFNγ+IL-12
Intracellular pathogens
Autoimmunity
IFNγ
IL-2
LTα
(IL-10)
TH-1
T-bet/Stat4
Foxp3/Stat5
TGFβ
IL-35
IL-10
iTreg
TGFβ+IL-2
IL-4+IL-2
GATA-3/Stat5
IL-4
IL-5
IL-13
IL-25
Amphiregulin
IL-10
TH-2
Immune tolerance
Lymphocyte homeostasis
Regulation of immune responses
Extracellular parasites
Allergy and asthma



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 (a 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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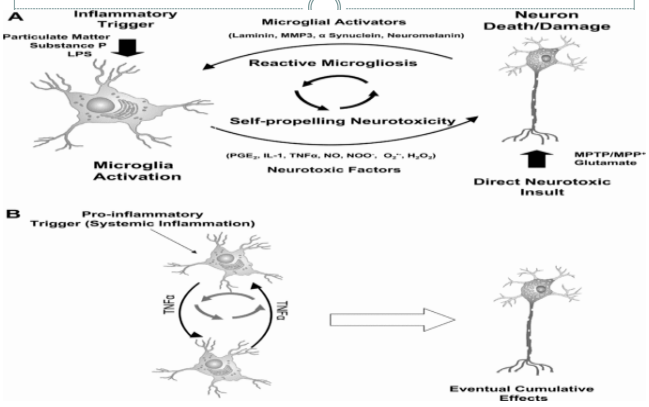
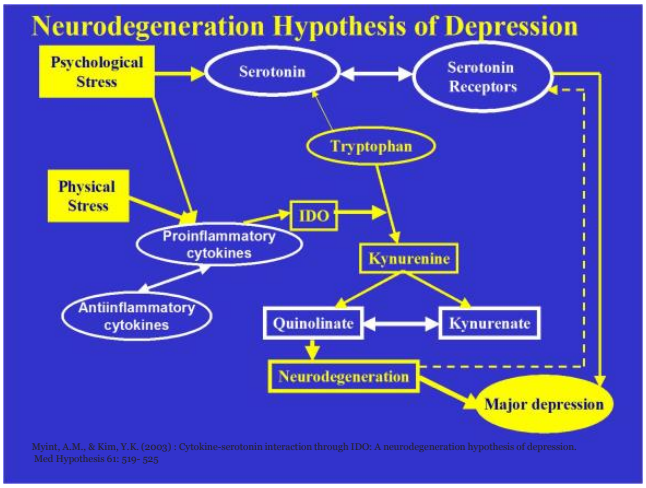
Available online 27 September 2006

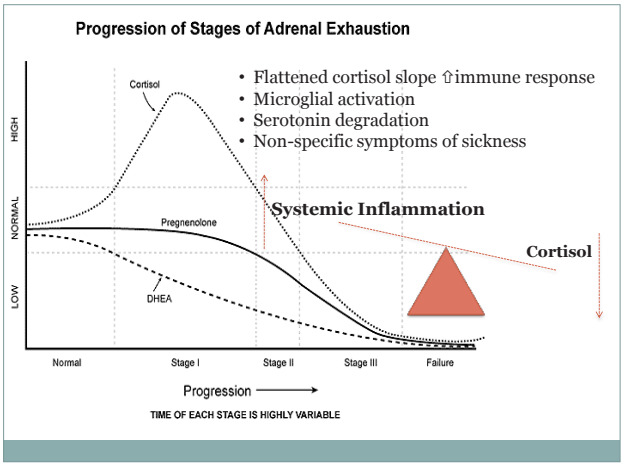
Abstract

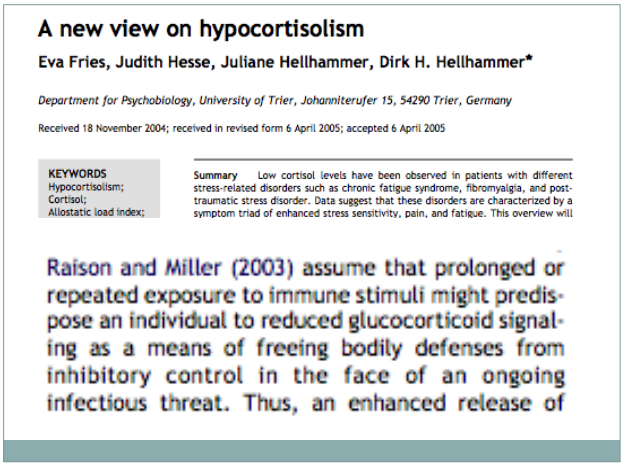
Fatigue is a common problem following cancer treatment and our previous studies suggest that a chronic inflammatory process might contribute to cancer-related fatigue. However, immune responses to challenge have not yet been evaluated among individuals with can-

Neuroinflammation: Microglial Cells









A new view on hypocortisolism

Eva Fries, Judith Hesse, Juliane Hellhammer, Dirk H. Hellhammer*

Department for Psychobiology, University of Trier, Johanniterufer 15, 54290 Trier, Germany

Received 18 November 2004; received in revised form 6 April 2005; accepted 6 April 2005

KEYWORDS
Hypocortisolism;
Cortisol;
Allostatic load index;

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 triad 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

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may be beneficial for health and survival. Most strikingly, the demonstration of a low allostatic load index in hypocortisolemic subjects suggests that a down-regulation of the HPA axis in chronically stressed subjects protects those subjects against the harmful effects of a high allostatic load index.

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 amd phellodendron
- Anti-anxiety and anti-stress properties similar benzodiazapenes, 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 it's 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

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-amino-butyric acid), and reduces restlessness, insomnia, and other disruptive conditions.
- Increases levels of dopamine and improves mental awareness.
- Increases alpha waves (meditative state)

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

↓

Aged Garlic Extract

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**

Aged Garlic Extract

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

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- Yamasaki, T. et al. 1994. Phytother. Res. 8: 408-412.
- 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.

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

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)

Bouic P, et al. Int J Sports Med 1999 May:20(4):258-62

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

Source: Bouic PJD et al. "The effects of B-sitosterol(BSS) and Beta-sitosterol glucoside (BSSG) mixture on selected immune parameters of marathon runners: Inhibition of post marathon immune suppression and inflammation." Int J Sports Med 1999; 20: 258-62.

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

Source: Louw,I et al. "A pilot study of the clinical effects of a mixture of beta-sitosterol and beta-sitosterol glucoside in active rheumatoid arthritis." Am J Clin Nutr 2002; 75(2), 351S[Abstract 40]

Plant Sterols: Allergies

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

Source: Myers, L and Bouic, PJD. "Flow cytometric analysis of the TH1-TH2 shift in allergic individuals using Moducare® (sterols/sterolins)." Proc. 26th Annu Cong Physiol Soc S. Afr. 1998; Abstract 178.

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

Source: Bouic PJD, Clark A, Brittle W, Lamprecht JH, Freestone M, Liebenberg RW. "Plant sterol/sterolin supplement use in a cohort of South African HIV-infected patients—effects on immunological and virological surrogate markers." South African Med J 2001; 91: 848–50.

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.

Rg3

- Rg3 is in a class of triterpene saponins called ginsenosides.
- Supports healthy neurotransmitter function in the brain
- Decreases 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.

Joo SS, Yoo YM, Ahn BW, Nam SY, Kim YB, Hwang KW, Lee do I. Prevention of inflammation-mediated neurotoxicity by Rg3 and its role in microglial activation. Biol Pharm Bull. 2008 Jul;31(7):1392-6.

Rg3

- 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

Joo SS, Yoo YM, Ahn BW, Nam SY, Kim YB, Hwang KW, Lee do I. Prevention of inflammation-mediated neurotoxicity by Rg3 and its role in microglial activation. Biol Pharm Bull. 2008 Jul;31(7):1392-6.

Rg3

- 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 goldenor '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 phenlyethanoids, 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

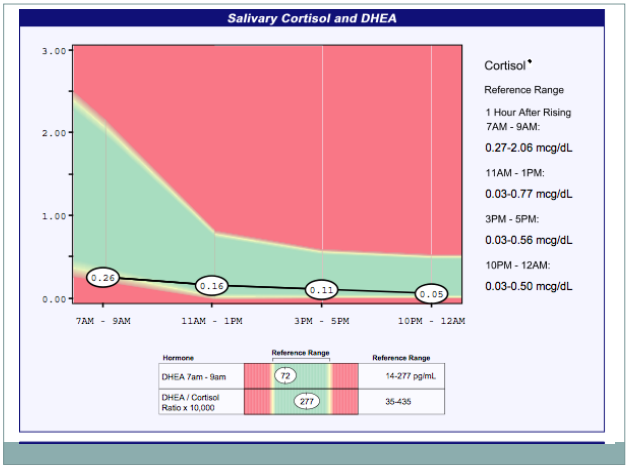
- RCT, cross over trial
- 56 male and female night shift physicians treated for (3) two week periods
- 20% improvement in Fatigue Index (mental performance, short-term memory, calculation, concentration
  - Darbinyan, 2000

Case

- 15 year old female with 3 year history of Postural Orthstatic 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

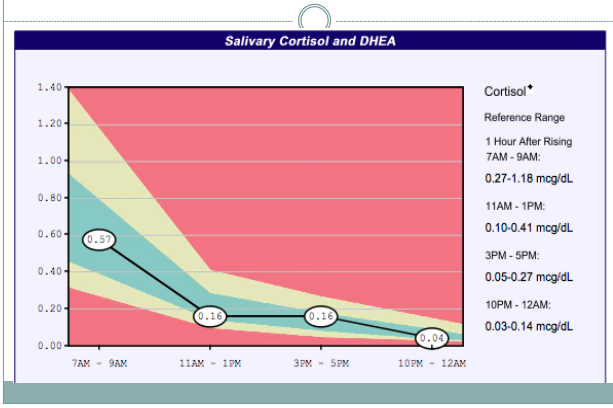


Follow Up Laboratory Values

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

- Treatment plan
  - Valtrex 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

ANDREW HEYMAN, MD MHSA

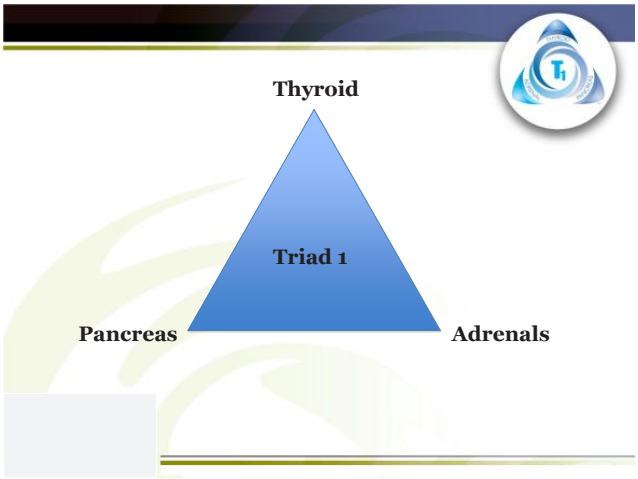
Triad 1: Adrenals | Thyroid | Pancreas

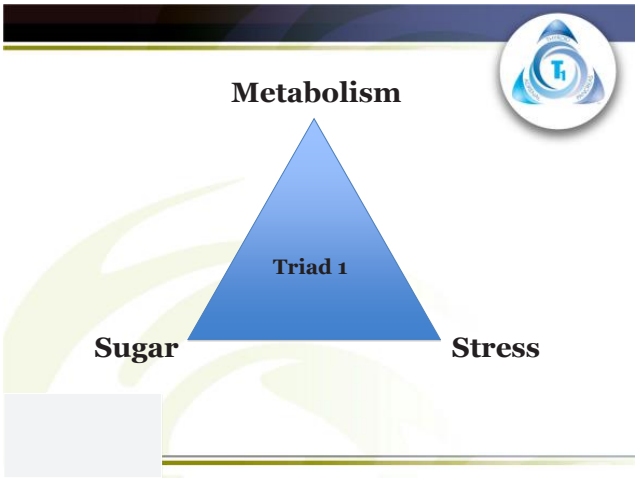
Adrenals-Thyroid-Pancreas

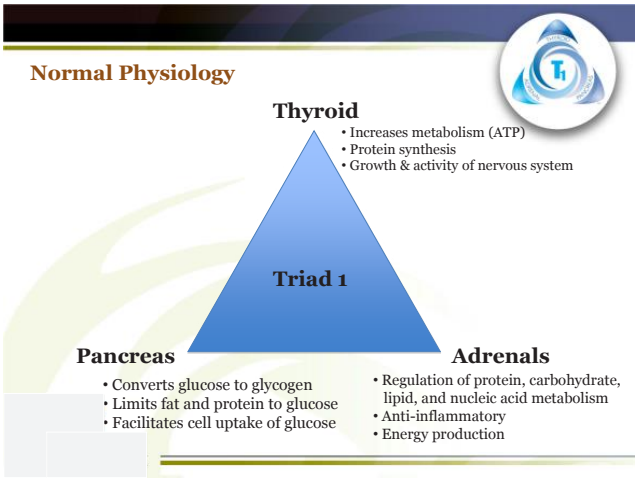
- Energy production and circulation
- Stress-metabolism-sugar
- Central regulator of physiology
- Normal: Vitality and Wellbeing
- Imbalanced: Fatigue and Obesity

Triad 1: Characteristics

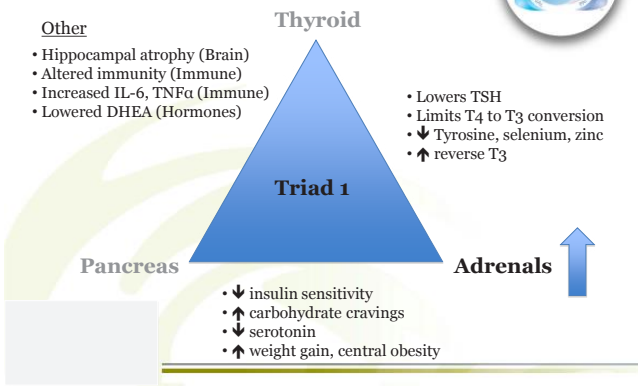
- Balance
- Movement
- Energy
- Rhythmicity
- Vitality
- Spirituality


Thyroid
Triad 1
Pancreas
Adrenals

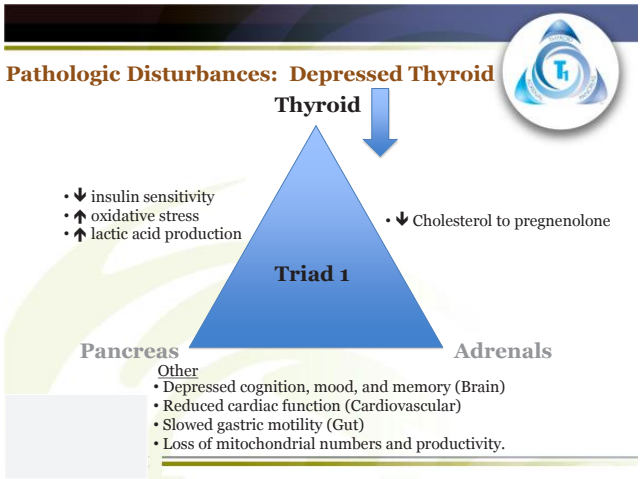

Metabolism
Triad 1
Sugar
Stress


Normal Physiology
Thyroid
• Increases metabolism (ATP)
• Protein synthesis
• Growth & activity of nervous system
Triad 1
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

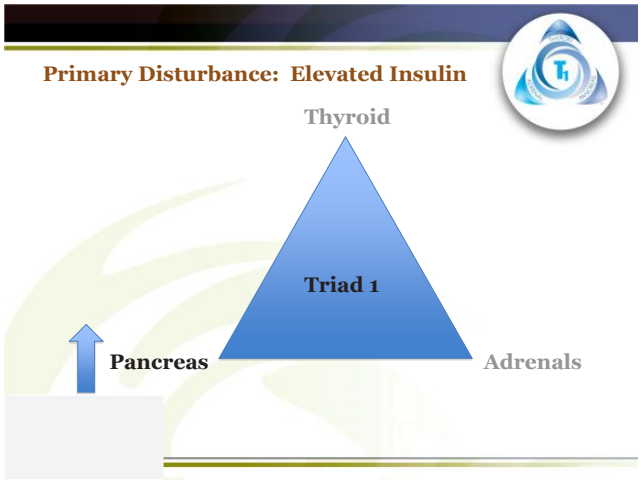
Pathologic Disturbances: Elevated Cortisol



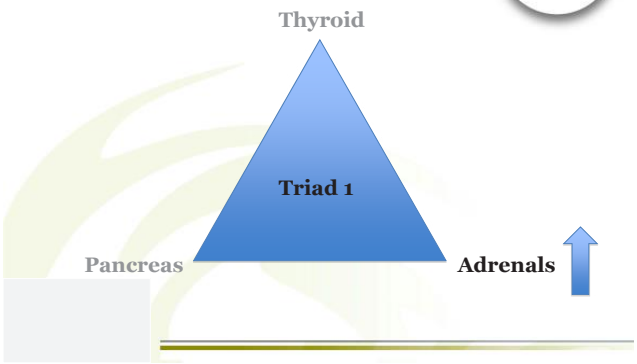
Pathologic Disturbances: Depressed Thyroid



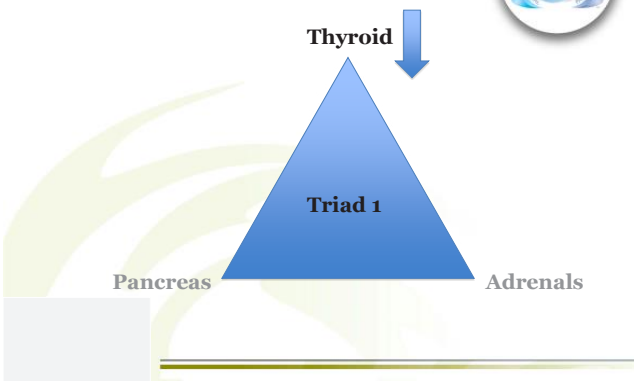
Primary Disturbance: Elevated Insulin



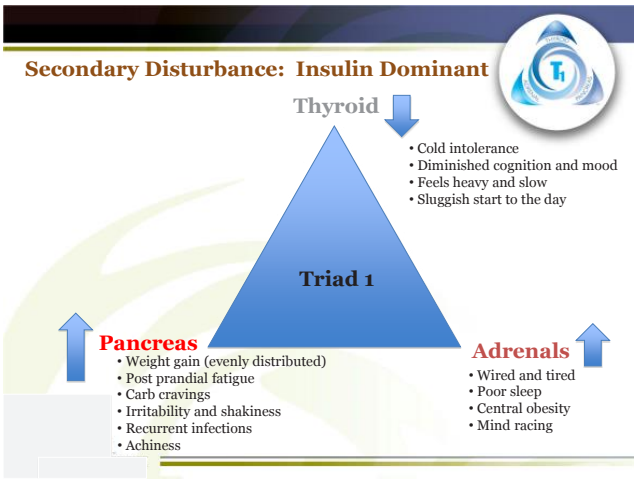
Primary Disturbance: Elevated Cortisol



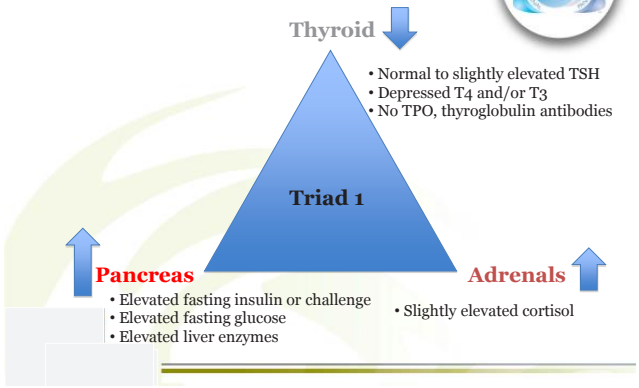
Primary Disturbance: Depressed Thyroid



Secondary Disturbance: Insulin Dominant



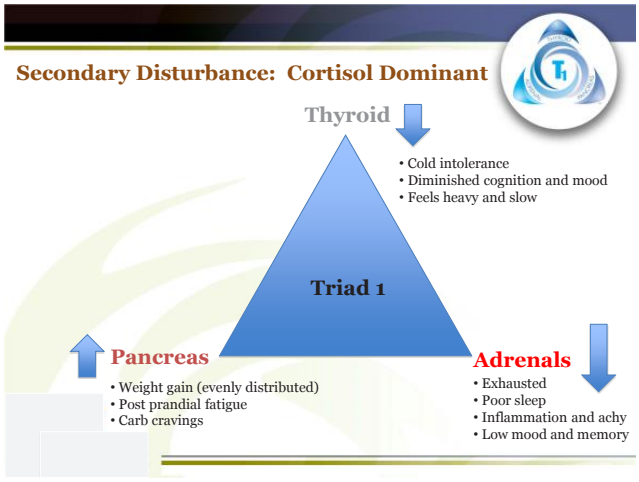
Secondary Disturbance: Insulin Dominant



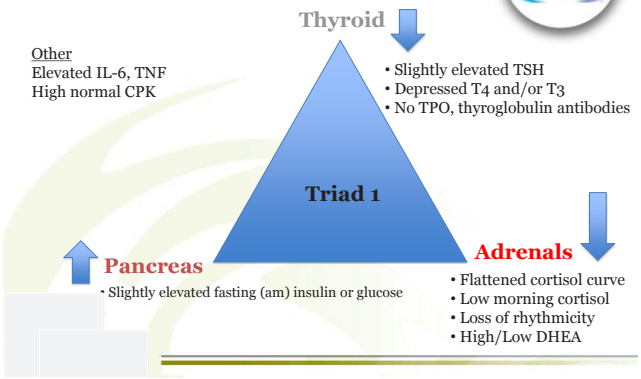
Sue B: Insulin Dominant

- 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



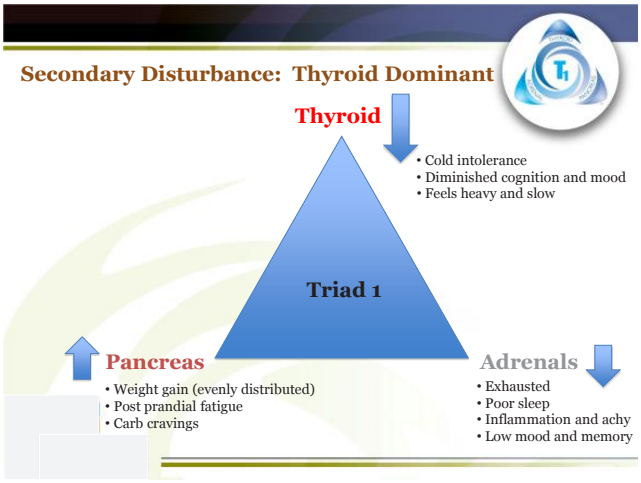
Secondary Disturbance: Cortisol Dominant



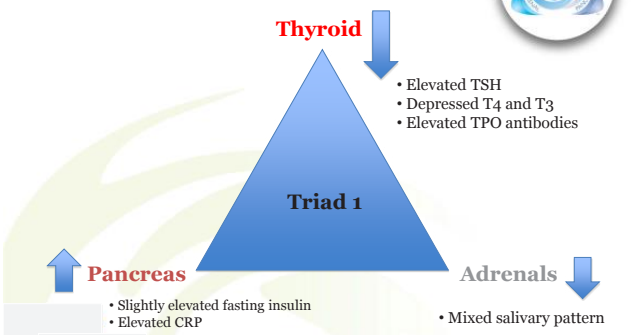
Frank J: Cortisol Dominant

- 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



Secondary Disturbance: Thyroid Dominant



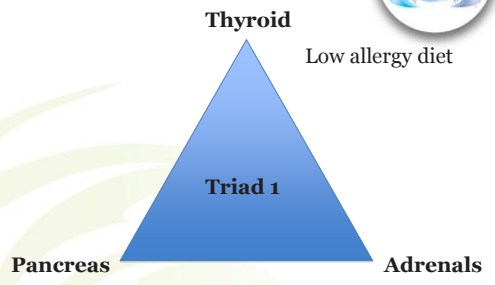
Betty R: Thyroid Dominant

- 52 year old house wife 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

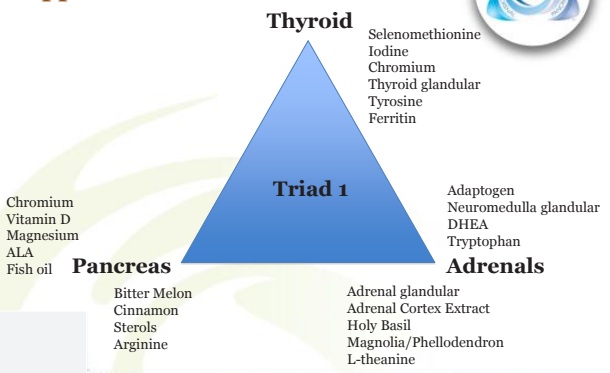


Caveman Diet
Low Glycemic Index diet

Dietary Guidelines

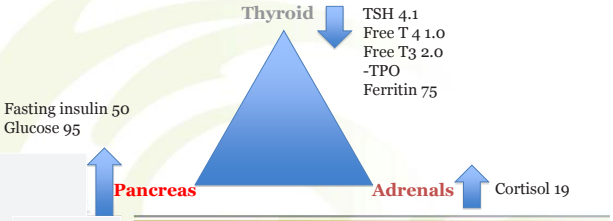
- Caveman Diet
- Modified Caveman Diet with evening carbs
- Low glycemic index diet
- Low glycemic index diet with lower carbohydrate
- Gluten free diet
- Handouts
- Challenges

Supplement Recommendations



Sue B: Insulin Dominant

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



Sue B: Clinical Strategy

- *Break Insulin Resistance*
- Manage Stress Response
- Enhance Thyroid Function

Sue B: Nutrition

Dietary Advice

Evening carb cravings?

yes

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

no

Caveman Diet
No grain/dairy/gluten
Low carbohydrate

Sue B: Insulin Management

FBS>90/⦸IR/↑Cortisol

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:

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

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)

Symptoms?

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

No → Selenomethionine 200 mcg/Iodine 1 mg

*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 x 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

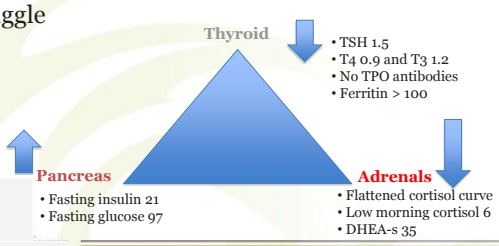
If insulin resistance, cravings and stress then add L-tryptophan 500 mg po TID-QID

Sue B: Summary

Hormone	Supplements
Pancreas	Caveman diet Trace minerals ALA Bitter Melon
Thyroid	Selenomethionine/Iodine Ferritin
Adrenals	Magnolia/Phellodendron Holy Basil L-tryptophan

Frank J: Cortisol dominant

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



Frank J: Clinical Strategy

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

Frank J: Nutrition

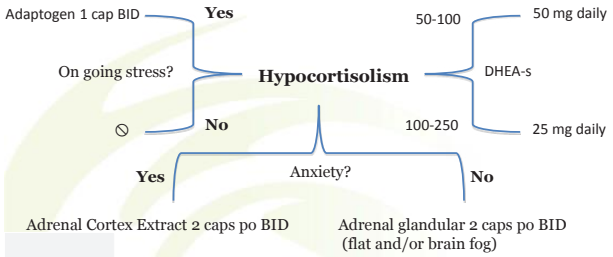
Dietary Advice

yes — Evening carb cravings? — no

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

Caveman Diet
No grain/dairy/gluten

Frank J: Stress Support



Key Concept

If patient reports difficulty sleeping,
add Neuromedulla glandular 2 caps at night
to reactivate 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 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:

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)

Symptoms?

Yes

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

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

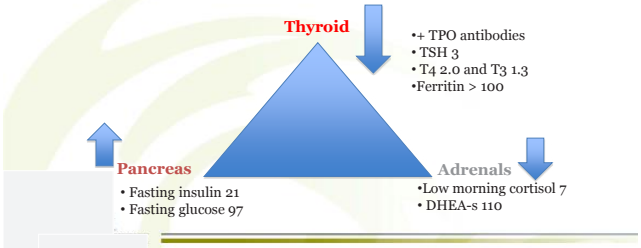
Add tyrosine when adrenals and thyroid are low due to preferential consumption under times of stress

Frank J: Summary

Hormone	Supplements
Pancreas	Caveman diet Trace Minerals and Vitamins
Thyroid	Selenomethionine/Iodine Tyrosine Thyroid USP 15-30 mg
Adrenals	Adrenal glandular Adaptogen Relora Tryptophan DHEA Neuromedulla glandular

Betty R: Thyroid dominant

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



Betty R: Clinical Strategy

- *Treat All Thyroid Abnormalities*
- Manage Growing Insulin Resistance
- Support Stress Response

Betty R: Nutrition

Dietary Advice

Evening carb cravings?

yes

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

no

Low Allergy emphasis
Caveman Diet
No grain/dairy/gluten

Betty R: Thyroid Support

Hypothyroidism

+TPO?

Yes

Selenomethionine 400 mcg/Iodine 1 mg*
Tyrosine 500 – 750 mg BID
Compounded T4/T3 only or…
Synthoid and/or Cytomel

No

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 auto-immune process, seek causative factors: food allergies, heavy metals, chronic infections, stress

Betty R: Thyroid Support

Hypothyroidism

+TPO?

Yes

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

No

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

On going stress?

Hypocortisolism

50-100 — 50 mg daily

DHEA-s

100-250 — 25 mg daily

⦸

No

Yes

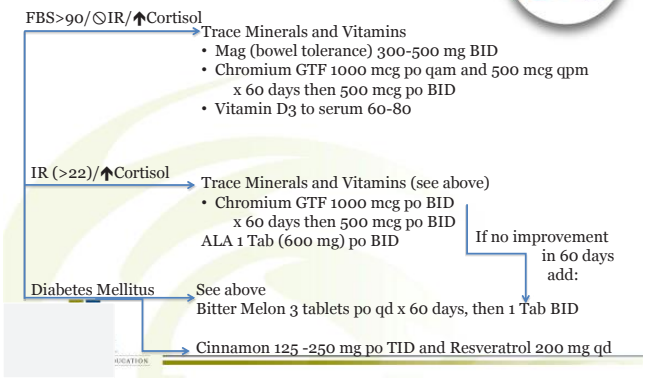
Anxiety?

No

Adrenal Cortex Extract 2 caps po BID

Adrenal gland 2 caps po BID (or brain fog)

Betty R: Insulin Management



Key Concept

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

Betty R: Summary

Hormone	Supplements
Pancreas	Caveman diet Trace Minerals and Vitamins
Thyroid	Selenomethionine/Iodine Tyrosine Sterols Compounded T4/T3
Adrenals	Adrenal glandular Adaptogen Tryptophan DHEA

Notes:

First in Nutritional and Environmental Medicine

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