HPA Axis Dysfunction: Helping Patients with Anxiety, Overwhelm and Fatigue

Nicole Fenske, DC
Five Common Causes of Chronic Disease

- Lack of physical activity
- Poor nutrition (too much sugar)
- Tobacco use
- Excessive alcohol consumption
- Stress
DISEASES

- Diabetes
- Cancer
- Auto-immune diseases
- Heart disease
- Obesity
- Arthritis
- Fibromyalgia

UNDERLYING CAUSES

- Inflammatory imbalances
- Hormonal imbalances
- Detoxification imbalances
- Structural imbalances
- Mitochondrial dysfunction
- Immune imbalances
- Digestive, absorptive, and microbiological imbalances
- Toxic emotions
  (anger, fear, resentment, etc.)
- Toxic chemical exposure
“Understood correctly, the HPA axis is truly one of the few systems that influences and controls, at least in part, nearly every other system in the body. Its influence on circadian regulation alone makes it one of the most powerful genomic regulators of the whole body.”

Thomas G. Guilliams Ph.D.
• Options?
• Individualized care?
• Patient-centered?
• Safe?
• Options?
• Individualized care?
• Patient-centered?
• Safe?
One Cause - One Solution
Limited paradigms – appealing, but effective???

- Antibiotics for chronic infection?
- Acid Blockers for acid reflux?
- SSRI drugs or St. John’s Wort for depression?
- Calcium supplement to prevent osteoporosis?
- Progesterone cream for PMS & perimenopause?
“When inappropriate or overwhelming signals begin to overpower our physiological resilience, the stretching of that system does not immediately resolve. Perhaps the best example of this is the slow progression of impaired glucose tolerance/insulin resistance, which is sometimes referred to as a ‘metabolic continuum’.”

Thomas G. Guilliams, Ph. D.
Our Culture Challenges our Physiological Resilience

Western culture

- High-tech solutions expected
- Quick fix expected
- Nutrient-deficient fast food common
- Preoccupation with youthfulness
- Lack of rest prevalent
- Modern conveniences replace activity
- Overuse of medications
- Treating the symptoms vs. addressing the cause of problems
Lifestyle as Intervention

Remember your chiropractic philosophy!

Thoughts
Trauma
Toxins

Mind the input into your nervous system!
“75% OF AN INDIVIDUAL’S HEALTH AFTER AGE 40 IS DEPENDENT UPON WHAT THE PERSON HAS DONE TO HIS OR HER GENES, NOT TO THE GENES THEMSELVES.”

Address a patient’s concerns with an understanding of the interconnected web of her individual body and the world in which she lives.
Keep in Mind . . . The World in Which She Lives

Peace?
Organic food?
Clean air & water?
People connected with nature?
Healthy ecosystems?
Healthy future for her children & future generations?

Noise & light pollution
EMF, microwave exposure
Polluted water, air
Toxic, devitalized soil & food
Environmental devastation
Urban sprawl
War
And the Web in Which She Lives

Loving family & friends
Connection to community
Caring for others
Safety
Balanced diet & life
Exercise
Sense of purpose
Self-efficacy
Nurturing the spirit
Faith, connection to the divine
Making a difference

OR

Stressful, dysfunctional primary relationships
Addictions
Isolated, fearful, Lonely
Excessive CHO’s
Poor diet
No vegetables
No exercise
Powerless, despair
No connection w/ nature
No connection w/ divine

OR

Healthy diet & life
Engagement in community
Relationships
Feel connected
Personal development
Spiritual practices
Beliefs & values
Living a purposeful life

OR

Stressful, dysfunctional primary relationships
Addictions
Isolated, fearful, Lonely
Excessive CHO’s
Poor diet
No vegetables
No exercise
Powerless, despair
No connection w/ nature
No connection w/ divine
The Interconnected Web of the Body: Foundational Health Factors

- Blood sugar regulation
- Body composition
- Gastrointestinal function
- Detoxification function
- Stress response/resilience
- Rest/relaxation
- Nutritional status
- Exercise
Overview of Presentation

• A functional medicine approach
• What is stress?
• Stress and its implications
• Quick review of HPA axis
• 4 key modifiable stressors
  ✓ Blood sugar imbalance
  ✓ Mental/emotional stress
  ✓ Sleep cycle disturbance
  ✓ Inflammatory imbalance
Overview of Presentation

• Nutritional support for the 4 key stressors
• Laboratory assessment of the HPA axis
• Lifestyle measures to support healthy HPA function
• Tools for the practitioner
• Summary of key points
What is stress?

- Do your patients know what stress truly is?
- If you were to ask a patient what is stress, what would be the most common answer?
  - Both physical and perceived
    - Not just the mental / emotional
- Do they understand the lifestyle contributors to the production of cortisol?
  - 4 key stressors
Fight and Flight
Life.
The autonomic nervous and the endocrine systems on fire.
Life.
The autonomic nervous and the endocrine systems on fire.
Stress in America

- 75-90% of all visits to family physicians are due to stress-related symptoms. [1]
- 43% of adults suffer adverse health effects of stress.
- Stress is linked to the six leading causes of death. [2]


Stress in America

According to the American Institute of Stress, some **44 percent of Americans feel more stressed than they did five years ago**, and **1 in 5 experience extreme stress**. In fact, **the AIS estimates that stress causes 60% of all human illness and disease** and that **3 out of 4 doctor’s visits are for stress-related ailments**. (Stress also costs the nation about $300 billion in medical bills and lost productivity every year.)
Our Leading Health Problem

Neuroscientists have recently clarified “stress” to mean...

“Conditions where an environmental demand exceeds the natural regulatory capacity of an organism, in particular situations that include unpredictability and uncontrollability.”

• Neurosci Biobehav Rev. 2011 Feb 21;35:1291-301.
The Fallout of Stress

Stress can lead or contribute to headaches, GI problems, sleep disorders, weight gain, mood changes, immune distress, memory impairment, addiction, fatigue, heart disease, hormone imbalances and cancer. These problems affect people’s productivity and in turn their success in all aspects of life.
Changes in Physiology and Function Due to Stress

- Poor glucose regulation
- Bone demineralization
- Menstrual cycle irregularities
- Poor wound healing
- Weakened mucosal lining
- Changes in thyroid function
- Increases in cytokines and prostaglandins
- Decrease in neurotransmitter levels
- Sleep cycle disruptions
- Impaired ATP production
- Increased urinary excretion of calcium
- Increased catabolism of amino acids and ligamentous tissues
• Major depression is associated with an increase in proinflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-alpha).

• These cytokines are potent modulators of corticotropin-releasing hormone (CRH), which produces heightened hypothalamic-pituitary-adrenal axis (HPA) activity characterized by increases in ACTH and cortisol.

• *A few minutes of stress may improve immune performance but longer periods of mental stress have detrimental effects that may lead to loss of immune integrity*

The GI System and Chronic Stress

- Cortisol and the proinflammatory cytokines interleukin (IL)-6 (together with its soluble receptor) and IL-8 were elevated in all IBS subgroups (diarrhea predominant, constipated, and alternators).
- Following CRH infusion, an exaggerated release of both ACTH and cortisol was observed in patients with IBS.
- *IBS is characterized by an over activation of the hypothalamic-pituitary-adrenal axis and a proinflammatory cytokine increase.*

Elevated Cortisol and Memory

• Long-term exposure to high endogenous levels of cortisol is associated with memory impairments.
• Results of the Douglas Hospital Longitudinal Study of Normal and Pathological Aging show that increased secretion of cortisol in the older human population is significantly associated with impairment of cognitive function during aging.

Osteoporosis and Chronic Stress

• Higher urinary cortisol (UFC) in persons with depression is associated with lower bone mineral density

• 684 men and women, aged 70 to 79 at baseline were assessed. In multiple adjusted models, higher baseline levels of UFC were significantly associated with incident fractures

• Higher baseline UFC is an independent predictor of future fracture

The Stress Response

Disruptions in homeostasis (i.e., stress) place demands on the body that are primarily met by the activation of **2 systems:**

1. the hypothalamic-pituitary-adrenal (HPA) axis and
2. the sympathetic nervous system (SNS)

Stressor-induced activation of the HPA axis and the SNS results in a series of neural and endocrine adaptations known as the “stress response” or “stress cascade.”
The Stress Response

In the face of an *acute* physical challenge, the body mobilizes the stress response which is central to surviving that challenge.

*Chronic* mobilization of the stress response carries a wide array of pathophysiologic risks.
Stress manifests in the brain chemistry and the centers in the brain that control the response to stress, not in the adrenal gland.
HPA Axis and the Stress Response System

- Stress activates Hypothalamus
- Hypothalamus releases CRF (Corticotropin Releasing Factor)
- CRF stimulates Pituitary
- Pituitary releases ACTH (Adrenocorticotropic Hormone)
- ACTH induces steroidogenesis in the Cortex
- Cortisol is produced by the Cortex
- Cortisol regulates the immune response and metabolism
- CRF = Corticotropin Releasing Factor
- ACTH = Adrenocorticotropic Hormone
- Cortisol actions:
  - Fat & protein mobilization
  - Gluconeogenesis (liver)
  - Normalized blood sugar
  - Prevents inflammation
  - Decreases size of lymphatic tissues

- Adrenal Gland
  - Norepinephrine
  - Epinephrine
What is Cortisol?

- A steroid hormone
- Made in the adrenal cortex so classified as a corticosteroid
- Glucocorticoid class of hormones
Functions of Cortisol

- Stimulates the liver to convert amino acids to glucose
- Stimulates increased glycogen in the liver
- Mobilizes fatty acids into the blood
- Increases coagulation
- Suppresses parts of the inflammatory response
- Prevents the loss of sodium in urine
- Maintains mood and emotional stability
But Prolonged Elevations in Cortisol result in...

- Stimulation of fat deposits
- Increases in blood pressure
- Increases in protein breakdown
- Demineralization of bone
- Suppression of the immune system
- Memory loss
- Depression
- Increases in blood sugar
Symptoms of Elevated Cortisol

- Irritability/anxiety or...fatigue/low energy
- Night sweats/muscular tremors
- Poor sleep/sleep disturbance/hot flashes
- Increased susceptibility to infection
- Shakiness between meals/sugar cravings
- Weight gain (around the middle)
Symptoms of Depressed Cortisol

- Fatigue, apathy, unmotivated
- Absent-minded/poor concentration
- Increased sleep but poor quality
- Increased susceptibility to inflammation and allergies (not infections)
- Depression
- Early onset perimenopause or menopause
- Muscle pains
Acute Physical Experiences, Elevated Cortisol and Hormones


- During acute stressful experiences, cortisol significantly increased, and remained significantly elevated at recovery.
- Testosterone was significantly reduced within 12 hours of the event.
- Total and free T4 and total and free T3 were reduced, TSH was increased.
Conditions shown to be associated with depressed HPA axis and depressed cortisol:

- Atypical depression
- Seasonal affective disorder (SAD)
- Postpartum depression
- Panic attacks/generalized anxiety disorder
- Bipolar II disorder
- PTSD
- Chronic Fatigue Syndrome
- Fibromyalgia
What is Epinephrine and Norepinephrine?

Epinephrine / adrenaline is primarily a hormone

Epinephrine / adrenaline is extra confusing because of its "sister molecule" norepinephrine / noradrenaline, which is primarily a neurotransmitter

Epinephrine / adrenaline is released by the adrenal gland into the bloodstream as a hormone whereas norepinephrine / noradrenaline is released by neurons in the brain as a neurotransmitter

Norepinephrine is also released as a hormone by the adrenal glands. What is released is 80% epinephrine and 20% norepinephrine.

Paul King, Computational Neuroscientist, Redwood Center for Theoretical Neuroscience
Epinephrine (adrenaline) prolongs and intensifies effects of the SNS:

- Causes the pupils of the eyes to dilate
- Increases the heart rate, force of contraction, and blood pressure
- Constricts the blood vessels of nonessential organs such as the skin
- Dilates blood vessels to increase blood flow to organs involved in exercise or fighting off danger, skeletal muscles, cardiac muscle, liver, and adipose tissue
Epinephrine (adrenaline) prolongs and intensifies effects of the SNS:

• Increases the rate and depth of breathing and dilates the bronchioles to allow faster movement of air in and out of the lungs
• Raises blood sugar as liver glycogen is converted to glucose
• Slows down or even stops processes that are not essential for meeting the stress situation, such as muscular movements of the gastrointestinal tract and digestive secretions
What is DHEA?

- Dehydroepiandrosterone (DHEA) is a steroid hormone produced in the adrenal glands (cortex), gonads and the brain.
- Leads to the production of androgens and estrogens.
- Levels decrease after age 30 and decrease more quickly in women.
- It has a short half-life and is usually converted to dehydroepiandrosterone sulfate.
What is DHEA?

• Lower levels are found in people with hormonal disorders, HIV/AIDS, Alzheimer's disease, heart disease, depression, diabetes, inflammation, immune disorders, and osteoporosis.

• Corticosteroids, birth control taken by mouth, and agents that treat psychiatric disorders may reduce DHEA levels.
Functions of DHEA

• A precursor for testosterone and estrogen.
• Reverses immune suppression caused by excess cortisol levels.
• Stimulates bone deposition and remodeling.
• LOWERS total cholesterol and LDL levels.
• Increases muscle mass.
Functions of DHEA

- Involved in conversion T4 to T3
- Accelerates recovery from acute stress
- Reverses many of the unfavorable effects of excess cortisol

The Big Picture: Hans Selye’s General Adaptation Syndrome

Stage 1: “Arousal”
– Both cortisol and DHEA increase with episodic stress, but recovery occurs to baseline
– This may be asymptomatic

Stage 2: “Adaptation”
– Cortisol chronically elevated, but DHEA declines
– “Stressed,” anxiety attacks, mood swings, depression

State 3: “Exhaustion”
– Adrenal insufficiency / low cortisol and DHEA
– Depression and fatigued
Rapid increases in catecholamines (adrenaline) with a concurrent but slower increase of corticosteroids
The Adaptation Stage is...

Characterized by sustained increased levels of corticosteroids and alarm molecules with consequent alterations long term in glucose tolerance, blood pressure, thyroid and sex hormone metabolism, etc.
The Exhaustion stage is . . .

– Characterized by the diminution of corticosteroids over time and the continued advance of many degenerative diseases.
– From a laboratory standpoint we may see:
  • Depressed cortisol over two to four time points
  • Depressed cortisol sum
  • Depressed DHEA
So in this model:

- With stress you get initial arousal and cortisol elevations.
- Long term you often get adaptation with elevated cortisol and depressed DHEA.
- With prolonged stress, you may get depressed OR elevated cortisol and depressed DHEA.

…the problem is, people don’t always respond the same way to stress, and symptoms are not always a differentiator.
A word of caution . . .

It is now recognized that Selye simplified a very complex system and that this model can be limiting. It is a starting point for understanding the stress response and the three stage model of stress adaptation we will discuss later in this presentation.
Multiple Set Points:

It appears the HPA axis has the capability of resetting itself at high or low cortisol values.
The HPA Axis Switch: Going from High to Low Cortisol Secretors

• It is hypothesized that in situations of initial elevated cortisol (and depression) a severe or prolonged stressor (e.g. viral illness) can “throw a switch” in the HPA Axis.
• This may lead to chronically re-set low cortisol levels such as are seen in PTSD, CFIDS, and fibromyalgia.

“The weight of current evidence supports the presence of the following factors related to hypothalamic-pituitary-adrenal (HPA) axis dysfunction in patients with chronic fatigue syndrome (CFS): mild hypocortisolism; attenuated diurnal variation of cortisol; enhanced negative feedback to the HPA axis; and blunted HPA axis responsiveness.”

“. . . many of the stress-induced changes in metabolic function are mediated by changes in gene-regulation triggered by glucocorticoids. These genomic changes are influenced by a person’s genetics, but are also greatly modified by many other lifestyle factors, which can modulate the eventual cellular changes influenced by cortisol.”

Thomas G. Guilliams, Ph.D.
“The challenge for today’s clinician is in assessing the status of and individual’s stress response system and relating that status to the individual’s clinical presentation. Ultimately, the goal is to discover the root cause(s) of the imbalance related to the stress response, helping patients regain their physiological balance, while slowing or reversing the chronic manifestations caused by stress.”

Thomas G. Guilliams Ph.D.
We need a model that organizes the modifiable categories of HPA axis stress to help us make this challenge manageable.

4 Key Stressors Model
4 Key Stressors

**Mental/Emotional**
- Anxiety
- Depression
- PTSD
- Fear, worry
- Restless mind

**Sleep Cycle Disturbances**
- Not sleeping enough hours
- Unable to fall into a deep sleep
- Difficulty falling asleep
- Inconsistent sleep schedule
- Shift work issues

**Blood Sugar Imbalances**
- Elevated blood sugar
- Hypoglycemia
- Increased oxidative stress (decreased antioxidant reserve)
- Abdominal obesity
- Metabolic syndrome
- Hyperlipidemia
- Hypertension

**Inflammation**
- Musculoskeletal: back, joint pain
- GI: dysbiosis, Crohn’s disease, diverticulitis
- Dermatological: eczema, psoriasis
- Auto-immune: MS, lupus, rheumatoid arthritis
- Immunological: food allergies, chronic infections
4 Key Stressors: Mental and Emotional Stress

• Some life events are universally painful like the death of a loved one.

• However many of the daily stressors one encounters can be controlled if you can perceive it differently or reframe it.

• One’s perception of an event is what creates stress – often more than the event itself.
Mental and Emotional Stress

- Gather a list of therapists and life coaches to share with your patients.
- Some patients may have clergy to whom they can turn.
Mental and Emotional Stress

- Depression
- Anxiety
- Irritation
- Inability to focus
- Addiction
- Eating disorders
- OCD
- PTSD
Mental and Emotional Stress

- Elevated adrenaline can cause anxiety and restlessness.
- Elevated cortisol can affect mood and memory.
What makes an event “stressful”?

• New
• Unpredictable
• Sense of threat (physical or emotional)
• Loss of control
Minimizing Mental and Emotional Stress

• Be aware of your stress level so you know when to ‘take a breather’
• Use stress management techniques
• Nutritional support (diet, supplements)
• Physical activity
Awareness of Stress Level

- Journaling
- Take time to do a stress inventory
Stress Management Techniques

• Journaling
• Cognitive behavior therapy (CBT helps you become aware of inaccurate or negative thinking so you can view challenging situations more clearly and respond to them in a more effective way)
• Simplify
• Say no, reorder priorities
• Don’t seek perfection
• Schedule down time
• Reduce exposure to electronic media
• Limit sugar, caffeine and alcohol
• Nourish loving and joyful relationships
• Reconnect with purpose, mission, and joy
Stress Management Techniques

- Do things you enjoy
- Avoid isolation, reach out
- Foam rolling [https://www.youtube.com/watch?v=sJwh1_RhYWY](https://www.youtube.com/watch?v=sJwh1_RhYWY)
- Exercise
- Spend time in nature
- Gratitude, compassion
- Laugh often
- 12-step groups
- Centering practice: meditation, prayer, relaxing music
Meditation and Stress Reduction

Research done by Sara Lazar, a neuroscientist at Massachusetts General Hospital and Harvard Medical School found differences in brain volume after eight weeks of meditation.

In the meditation group there was thickening in four brain regions:

1. The posterior cingulate, which is involved in mind wandering, and self relevance

2. The left hippocampus, which assists in learning, cognition, memory and emotional regulation

3. The temporo parietal junction, associated with perspective taking, empathy and compassion

4. The Pons, where a lot of regulatory neurotransmitters are produced
Meditation and Stress Reduction

- The amygdala is the fight or flight part of the brain which is important for anxiety, fear and stress in general. That area got smaller in the group that went through the mindfulness-based stress reduction program.
- The change in the amygdala was also correlated to a reduction in stress levels.
- In her study, the average was 27 minutes a day. Or about a half hour a day.
- There isn’t good data yet about how much someone needs to practice in order to benefit.
- Anecdotal comments from students suggest that 10 minutes a day could have some subjective benefit.
“Regular moderate physical activity, especially in the form of routine exercise, improves many of the metabolic signals that drive the HPA axis, primarily by promoting tighter control on blood glucose levels and reducing inflammatory signaling. . . . Realizing that the benefit of regular exercise is both physical and psychological, there are increased benefits along the scale form sedentary behavior to athletic fitness.”

Thomas G. Guilliams, Ph.D.
Healthy Relationships
Elevated Cortisol and Depression

• The HPA-axis is hyperactive in depression, due to genetic factors or to ‘stimuli’ that may occur during early development or adult life.

• Additionally, rat studies have shown that these high levels of cumulative corticosteroid exposure have long term effects by inducing neuronal damage that selectively affects hippocampal structure.

Hypercortisolemia has been attributed to a breakdown in glucocorticoid receptor-mediated negative feedback mechanisms within the HPA axis, and may be central to the pathogenesis of depressive symptoms.

Elevated Cortisol and Depression

• Data was collected in 2002-2004 on almost three thousand participants living in London.
• Salivary cortisol was assessed on waking, 30 minutes later, and four times throughout the day and evening.
• Salivary cortisol averaged over the day was inversely associated with positive affect (after controlling for other variables).

Norepinephrine

- Alertness
- Concentration
- Energy
GABA and Serotonin

• GABA and serotonin are released to help counter-act stress
• Chronic stress can lead to depletion of these and other neurotransmitters
Dopamine

- Pleasure/reward
- Motivation and drive
- Interest in life
- Focus and memory
Natural Therapies to Restore Mental and Emotional Balance

Maintaining the right amounts of cortisol and DHEA as well as ample amounts of Serotonin and GABA are important steps in maintaining a positive and relaxed mental outlook.
Supplements to Support Mental/Emotional Health

(see slides at end of presentation for more info/doses)

- Pharma GABA
- Phosphatidylserine
- 5HTP
- Taurine
- L-theanine
- L-tyrosine
- Inositol
- Calcium/Magnesium
- 5-MTHF, B6, C, Zn

- Combination products are available
Supplements to Support Mental/Emotional Health
(see slides at end of presentation for more info/doses)

• Mucuna pruriens
• Rhodiola rosea
• Eleuthero
• Ashwaghanda
• Valerian root
• Passionflower
• Wild Jujube extract
• Hops
• German chamomile
• Schizandra berry
• Combination products are available
4 Key Stressors: Blood Sugar Imbalance

"STRESSED" is "DESSERTS" spelled backwards
The diagram illustrates the relationship between stress, circadian disruption, glycemic dysregulation, and inflammatory signals. It highlights factors contributing to stress, such as lack of control, burnout, relationships, and sleep issues. Circadian disruption factors include shift work, jet lag, and daylight savings. Glycemic dysregulation is influenced by poor diet choices, high GI meals, insulin resistance, and stress eating. Inflammatory signals involve low physical activity, obesity, and conditions like arthritis, cardiovascular disease, allergies, and infectious diseases. The diagram emphasizes the interconnectedness of these factors in maintaining overall health.
Key Point

A healthy adrenal response requires **blood sugar control.**
Blood sugar regulation is one of the keys to health. Focus on this and many other health challenges will be addressed and many diseases will be prevented.
How do blood sugar imbalances affect the adrenals?

The body, in an attempt to normalize blood sugar, initiates a counter-regulatory process during which the adrenals are stimulated to secrete increased levels of cortisol.

When insulin is high and glucagon is low, the adrenals are called upon to produce excess cortisol as a back-up response to help raise blood sugar in the absence of adequate glucagon. This occurs at the expense of the adrenal glands.
General Summary of the Influences of Blood Sugar Regulation

- Adrenal function
- Balance of sex steroid hormones
- **Balance of neurotransmitters**
- Energy production and utilization
- Detoxification
- Gastrointestinal function
- Libido
- Risk of breast cancer, cardiovascular disease and osteoporosis
Key Point:

Dysglycemia occurs along a spectrum and even mild dysglycemia can profoundly influence hormonal health!
**Spectrum of dysglycemia**

• Moderate dysglycemia causing:
  • Fatigue, mood disorders, abdominal weight gain, and SX of sex steroid and androgen dysregulation

• Insulin resistance causing, in addition:
  • Very significant abdominal weight gain, dysfunctional uterine bleeding, hirsuitism, PCOS, increased risk of cancer, cardiovascular disease, and early degenerative changes

• Type II diabetes
Selected Symptoms of Blood Sugar Dysregulation

- Fatigue or shakiness, especially energy highs and lows
- Sugar cravings
- “I just don’t get energy out of my food”
- Rapid weight gain, especially abdominal
- Patient’s body fat disproportionate to caloric intake and exercise
- History of gestational diabetes
Selected Symptoms of Blood Sugar Dysregulation

• Alzheimer’s

• A study recently published in the journal *Neurology* showed that people with diabetes are twice as likely to develop dementia as people with normal blood sugar levels
Laboratory Assessment

- Moderate dysglycemia
  - May see very little abnormal lab findings

- Insulin resistance (full-blown or borderline)
  - Normal or mildly elevated fasting serum glucose
  - Normal, borderline, or elevated Hemoglobin A1C
  - Triglyceride/ HDL ratio approaching or exceeding 5
  - Serum insulin: fasting > 15 (< 6 healthy)
  - Waist:hip ratio > .9 women, >1.0 men (appearance of pregnancy)

- Type II diabetes
  - Elevated fasting serum glucose of 126 or higher (95 and below healthy)
  - Elevated hemoglobin A1C of 6.5 or higher (5/7 and below healthy)
• Evidence suggests that progressive dysfunction of the HPA axis, with elevated levels of circulating cortisol, is implicated in the development of visceral obesity.
• Central adiposity is likely, at least in part, an effect of increased cortisol secretion.

Fat, Sick, and Tired

High Blood Sugar: ↑ Fat Storage  ↑ Mood swings  ↑ Insulin

Normal Blood Sugar Levels

Low Blood Sugar: ↑ Cravings  ↑ Fatigue  ↑ Cortisol

http://completewellbeing.com/static/img/articles/2011/12/graph-
Vicious Cycle

Eat high carb foods $\rightarrow$ insulin production $\rightarrow$ decrease blood glucose $\rightarrow$ cortisol production to produce more glucose $\rightarrow$ repeat over and over $\rightarrow$ HPA axis stress
Taxing the System

- Cortisol is naturally high in the morning
  - Insulin Sensitivity is low
    - Less efficient at processing sugar

**Figure 1** shows the effect of high-glycemic meals, skipping meals or going longer than three to four hours between meals, which causes stress on the HPA axis and a cortisol-induced response.
Dysglycemia Lifestyle Recommendations

- Exercise
- Sleep
- Stress management
- Eat a macronutrient-balanced diet
Macronutrient Balancing
(balancing fats, carbs and proteins)

Unbalanced Breakfast
Balanced Breakfast
Macronutrient Balancing

Balanced Lunch

Unbalanced Lunch
Macronutrient Balancing

Balanced Dinner

Unbalanced Dinner
Rules of Thumb for Blood Sugar Balance

• Avoid refined carbohydrates and simple sugars
• Avoid processed foods (most contain added sugar)
• Eat protein at every meal
• Eat lots of fiber (fruits, veggies, nuts, seeds, beans)
• Eat healthy fats
• Avoid liquid sugar
• "Eat food, not too much, mostly plants."  Michael Pollan
“When given the choice between sugar and healthy food, the rats pushed the healthy food away because they wanted nothing but sugar. When the rats were given a choice between plain water and sugar water, they chose the sugar water. Taking the sugar water away caused the rats to experience withdrawal symptoms”.

Study from Princeton University
Problem

Sugar addiction is socially acceptable and sugar is everywhere.
Sugar Woes

- The average American now consumes 22 to 28 teaspoons of added sugars a day – mostly high-fructose corn syrup and table sugar. That’s 350 to 440 empty calories that few of us can afford.
- A 12 oz. can of soda has about 10 teaspoons of sugars (roughly half fructose and half glucose)
- The AHA recommends that children consume no more than 3 teaspoons of sugar a day.
- Preschoolers consume an average of 10-12 tsp/day.
Sugar Woes

• Kellogg’s Original All-Bran contains 1.5 tsp of sugar in ½ cup.
• Honey Roasted Honey Bunches of Oats contains 3.5 tsp of sugar in 2/3 cup.
• Kashi GoLean Crunch contains 3.5 tsp in 1 cup.
Why Do We Care?

- Juvenile delinquency
- Anxiety
- Hyperactivity
- Inability to concentrate
- Irritability
- Learning disorders
- Depression
Mood

- Our brain’s biochemistry depends on what we eat. Or don’t eat. Neurotransmitters are built upon nutrients, particularly amino acids (protein building blocks) and B-complex vitamins. Even our genes depend on nutrients to work properly.

- When our blood sugar falls and we crash, ancient parts of our brain light up. We become aggressive, irritable, impatient. Eating a sugary or starchy food solves the problem quickly, but starts a new up-and-down blood sugar cycle.
Supplements to Support Blood Sugar Balance
(see slides at end of presentation for more info/doses)

- Biotin
- Alpha Lipoic Acid
- Chromium
- Cinnamon Bark Extract (Cinnulin)
- Vanadyl Sulfate Hydrate
- Berberine
- Water-soluble fibers
- Combination products are available
4 Key Stressors: Sleep Disturbance
Sleep

• Sleep is the body’s way of metabolically and psychologically resetting itself.
• Sleep helps the body readjust to the stress placed upon it each day.
• Many repair processes occur during the deep, slow-wave stages of sleep.
• “Helping patients understand how to manage their daytime activities to ensure the proper quantity and quality of regular sleep they experience, is one of the most...”

Thomas G. Guilliams, Ph.D.
“Helping patients understand how to manage their daytime activities to ensure the proper quantity and quality of regular sleep they experience, is one of the most powerful ‘therapies’ available for reducing HPA axis dysfunction.”

Thomas G. Guilliams Ph.D.
Sleep

- The pituitary gland secretes growth hormone primarily at night, which is essential for maintaining strength, muscle mass and liver function, normalizing blood sugar, and keeping the immune system healthy.
- Serotonin, dopamine and norepinephrine are synthesized during deep stages of sleep.
Sleep

• Sleep functions as an “antioxidant” for the brain because free radicals are removed during the sleep cycle.
Sleep

• Poor sleep can dampen immune defenses, change the body’s response to hunger hormones, increase risk of diabetes/obesity/CVD.

• Sleep deprivation can result in an overproduction of cortisol and epinephrine which affects stress, anxiety, blood sugar, heart rate and blood pressure.
Sleep

Shift work has been linked to an increased risk for cancer, autoimmune diseases, metabolic-inflammatory disorders (e.g., CVD, diabetes, obesity) and moods disorders.
Improving the Sleep Cycle

• Restore more natural sleep / waking habits (i.e. wake and sleep with the sun)
• No “fugitive” light at night
• Walk or be outdoors daily, with daily sun exposure, glasses off (especially in the morning)
Improving the Sleep Cycle

- Maintain a consistent sleep schedule
- Aim for 7-8 hours
- Aim to be in bed before 10 pm
- Minimize naps
- Avoid caffeine late in the day
- Limit alcohol
- Dim lights and minimize electronics and hour before bed
Improving the Sleep Cycle

- Keep the bedroom cool (65-67 degrees)
- Invest in a quality mattress and pillow
- Exercise regularly
- Do relaxing activities before bed
- Turn off wireless at night
- Meditation
A Silicon-valley engineer turned technology health advocate, Jeromy Johnson discusses our attachment to technology and the health hazards such an addiction may hold.

16 minutes well-spent.
What is Causing the Disturbance?

- Stress?
- Pain?
- Restless legs?
- Neurotransmitter imbalances?
- Hormonal imbalances (cortisol, melatonin)?
Supplements to Support Sleep
(see slides at end of presentation for more info/doses)

- 5HTP
- PharmaGABA
- L-theanine
- Calcium/magnesium
- Phosphatidylserine
- Valerian root
- Passionflower
- Wild jujube extract
- German chamomile
- Hops
- Melatonin
- Combination products available
Sleep Deprivation and Elevated Cortisol

Chronic sleep deprivation:
• increases evening cortisol levels
• Increases insulin and blood glucose
• decreases parasympathetic and increases sympathetic tone
• increases appetite and energy expenditure
• increases levels of proinflammatory cytokines
• increases blood pressure

4 Key Stressors: Inflammation

Inflammation in the body not only manifests as pain and disease, it also sends signals to the HPA axis to send cortisol to the rescue to help the inflammation. This creates a vicious cycle for both the stress-response and immune systems.
Inflammation

• Part of our body’s normal immune response
• Normal for short periods of time
• The body’s first line of defense against infection and trauma
Inflammation

• Inflammatory proteins are destructive for a reason.

• When it becomes the body’s “way of life” then it is a problem.

• These proteins can start to attack healthy tissue.
Inflammation

• It can be quite overt like Rheumatoid Arthritis or a “silent killer” as it is with cardiovascular disease.

• Most common health problems have an inflammatory component, such as joint pain, heart disease, thyroiditis, autoimmune conditions, cancer, GI problems, skin conditions, dementia, Fibromyalgia.
A wide range of triggers (whether it’s Candida Albicans, E. Coli, food or a cut) set off the same inflammatory pathways. And you can treat this inflammation from these various triggers with the same interventions, like fish oil, while looking for the root cause.
Signs of Chronic Inflammation and Disease Processes

- Skin: psoriasis and eczema
- Bowels: IBD, Celiac
- Nervous system: Alzheimer’s, MS
- Joints: Rheumatoid arthritis
- Respiratory system: Allergies/asthma
- Cardiovascular system: Atherosclerosis
- Cancer
- Diabetes
Triggers for Inflammation

- Infections
- Trauma and injury
- Toxins
- Blood sugar dysregulation (insulin)
- Antigens
- Certain foods
- Stress
Triggers for Inflammation

• Obesity – fat tissue produces pro-inflammatory molecules
• A diet high in refined carbohydrates, low in “good” fats and high in “bad” fats
• Nutrient deficiencies, including vitamin D
• Sleep deprivation
• Gastrointestinal problems
• Food allergens/sensitivities
To inflame your body, try this.
Chronic Inflammation: How and Why?

- Genetic susceptibility to triggers
- Overabundance of inflammatory precursors (glycating diet)
- Lack of antioxidant phytochemicals
- Insufficient dampening or excessive upregulation by endogenous mediators
- Malfunctioning “off switch”
  - Inadequate priming of T regulatory cells
  - Imbalanced Th1/Th2 lymphocytes
Nutrients for Modulating the Inflammatory Response

Essential Fatty Acids

- Gamma-linolenic Acid (GLA) belongs to the Omega-6 family, but has an almost identical structure to Alpha-linolenic Acid (Omega-3)
- May help to displace Arachidonic Acid from membrane phospholipids
- Studies have indicated that Omega-3 fatty acids and GLA are effective anti-inflammatory agents.
- Enhancement of Omega-3 status improves pain tolerance

Arachidonic acid found in meat, diary, poultry, and shellfish is a precursor to inflammatory PGE2.

- Omega-3s, particularly EPA/DHA found in cold-water fish, are precursors to anti-inflammatory series-3 eicosaanoids.
- EPA blocks metabolism of AA by inhibiting delta 5 desaturase.

- A lower ratio of omega-6 to omega-3 lowers enzyme competition (delta 6 desaturase) and reduces shunting to AA.
- Zinc, magnesium, ascorbate, niacin, and pyridoxine are coenzymes for desaturase metabolism of omega-3 PUFAs.
- Trans fatty acids increase inflammation by various mechanisms.

**Summary:**

Fatty Acids and Inflammation
Most chronic diseases have been linked to excessive or persistent inflammation.

Chronic inflammation occurs when the injury is ongoing or a predisposed immune system fails at counter-regulation.

Conventional pharmacological treatment focuses on specific pathways, and often on the downstream consequences of inflammation.
Key Concepts in Inflammation

• Inflammatory diseases are not distinct entities - they are inseparable from the context in which they developed.
• The respiratory and GI mucosa are the single biggest sources of fuel (triggers) for chronic inflammation mediated through the MALT (mucosal associated lymphoid tissue).
• Botanical & nutritional therapies can act as biological response modifiers that dampen the inflammatory cascade without contributing to additional pathology.
Top 11 List for Decreasing Chronic Inflammation:

1. Restrict dietary arachidonic acid (AA) intake through meat, dairy, poultry, shellfish. Choose grass-fed.
2. Increase and/or supplement omega-3s, particularly EPA/DHA in cold-water fish. (Omega 3s increase series-3 eicosanoids, and block metabolism of AA by inhibiting delta 5 desaturase).
3. Target a lower ratio of omega-6 to omega-3 by limiting intake of plant-source omega-6 PUFAs, thus lowering enzyme competition (delta 6 desaturase) and reducing shunting to AA.
4. Ensure adequate intake of zinc, magnesium, ascorbate, niacin, and pyridoxine (coenzymes for desaturase metabolism of omega-3 PUFAs).
5. Increase dietary antioxidants/phytonutrients by increasing intake of deeply pigmented fruits and vegetables, thereby reducing oxidative biosynthesis of inflammatory eicosanoids and isoprostanes.

6. Eliminate hydrogenated/partially hydrogenated and trans-fatty acids, alcohol, simple sugars, and refined carbohydrates, which are inhibitors of desaturase enzymes.

7. Optimize blood glucose regulation and address hyperinsulinemia as excess insulin shifts dihomogammalinolenic (DGLA) acid toward PGE2 synthesis.

Top 11 List for Decreasing Chronic Inflammation:
Top 11 List for Decreasing Chronic Inflammation

8. Maintain GI health.
9. Get enough sleep.
10. Improve body composition (fat cells produce inflammatory compounds).
11. Avoid toxin exposure.
Inflammation Summary

• Treat the CAUSE of the inflammation (see Top 11 List).

• In the meantime, if you need to treat the inflammation, use a natural substance.

• Use antiinflammatory medications sparingly as they can cause kidney, liver and GI damage as well as slow down joint repair.
Supplements to Treat Inflammation
(see slides at end of presentation for more info/doses)

- Vitamin D3
- Omega 3 essential fatty acids (4,000 mg/day of combined EPA and DHA)
- Curcumin
- Ginger
- Skullcap root
- Quercetin
- Green tea leaf extract
- Bromelain
- Combination products available
Ginger and Turmeric

- Have long been used in East Indian medicine for a variety of both acute and chronic inflammatory conditions.
- Studies have demonstrated significant anti-inflammatory and antioxidant activities for both ginger and turmeric.
- Studies suggest that both herbs may block cyclooxygenase and lipoxygenase activity thereby inhibiting inflammatory prostaglandin and leukotriene release.


Bioflavonoids

– Quercetin, a flavonoid of high biological activity, is an effective inhibitor of lipoxygenase.

– Quercetin also prevents the overproduction of tumor necrosis factor-alpha, and nitric oxide, which can induce several pathophysiological conditions during acute and chronic inflammation.


– Derived from plant and animal sources
– Anti-inflammatory effect centers around acute injuries, post-surgery and degenerative joint conditions
– Can invoke a significant reduction in pain and inflammation and faster recovery rates compared with a placebo

Hormonal Dysfunction and Inflammation

Inflammation alters the adrenal response, results in an alteration of the HPA stress response causing inappropriately low cortisol secretion in relation to ACTH secretion (e.g., RA) and lowers DHEA-sulfate as shown in patients with chronic inflammatory diseases.

Laboratory Assessment of the HPA Axis
Does “Adrenal Fatigue” Exist?

• Low cortisol/DHEA is often related to chronic stress.
• This most likely reflects HPA axis down-regulation to protect tissues form excess cortisol.
• This has little to do with the capacity of the adrenal glands to produce hormones.
• While we often refer to “testing the adrenals”, it is more accurate to say we are assessing the status of the HPA axis using adrenal hormone measurements as surrogate markers.
Does “Adrenal Fatigue” Exist?

- This term is not used in the peer-reviewed literature.
- True adrenal insufficiency will require hydrocortisone replacement therapy (i.e. Addison’s disease).
- More appropriate terms are used later in this talk we discuss the three stages of stress adaptation.
Labs to Assess Function: Who Should We Test?

- Fatigue
- Insomnia (most common causes are high cortisol, low progesterone, low melatonin)
- Depression (responds well to neurotransmitter support, adrenal support and decreasing inflammation)
- Hypothyroidism
- Perimenopause/menopause (hot flashes, low libido)
Laboratory Assessment of the HPA Axis

- Cortisol can be measured in serum, urine, saliva, hair and fingernails.
- Serum cortisol represents both bound and free cortisol concentrations.
- **Salivary free cortisol measurements are the best and most easily sampled surrogate marker for the glucocorticoid action (serum free cortisol) available to most target tissues.**
Laboratory Assessment of the HPA Axis

- When comparing lab results always use the same lab as methodological variances can result in differences in reported values.
Laboratory Assessment of the HPA Axis

- One of the most important features of the HPA Axis is its circadian rhythm, resulting in a predictable diurnal cortisol secretion pattern.

- The most important measurements are the first morning cortisol and the last sample prior to bedtime.
Cortisol Rhythm

The graph shows the cortisol rhythm over different stages and times of the day. It indicates the normal diurnal range and the cortisol levels at specific times:

- **Stage 1**: Highest cortisol levels in the morning (7-9 am) with a peak of 30 nM cortisol. The levels gradually decrease throughout the day.
- **Stage 2**: Moderate cortisol levels with a peak of 16 nM cortisol in the morning. The levels decrease to 13 nM by the afternoon and rise again in the evening.
- **Stage 3**: Lowest cortisol levels, with a peak of 3 nM in the morning. The levels decrease to 1 nM by the afternoon and remain low throughout the evening.

The graph illustrates the typical diurnal pattern of cortisol levels, with peak levels in the morning and a decrease throughout the day.
Laboratory Assessment of the HPA Axis

- Note that significant elevations in salivary cortisol follows moderate to intense exercise, peaking near the end of a session and resolving over the following one to two hours.
Cortisol awakening response (CAR) is one of the most distinctive features of the 24-hour circadian rhythm of cortisol secretion. This is the predictable increase of cortisol that occurs in the morning, just after awakening. This is the highest peak of cortisol of the day.
**Cortisol Awakening Response**

- **“Flip flop” switching of regional brain activation associated with the attainment of consciousness.**
- **Attainment of full alertness associated with restoration of full cerebral blood flow to cortical areas.**

- **Rising cortisol levels are blunted in comparison to rising ACTH levels due to reduced adrenal sensitivity to ACTH controlled by direct signals from SCN.**

- **The CAR: dynamic increase in cortisol post awakening.**

- Dynamic increase as a result of:
  1. Flip flop switching of regional brain activation
  2. HPA axis activation
  3. Release of reduced adrenal sensitivity to ACTH
  4. Enhanced adrenal sensitivity to ACTH in the presence of light, via an extra-pituitary neural pathway from the SCN.
Laboratory Assessment of the HPA Axis

- Cortisol awakening response (CAR) is influenced by a person’s anticipation of stress.
- A lower cortisol response to awakening is seen in subjects with a high amount of psychosocial burnout, chronic fatigue and PTSD, while it is higher in those with ongoing job-related and perceived stress.
Laboratory Assessment of the HPA Axis

- In those experiencing high work stress, the CAR is higher on workdays than weekends.
- General depression disorders often result in a higher CAR, but those with SAD have a lower CAR, though only in the winter months.
- CAR is significantly elevated during ovulation.
Laboratory Assessment
CAR – Key Point

- The use of the CAR alone or with a diurnal pattern is the best single biomarker for a “snapshot” assessment of the HPA axis.

- To capture CAR, collect the first sample 30-40 minutes after waking.
Laboratory Assessment Instructions

- To measure the CAR, collect the morning sample strictly between 30-40 minutes after waking and restrict activity at this time to simple morning tasks like showering and dressing. Do not brush teeth, eat or exercise.

- Test on a typical day (for example on a typical work day not a weekend).
Laboratory Assessment
Instructions

- If the patient has an unusually stressful day, they can rinse out the tubes and repeat on the next normal day.
- Wake up on the testing day at the usual time and manner.
- Record when morning light comes into the room in order to match sunlight access on subsequent follow-up tests (light increases morning cortisol).
Patients who work second or third shift should collect saliva samples “mid-week” during their normal work week at their normal waking time, shifting subsequent sample collections accordingly.
Laboratory Assessment
DHEA/DHEA-S

- Test first thing in the morning
- Collect passive drool. Do not use chemical stimulants or chewing methods to avoid contamination with gingival fluids or serum.
- Ask the lab to report an age and sex-specific reference range
Exogenous corticosteroids such as prednisone inhibit cortisol production.

Clinicians should ask about previous corticosteroid use in all subjects with a flattened hypocortisol salivary profile.

The HPA axis may normalize after corticosteroid-induced adrenal insufficiency using slow withdrawal of treatment over 9-12 months.
Cushing’s Disease

Cushings disease (CD) is caused by an ACTH-secreting pituitary adenoma leading to a chronic overproduction of cortisol, and has an incidence of 13 cases per million people annually.
Cushing’s Disease

Common signs and symptoms involve progressive obesity and skin changes, such as:

- Weight gain and fatty tissue deposits, particularly around the midsection and upper back, in the face (moon face), and between the shoulders (buffalo hump)
- Pink or purple stretch marks (striae) on the skin of the abdomen, thighs, breasts and arms
- Thinning, fragile skin that bruises easily
- Slow healing of cuts, insect bites and infections
- Acne
Cushing’s Disease

Women with Cushing syndrome may experience:
• Thicker or more visible body and facial hair (hirsutism)
• Irregular or absent menstrual periods

Men with Cushing syndrome may experience:
• Decreased libido
• Decreased fertility
• Erectile dysfunction
Addison's disease is a disorder that occurs when your body produces insufficient amounts of certain hormones produced by your adrenal glands. In Addison's disease, your adrenal glands produce too little cortisol and often insufficient levels of aldosterone as well.
Addison’s Disease

- Extreme fatigue
- Weight loss and decreased appetite
- Darkening of your skin (hyperpigmentation)
- Low blood pressure, even fainting
- Salt craving
- Low blood sugar (hypoglycemia)
- Nausea, diarrhea or vomiting
- Abdominal pain
- Muscle or joint pains
- Irritability
- Depression
- Body hair loss or sexual dysfunction in women
Addison’s Disease

Refer to a medical doctor if a patient’s salivary cortisol level are way out of range and the patient exhibits any of these symptoms. We do not treat Addison’s or Cushing’s disease.
Stage 1
Acute HPA Axis Activation

• AKA “Adrenal Stress” or “Alarm” or “Fight or Flight”
• Characterized by increase in cortisol (total cortisol sum in high, at least one cortisol is high)
• DHEA is borderline low, low or normal
Stage 1
Supplemental Strategies

- B complex
- Magnesium
- Phosphatidyl serine (lowers cortisol)
- Ashwagandha
- Skullcap Root Extract
- Eleuthero Root Extract
- Rhodiola rosea Root Extract
- L-Theanine
- Combination products are available
Stage 2
Stress Maladaptation

• AKA “Adrenal Fatigue” or “Resistance”
• Characterized by low DHEA relative to cortisol, irregular cortisol rhythm
• DHEA is borderline low or low
• Cortisol sum is normal
• AM, noon or afternoon cortisols are low or borderline low
Stage 2
Supplemental Strategies

• Vitamins B5 (pantothenic acid), B6 and B12
• Vitamin C
• Ashwagandha
• Eleuthero Root Extract
• Rhodiola rosea Root Extract
• Schisandra Berry Extract
• Licorice Root Extract
• DHEA (need to measure in saliva first to make sure it is low, need to monitor)
• Combination products are available
Stage 3
HPA Axis Down-regulation

• AKA “Adrenal Exhaustion”
• Characterized by low DHEA and low cortisol
Stage 3
Supplemental Strategies

- Vitamins B5 (pantothenic acid), B6 and B12
- Vitamin C
- Adrenal glandular concentrate
- Eleuthero Root Extract
- Rhodiola rosea Root Extract
- Schisandra Berry Extract
- Licorice Root Extract
- DHEA (need to measure in saliva first to make sure it is low, need to monitor)
- Combination products are available
A Word of Caution

• The three-stage model is a common way to explain HPA axis progression.
• The body is complex, these phases are fluid and we do not all fit nicely into these three phases.
• We cannot neatly place patients in these stages.
• Clinicians should rely upon all of their diagnostic and history-taking skills, in addition to lab findings, to assess the status and function of the HPA axis.
But there’s good news . . .

With a few exceptions, the core therapies designed to improve HPA axis function will be fundamentally similar in most patients and independent of their “stage” of HPA axis progression.
And let’s not forget the thyroid…Symptoms of thyroid dysfunction may mimic HPA dysfunction.
Assessment of Thyroid Function

BRIEFLY…

• History, examination, palpation
• Free T3, Free T4, rT3, TSH, antithyroid antibodies
• Remember, thyroid is considered a “sentinel” gland for environmental sensing. Therefore, thoroughly assess for need for heavy metal and general detoxification program. Also, thoroughly evaluate for food sensitivities; suspect gluten.
Therapeutic Strategies for HPT Hypofunction: Diet and Lifestyle

- Same as for HPA
- Avoid food sensitivities, especially grains containing gliadin
- Minimize toxic exposure
Therapeutic Strategies for HPT Hypofunction: Nutritional Supplementation

- Detoxification support
- Iodine (or seaweed)
- L-Tyrosine
- Selenium (with caution)
- Vitamins A, E and D
- Zinc
Women in Midlife and HPA Axis Dysfunction

A bit of a tangent . . .
HPA Dysfunction and Menopause

• HPA axis has a profound effect on the menopausal transition

• Should be at optimal function during perimenopause and menopause in order to support:
  – Non-ovarian estrogen and testosterone
  – And of course, general well-being, neuroendocrine health, mental, cardiovascular health, as well a bone integrity
Key Indications of HPA Dysfunction in the Peri/menopausal Woman

- Hot flashes
- Abdominal weight gain
- Insomnia
- Reduced ability to manufacture non-ovarian progesterone and estrogen
- Fatigue
- Impaired temperature regulation (↑ or ↓)
  - (cold extremities, cold core temp. hot flashes)
Dysglycemia, estrogen dominance, and HPA hyperactivation produce overlapping and very similar symptom complexes, with interwoven causes.
Enhancers of Estrogen Production in Body Fat

• Anything that increases insulin
  — Excess carbohydrates of any kind, especially refined
  — or inadequate protein and/or fats relative to carbohydrates
  — extended exposure to artificial light after sunset

• Anything that increases stress hormone production
  — Stress, caffeine, skipping meals, inadequate sleep, too much sugar
For the majority of women, the causes of most hormone challenges are overlapping and interwoven, and stem from NON-Hormonal causes.
Key Perimenopausal Foundational Health Issues

- Blood sugar regulation
- HPA axis function
- Sleep support
- Detoxification function
- Gastrointestinal function
- Status of vitamin, mineral and essential fatty acids
- Exercise
- Body composition
Key Point

Women handle stress differently than men do!
We propose that behaviorally, females’ responses are more marked by a pattern of ‘tend and befriend.’ Tending involves nurturant activities designed to protect the self and offspring that promote safety and reduce distress; befriending is the creation and maintenance of social networks that may aid in this process. “...neuroendocrine evidence from animal and human studies suggests that oxytocin, in conjunction with female reproductive hormones and opioid peptide mechanisms, may be at its core. This previously unexplored stress regulatory system has manifold implications for the study of stress.”
Facilitating Lifestyle Change...

• It’s not enough to simply give patients recommendations without educating them regarding implementation.
• In fact, this can simply add to a patient’s stress.
• *The more recommendations you give without instruction, the more stressful and ineffective your care becomes.*
Stress Recovery Program Tools

• Questionnaire about the 4 key stressors

• Handouts that explain HPA axis dysfunction

• Handouts/handbook that explains the 4 key stressors and offers overviews of supplements and lifestyle strategies
Supplement Information and Dosages
5-Hydroxytryptophan (5-HTP)
(Sleep and M/E Stress)

- Amino acid that converts into serotonin
- Serotonin levels are connected to regulating stress sensitivity and decreases pain sensitivity
- Promotes a positive mood, decreases anxiety
- Helps regulate appetite
- Serotonin deficiency linked to aggression

- 50-400 mg/day. Higher dose often used to help with sleep and severely compromised mood
L-Taurine
(M/E Stress)

- Amino acid found in the brain and has brain-protective properties
- Calms by binding to GABA receptors and activating glycine receptors in the brain
- 100-1000 mg/day
PharmaGABA
(Sleep, M/E Stress)

- Natural form of GABA, found to promote a relaxed and effortless state of focus by increasing alpha waves and decreasing beta waves in the brain.
- An important counterpart to the excitatory activities of glutamate.
- 100-400 mg/day
L-theanine
(Sleep, M/E Stress)

- Amino acid naturally found in green tea; increases serotonin and dopamine production
- Increases attention and promotes relaxation by increasing alpha wave activity
- 100-400 mg/day
L-tyrosine
(M/E Stress)

- Converts to dopamine which brightens mood, supports memory and fights addiction
- Supports thyroid function
- 200-2000 mg/day
Magnesium
(Sleep, M/E Stress, Blood Sugar)

- “Nature’s tranquilizer”
- Relaxes muscles, calms the mind
- Reduces anxiety and increases production of calming neurotransmitters such as serotonin
- Modulates glutamate
- Improves insulin and glucose metabolism.

100-800 mg/day
Melatonin
(sleep)

- Used for insomnia and to reset the sleep-wake cycle
- 1-3 mg before bed
5-MTHF
(5-methyltetrahydrofolate)
(M/E Stress)

- Bioactive form of folate. Works with B12 as methyl donor, which increases serotonin and melatonin production
- Deficiency can cause neurological, cognitive and psychiatric dysfunction
- 400 mcg - 1mg/day
Inositol
(M/E Stress, Blood Sugar)

- B vitamin that is an important component of cell membrane signaling. Helps release neurotransmitters from within nerve cells.
- A deficiency can cause anxiety and depression.
- Reduces insulin resistance.
- 1000-12,000 mg/day
Calcium
(Sleep)

- Aids in the release of melatonin from the pineal gland resulting in deeper stage of sleep.
- 200-1000 mg/day
Phosphatidyl Serine
(Sleep)

- Phospholipid found in the brain.
- Supports brain health.
- Lowers elevated cortisol levels that can contribute to frequent waking by interfering with slow wave sleep.
- Works four hours after you take it (i.e. take it at 6 PM to reduce cortisol at 10 PM).

- 100-800 mg/day
The term “adaptogen” describes plants that support the resistance phase of stress response and promote recovery from stress.

Common adaptogens: eleuthero, schisandra, rhodiola, ashwagandha

Rarely used in isolation, often used in mixes
Eleuthero

(*Eleutherococcus senticosus*)

(M/E Stress)

- Shown to improve mental performance during stressful conditions.
Schizandra berry 
(M/E Stress)

- Used for centuries in China and Russia to support stress response and mental clarity.
- Supports overall brain function, including learning and memory.
- Shown to increase concentrations of nitric oxide resulting in increased blood flow.
Rhodiola rosea
(M/E Stress)

- Supports mood, memory and mental performance
- Decreases anxiety
Ashwagandha
(*Withania somnifera*)
(M/E Stress)

- Shown to decrease symptoms of chronic stress, including anxiety and depression.
Licorice Root Extract
(Fatigue)

- Contains glycyrrhhetic acid and glycyrrhizin
- Blocks the enzyme responsible for the conversion to cortisol the inactive cortisone so helps to maintain cortisol levels
- Avoid using with high cortisol and those with high blood pressure
Mucuna pruriens
(M/E Stress)

- Naturally contains L-dopa, the precursor to dopamine.
Valerian root
(*Valeriana officinalis*)
(Sleep, M/E Stress)

- Components of valerian (including valerenic acid) relax muscles and promote relaxation by stimulating the release of GABA in the CNS and binding to GABA receptors.
Passionflower extract
(Passiflora incarnata)
(Sleep, M/E Stress)

- Decreases anxiety by interacting with GABA receptors.
- Eases feelings of overstimulation and scattered thoughts.
Wild Jujube Extract  
(Ziziphus jujube)  
(Sleep, M/E Stress)

- Calms and promotes sleep.
- Great for fighting nervous exhaustion, fatigue, irritability and insomnia.
Hops
(\textit{Humulus lupulus})
(Sleep, M/E Stress)

- Mild sedative often used for anxiety, nervousness and insomnia.
German chamomile
(Matricaria chamomilla)
(Sleep, M/E Stress)

- Decreases anxiety and has been shown to have a mild sedative effect.
Adrenal Concentrate
(Fatigue)

- The concept of glandular therapy states that similar organ extracts from animals will support the same organ within humans by stimulating its activity.
Alpha Lipoic Acid
(Blood Sugar)

- Potent antioxidant shown to improve blood sugar metabolism and increase insulin sensitivity.
- Shown to improve diabetic neuropathy.
- 300-600 mg/day
Biotin
(Blood Sugar)

- B vitamin that stimulates glucose-induced insulin secretion, enhances insulin sensitivity and accelerated glucose metabolism in the liver and pancreas.
- 1000-6000 mcg/day
Chromium
(Blood Sugar)

- Helps maintain normal glucose levels by facilitating the uptake of glucose into cells, increasing insulin sensitivity and decreasing blood lipids.
- 200-800 mcg/day
Vanadyl Sulfate
(Blood Sugar)

- Mineral that mimics the action of insulin.
- Increases insulin sensitivity, increases transport of glucose into cells.
- Decreases glucose production.

- 25-50 mg/day
Cinnamon Bark Extract
(Blood Sugar)

- Improves blood sugar levels by increasing insulin sensitivity.
- Supports healthy body composition by increasing lean body mass while reducing body fat.
- Doses vary according to the concentrated extract being used.
Berberine
(Blood Sugar)

- A plant extract found in botanicals such as goldenseal, oregon grape and barberry.
- Helps activate specific proteins that improve insulin sensitivity, and down-regulates genes involved in fat storage, while activating genes involved in burning fat.
- 600-1500 mg/day
Water-Soluble Fibers that Support Blood Sugar Regulation

- **Glucomannan from Konjac root:** Shown to lower fasting glucose levels, LDL cholesterol and triglycerides in diabetic patients.

- **Inulin:** Derived from chicory root, inulin is a fiber that lowers blood sugar levels and triglycerides and promotes beneficial bacteria in the gut.

- **Arabinogalactan:** A fermentable fiber that slows the absorption of glucose into the bloodstream and supports the health of good bacteria.
Water-Soluble Fibers that Support Blood Sugar Regulation

- Flaxseed, ground meal or powder: high in fiber and omega-3 fatty acids which have a balancing effect on blood sugar and lipid levels.
- Psyllium: A rich source of soluble fiber best known as a bulk-forming laxative. Has been shown to lower fasting blood sugar in patients with Type II Diabetes.
Tumeric
(Inflammation)

- Reduces inflammation throughout the body.
- Helps fight depression, reduce adrenal fatigue, and destroy infectious microbes.
- 600-1200 mg/day
Skullcap Root
(Inflammation)

- Chinese herb and potent antioxidant.
- Reduces pro-inflammatory compounds in the body.
- 200-600 mg/day
Green Tea Extract
(Inflammation)

- Reduces free radical damage and histamine release from cells.

- 100-300 mg/day
Quercetin
(Inflammation)

- Flavonoid found in fruits and vegetables which inhibits inflammation and supports the epithelial barrier in the gut.
- Boosts the immune system and reduces allergic reactions.
- 200-600 mg/day
Vitamin D
(M/E Stress, Inflammation)

- Too little has been linked to inflammatory diseases including Lupus, RA, IBS and MS.
- Shows significant anti-inflammatory effect on cells. There's also some evidence that D can lessen the ongoing pain from inflammation.
- 1000 - 10,000 IU/day
Bromelain
(Inflammation)

- Natural protein digesting enzyme from the pineapple plant.
- Helps alleviate pain and swelling.
- 240-500 mg/day
DHEA

- A crucial counterpart to cortisol.
- Provides inflammatory balance and protection to brain tissue in the hippocampus, where excessive cortisol secretion can affect mood regulation and memory.
- Do not supplement if it has not been measured.
Key/Summary Slides for Reference
Five Common Causes of Chronic Disease

• Lack of physical activity
• Poor nutrition (too much sugar)
• Tobacco use
• Excessive alcohol consumption
• Stress
4 Key Stressors

Mental/Emotional
- Anxiety
- Depression
- PTSD
- Fear, worry
- Restless mind

Sleep Cycle Disturbances
- Not sleeping enough hours
- Unable to fall into a deep sleep
- Difficulty falling asleep
- Inconsistent sleep schedule
- Shift work issues

Blood Sugar Imbalances
- Elevated blood sugar
- Hypoglycemia
- Increased oxidative stress
  (decreased antioxidant reserve)
- Abdominal obesity
- Metabolic syndrome
- Hyperlipidemia
- Hypertension

Inflammation
- Musculoskeletal: back, joint pain
- GI: dysbiosis, Crohn’s disease, diverticulitis
- Dermatological: eczema, psoriasis
- Auto-immune: MS, lupus, rheumatoid arthritis
- Immunological: food allergies, chronic infections
Stress Management Techniques

• Journaling
• Cognitive behavior therapy (CBT helps you become aware of inaccurate or negative thinking so you can view challenging situations more clearly and respond to them in a more effective way)
• Simplify
• Say no, reorder priorities
• Don’t seek perfection
• Schedule down time
• Reduce exposure to electronic media
• Limit sugar, caffeine and alcohol
• Nourish loving and joyful relationships
• Reconnect with purpose, mission, and joy
Stress Management Techniques

- Do things you enjoy
- Avoid isolation, reach out
- Foam rolling (https://www.youtube.com/watch?v=sJwh1_RhYWy)
- Exercise
- Spend time in nature
- Gratitude, compassion
- Laugh often
- 12-step groups
- Centering practice: meditation, prayer, relaxing music
Supplements to Support Mental/Emotional Health
(see slides earlier in presentation for more info/doses)

- Pharma GABA
- Phosphatidylserine
- 5HTP
- Taurine
- L-theanine
- L-tyrosine
- Inositol
- Calcium/Magnesium
- 5-MTHF, B6, C, Zn
- Combination products are available
Supplements to Support Mental/Emotional Health

(see slides earlier in presentation for more info/doses)

- Mucuna pruriens
- Rhodiola rosea
- Eleuthero
- Ashwagandha
- Valerian root
- Passionflower
- Wild Jujube extract
- Hops
- German chamomile
- Schizandra berry
- Combination products are available
Blood sugar regulation is one of the keys to health. Focus on this and many other health challenges will be addressed and many diseases will be prevented.
Rules of Thumb for Blood Sugar Balance

• Avoid refined carbohydrates and simple sugars
• Avoid processed foods (most contain added sugar)
• Eat protein at every meal
• Eat lots of fiber (fruits, veggies, nuts, seeds, beans)
• Eat healthy fats
• Avoid liquid sugar
• "Eat food, not too much, mostly plants.“ Michael Pollan
Supplements to Support Blood Sugar Balance
(see slides earlier in presentation for more info/doses)

- Biotin
- Alpha Lipoic Acid
- Chromium
- Cinnamon Bark Extract (Cinnulin)
- Vanadyl Sulfate Hydrate
- Berberine
- Water-soluble fibers
- Combination products are available
Improving the Sleep Cycle

• Restore more natural sleep / waking habits (i.e. wake and sleep with the sun)
• No “fugitive” light at night
• Walk or be outdoors daily, with daily sun exposure, glasses off (especially in the morning)
Improving the Sleep Cycle

• Maintain a consistent sleep schedule
• Aim for 7-8 hours
• Aim to be in bed before 10 pm
• Minimize naps
• Avoid caffeine late in the day
• Limit alcohol
• Dim lights and minimize electronics and hour before bed
Improving the Sleep Cycle

• Keep the bedroom cool (65-67 degrees)
• Invest in a quality mattress and pillow
• Exercise regularly
• Do relaxing activities before bed
• Turn off wireless at night
• Meditation
Supplements to Support Sleep
(see slides earlier in presentation for more info/doses)

- 5HTP
- PharmaGABA
- L-theanine
- Calcium/magnesium
- Phosphatidylserine
- Valerian root
- Passionflower
- Wild jujube extract
- German chamomile
- Hops
- Melatonin
- Combination products available
Triggers for Inflammation

- Infections
- Trauma and injury
- Toxins
- Blood sugar dysregulation (insulin)
- Antigens
- Certain foods
- Stress
Triggers for Inflammation

- Obesity – fat tissue produces pro-inflammatory molecules
- A diet high in refined carbohydrates, low in “good” fats and high in “bad” fats
- Nutrient deficiencies, including vitamin D
- **Sleep deprivation**
- Gastrointestinal problems
- Food allergens/sensitivities
1. Restrict dietary arachidonic acid (AA) intake through meat, dairy, poultry, shellfish. Choose grass-fed.
2. Increase and/or supplement omega-3s, particularly EPA/DHA in cold-water fish. (Omega 3s increase series-3 eicosanoids, and block metabolism of AA by inhibiting delta 5 desaturase).
3. Target a lower ratio of omega-6 to omega-3 by limiting intake of plant-source omega-6 PUFAs, thus lowering enzyme competition (delta 6 desaturase) and reducing shunting to AA.
4. Ensure adequate intake of zinc, magnesium, ascorbate, niacin, and pyridoxine (coenzymes for desaturase metabolism of omega-3 PUFAs).
5. Increase dietary antioxidants/phytonutrients by increasing intake of deeply pigmented fruits and vegetables, thereby reducing oxidative biosynthesis of inflammatory eicosanoids and isoprostanes.
6. Eliminate hydrogenated/partially hydrogenated and trans-fatty acids, alcohol, simple sugars, and refined carbohydrates, which are inhibitors of desaturase enzymes.
7. Optimize blood glucose regulation and address hyperinsulinemia as excess insulin shifts dihomogammalinolenic (DGLA) acid toward PGE2 synthesis.

Top 11 List for Decreasing Chronic Inflammation:
Top 11 List for Decreasing Chronic Inflammation

8. Maintain GI health.
9. Get enough sleep.
10. Improve body composition (fat cells produce inflammatory compounds).
11. Avoid toxin exposure.
Supplements to Treat Inflammation
(see slides earlier in presentation for more info/doses)

- Vitamin D3
- Omega 3 essential fatty acids (4,000 mg/day of combined EPA and DHA)
- Curcumin
- Ginger
- Skullcap root
- Quercetin
- Green tea leaf extract
- Bromelain
- Combination products available
Labs to Assess Function: Who Should We Test?

- Fatigue
- Insomnia (most common causes are high cortisol, low progesterone, low melatonin)
- Depression (responds well to neurotransmitter support, adrenal support and decreasing inflammation)
- Hypothyroidism
- Perimenopause/menopause (hot flashes, low libido)
Stage 1
Acute HPA Axis Activation

• AKA “Adrenal Stress” or “Alarm” or “Fight or Flight”
• Characterized by increase in cortisol (total cortisol sum in high, at least one cortisol is high)
• DHEA is borderline low, low or normal
Stage 1
Supplemental Strategies

- B complex
- Magnesium
- Phosphatidyl serine (lowers cortisol)
- Ashwagandha
- Skullcap Root Extract
- Eleuthero Root Extract
- Rhodiola rosea Root Extract
- L-Theanine
Stage 2 Stress Maladaptation

• AKA “Adrenal Fatigue” or “Resistance”
• Characterized by low DHEA relative to cortisol, irregular cortisol rhythm
• DHEA is borderline low or low
• Cortisol sum is normal
• AM, noon or afternoon cortisols are low or borderline low
Stage 2
Supplemental Strategies

- Vitamins B5 (pantothenic acid), B6 and B12
- Vitamin C
- Ashwagandha
- Eleuthero Root Extract
- Rhodiola rosea Root Extract
- Schisandra Berry Extract
- Licorice Root Extract
- DHEA (need to measure in saliva first to make sure it is low, need to monitor)
Stage 3
HPA Axis Down-regulation

• AKA “Adrenal Exhaustion”
• Characterized by low DHEA and low cortisol
Stage 3
Supplemental Strategies

- Vitamins B5 (pantothenic acid), B6 and B12
- Vitamin C
- Adrenal glandular concentrate
- Eleuthero Root Extract
- Rhodiola rosea Root Extract
- Schisandra Berry Extract
- Licorice Root Extract
- DHEA (need to measure in saliva first to make sure it is low, need to monitor)
Facilitating Lifestyle Change...

• It’s not enough to simply give patients recommendations without educating them regarding implementation.
• In fact, this can simply add to a patient’s stress.
• *The more recommendations you give without instruction, the more stressful and ineffective your care becomes.*
Stress Recovery Program Tools

• Questionnaire about the 4 key stressors

• Handouts that explain HPA axis dysfunction

• Handouts/handbook that explains the 4 key stressors and offers overviews of supplements and lifestyle strategies
Two Simple Questions: Causes and Function

• Does this person need to be rid of something (toxic, allergic, infectious, poor diet, stress)?

• Does this person have some unmet individual need required for optimal function?
Gratitude

• Thomas G. Guilliams, PhD

• Christopher Mote, DO, DC
A Few More Thoughts About Stress... and Our Freedom to Choose

“Between stimulus and response, there is a space. In that space lies our freedom and power to choose our response. In our response lies our growth and our happiness.”

- Stephen Covey,
  The Seven Habits of Highly Effective Families
To cause distress in the body, try this...
...and this...
...and this!
To normalize stress hormones, try this...
Lifestyle as Intervention

Remember your chiropractic philosophy!

Thoughts
Trauma
Toxins

Mind the input into your nervous system!
“Don't be afraid to go out on a limb. That's where the fruit is.”

~ H. Jackson Brown Jr.
Baby Steps
Making Peace with the Stress of Life...
“Security is mostly a superstition. It does not exist in nature, nor do the children of men, as a whole, experience it. Avoiding danger is no safer in the long run than outright exposure. Life is either a daring adventure or nothing.”

- Helen Keller