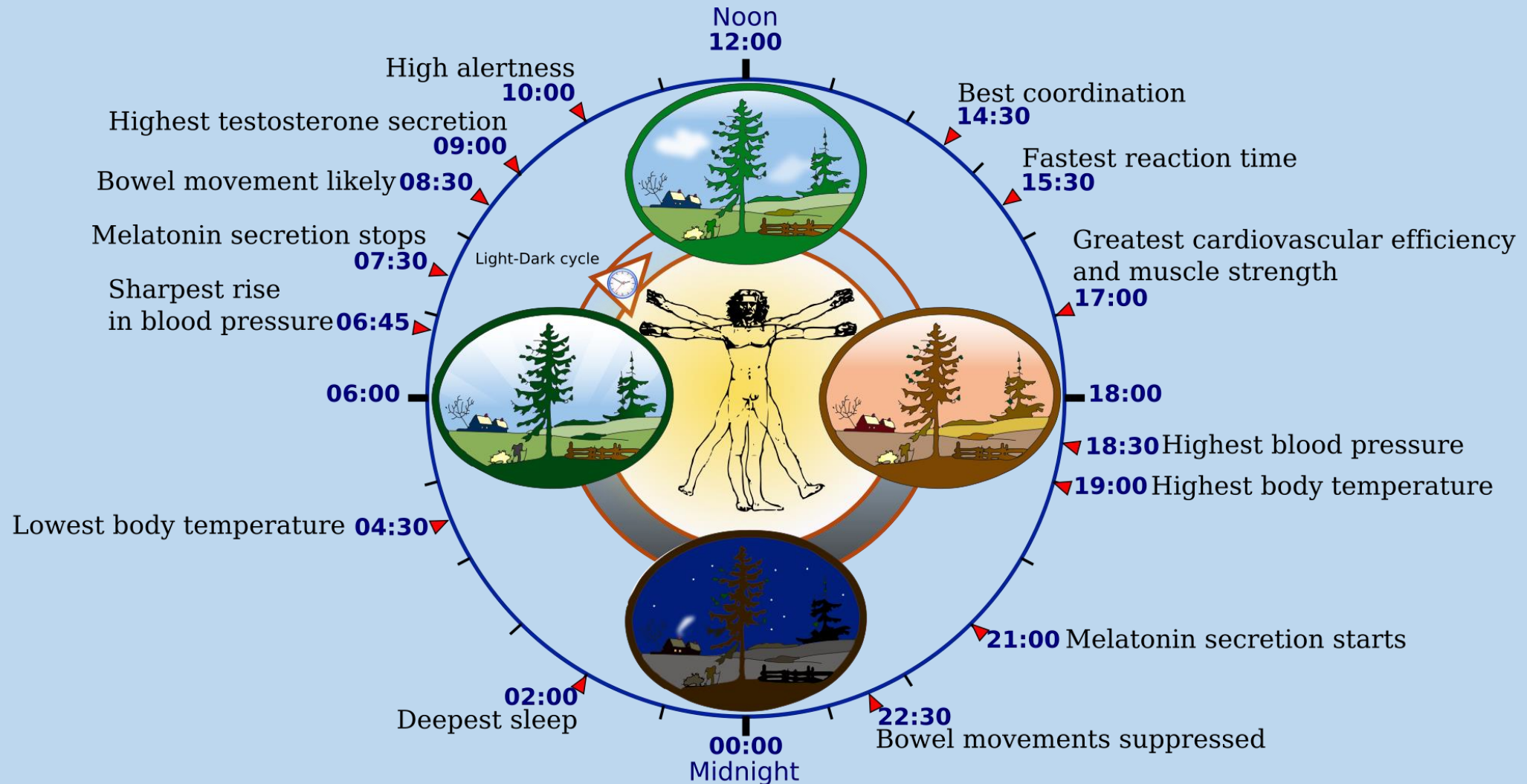


Resetting the 24 Hour Circadian Cycle

Dr Mary Bove



Human Circadian Cycle



NeuroEndocrine System

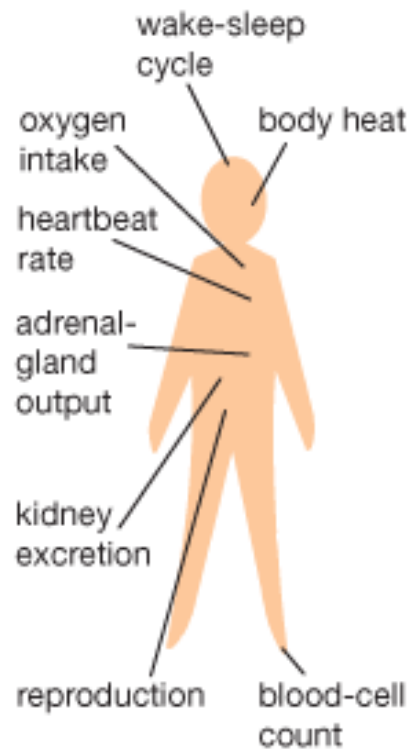
- Control System
- A constant adaptation to internal and external events
- Allostatisis- process of regulation
- Involves both the nervous and endocrine systems
- Dysfunction with in this process contributes strongly to health and wellness in the body

A Network

- Glands communicate via the nervous system to stimulate the release of hormones carrying essential messages to many aspects of the body's physiology
- Hormones regulate metabolism via
 - Controlling the rate of chemical reactions in the cell
 - Facilitating transportation of substances across the cell membrane
 - Promoting activities related to growth and reproduction

Human Biological Rhythms

Some biological rhythms in humans



Wake-sleep cycle

The rhythm of wakefulness and sleep is tied to the daily 24-hour period of the Earth's rotation.

Body heat

The heat of the body varies throughout the day. However, body temperature falls to its lowest point during the very early morning hours.

Oxygen intake

Regulated by a control center in the brain, oxygen intake increases during the body's normal peak hours of activity, even in the absence of activity.

Heartbeat rate

The heartbeat rate, about 70 beats per minute, dips somewhat between the evening and early morning hours.

Adrenal-gland output

The secretion of cortisone and other adrenal hormones involved in metabolism is low during sleeping hours but increases before waking to ready the body for normal activity.

Kidney excretion

Sodium, potassium, and other metabolic wastes are usually removed from the blood by the kidneys during the afternoon hours.

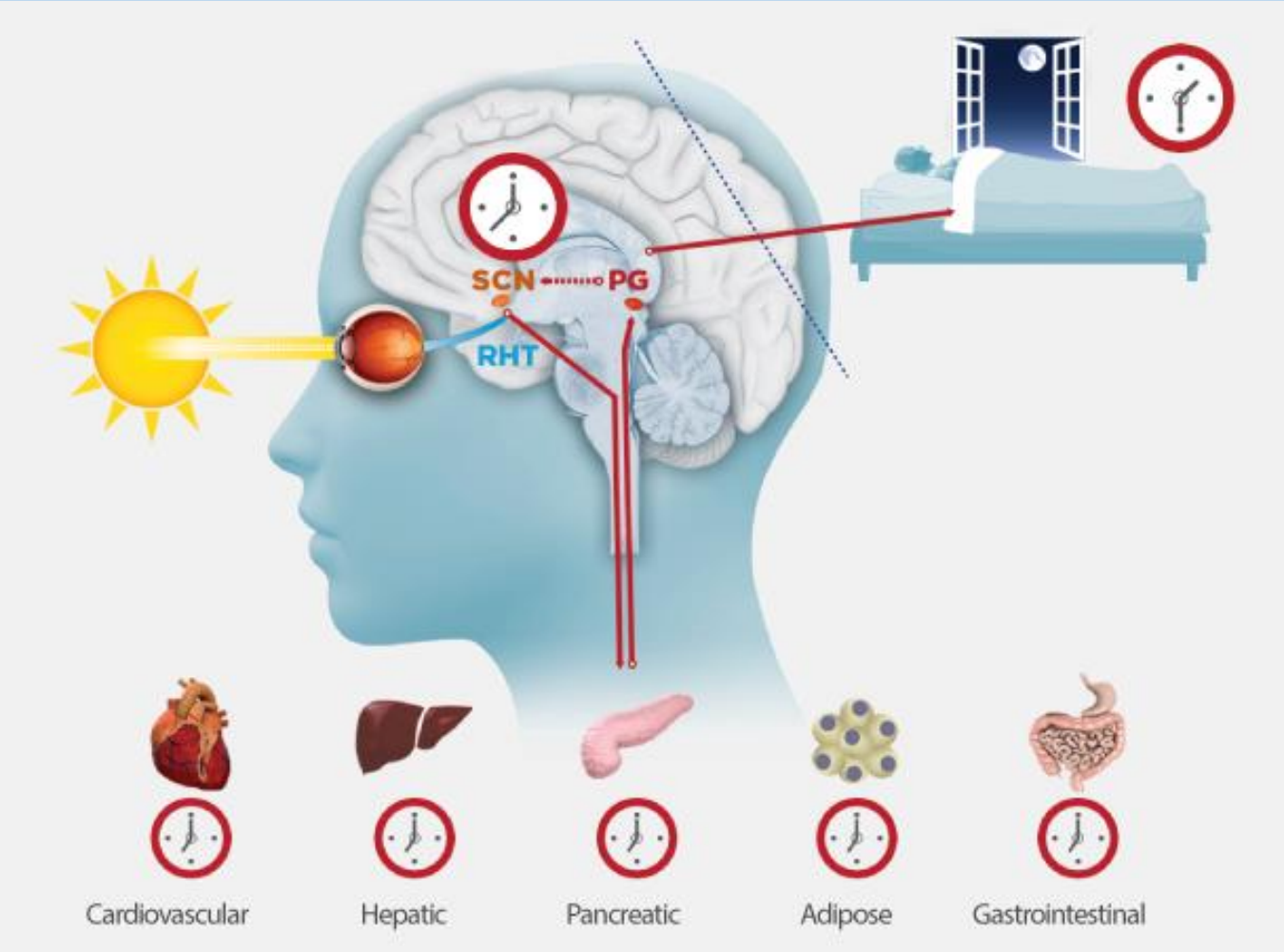
Blood-cell count

White blood cells called eosinophils are most numerous during the early morning hours when most other rhythms are at their lowest levels. Thus the eosinophil rhythm is out of phase with the body's typical activity rhythms.

Reproduction

The reproductive cycle is not a daily rhythm. Eggs are released from the ovaries of the female about once every 28 days, in phase with the lunar cycle.

CIRCADIAN RHYTHMS Effect all Organs and Systems



<https://www.non-24pro.com/physiology-of-non-24.php>

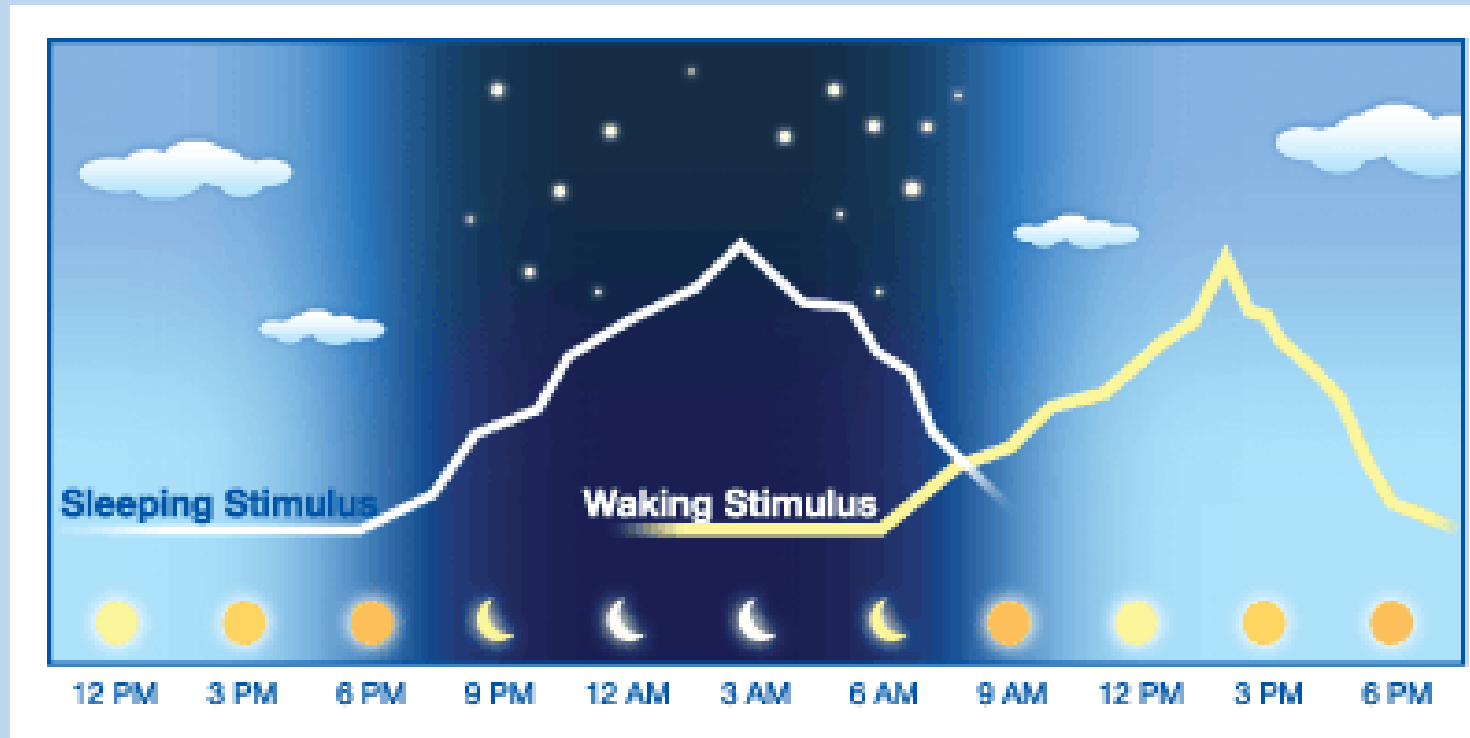
Circadian Sleep/Wake Brain

Circadian nocturnal sleep-daytime wakefulness:

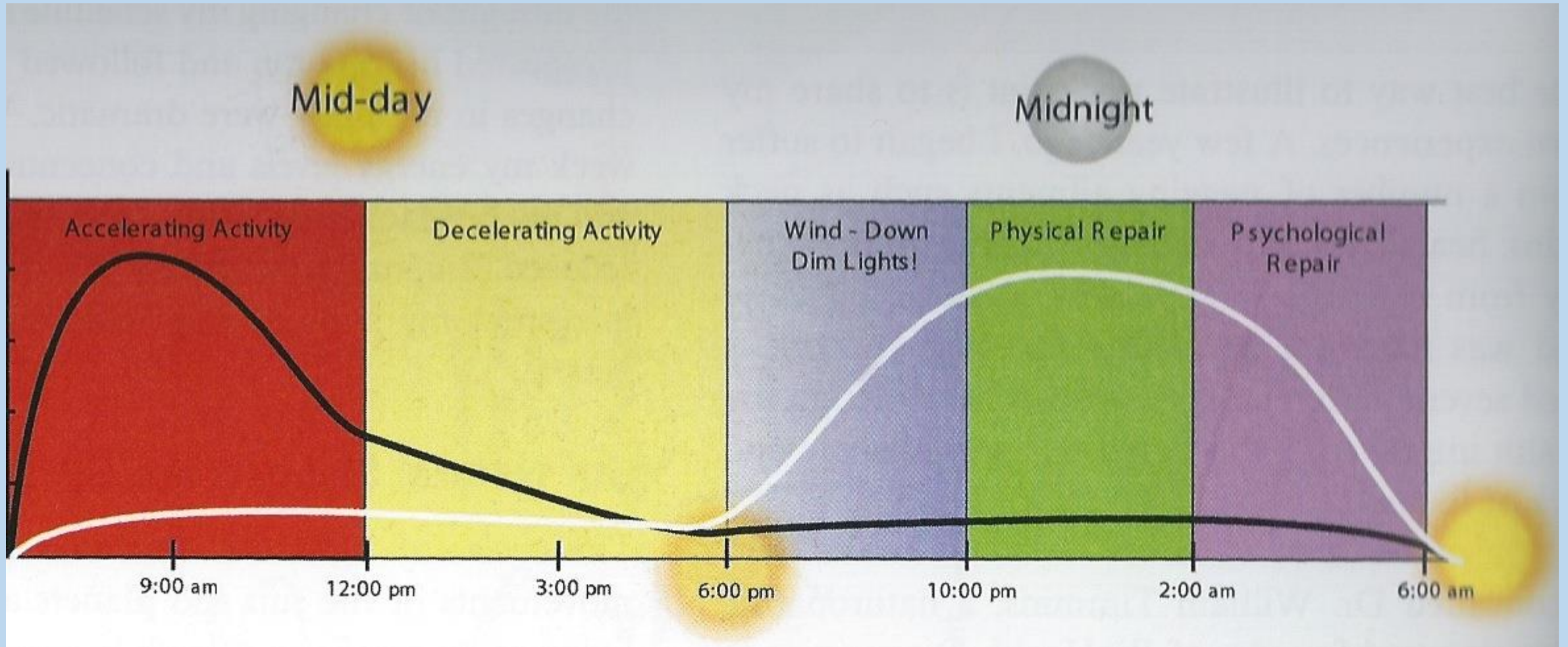
- changes in peripheral cytokines
- immune function
- endocrine influences

The interaction between the circadian sleeping/waking brain and the cytokine-immune-endocrine system are integral to preserving homeostasis.

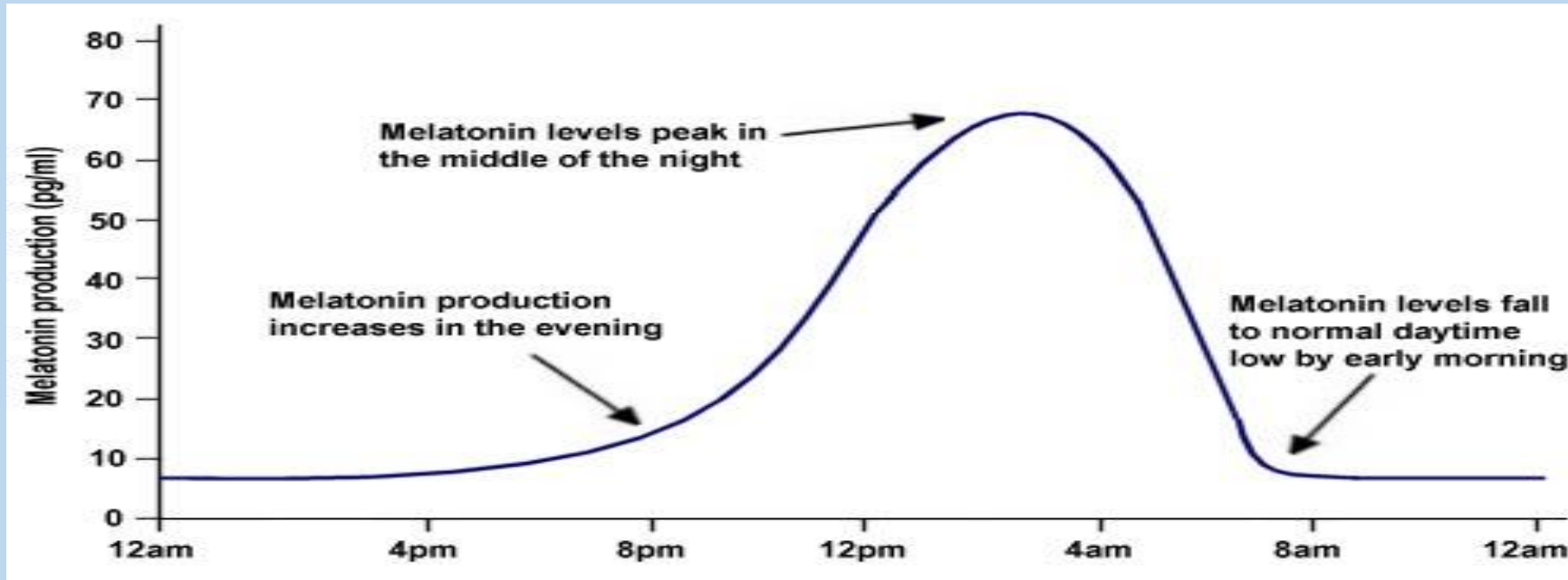
Circadian Sleep Rhythm



Restoration Happens at Night



Pineal Secretes Melatonin



The pineal gland is activated in the dark, and actively produces melatonin (N-acetyl-5-methoxytryptamine) and its precursor, serotonin (5-hydroxytryptamine) .

Tryptophan is required for the body to manufacture melatonin.
Found in Fenugreek, Spearmint, Fennel Seeds

Meditation can also increase melatonin.

3 Phases of Stress

1. Acute, non-recurring, mild response
2. Acute, recurring and poor recovery
 - Excess cortisol levels, anxiety, poor sleep
3. Chronic, prominent symptoms, poor recovery
 - Pronounced adrenal fatigue: symptoms usually match lab values
 - Really poor sleep, awake un-refreshed, cannot remember last time they had a “good night’s sleep”; short term memory affected

Healthy Response to Stress

- Alarm: inflammatory in nature
 - Stimulates tissue defenses
 - Increased sympathetic tone (epinephrine, etc.)
 - Short lived
- Response: anti-inflammatory in nature
 - HPA axis activity
 - Somewhat longer in duration
- Adaptation: both inflammatory and anti-inflammatory activity resolve

Continued or Repeated Stress

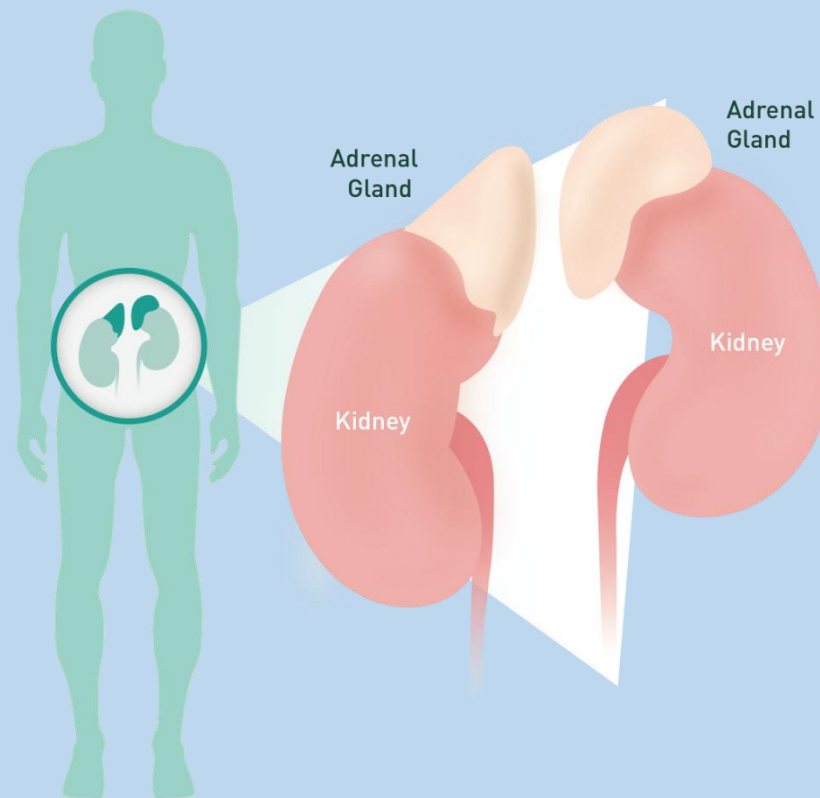
- Habituation leads to chronic HPA activation
- Elevated cortisol stops turning down the reaction
- Persistent inflammation at this point
- Elevated cortisol also stimulates gluconeogenesis in liver, leading to increased fat production
- TNF alpha, IL-1, IL-6, CRP lead to peripheral insulin resistance
- Increased fat production stimulates insulin production as part of inflammatory response

Cortisol/Insulin effects

- Prolonged elevated cortisol leads to insomnia, fatigue
- Prolonged elevated cortisol leads to dysglycemia
 - Decreased glucose uptake and use by cells
 - Increased gluconeogenesis, glycogenolysis
- Prolonged elevated cortisol leads to increased insulin and leptin
 - Also decreased insulin/leptin effect in CNS

Meet Your Adrenals

These walnut-size glands that sit atop the kidneys are a powerhouse in your endocrine system. Get to know them, learn how to take care of them and uncover the diverse roles they play in the body.*



- 1 Stress Response:** They produce adrenaline and cortisol, hormones that determine how your body reacts to stress.*
- 2 Sleep Patterns:** They set your body's normal sleeping patterns through the production of cortisol.*
- 3 Immune Health:** When the body is balanced, they produce optimal cortisol levels, which help naturally build resilience.*
- 4 Mood & Mental Clarity:** By directing the body's hormonal orchestra, they are ultimately responsible for a healthy mood.*

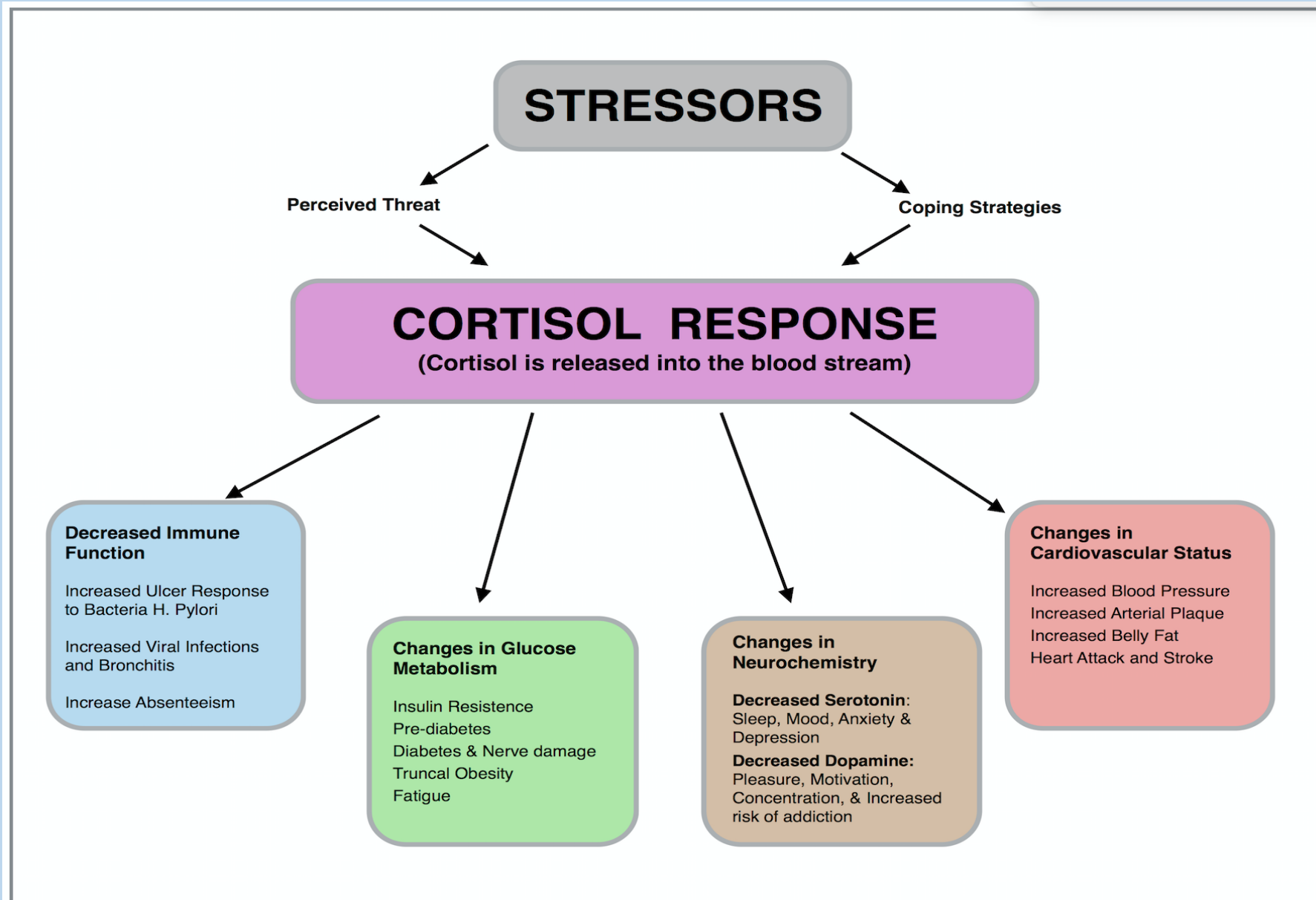
Role of Cortisol

- Cortisol has two modes of operation:
 - Proactive mode - It promotes coordination of circadian events, such as the sleep/wake cycle and food intake and is involved in processes underlying selective attention, integration of sensory information, and response selection.
 - Reactive mode - It facilitates our ability to cope with, adapt to, and recover from stress; cortisol promotes learning and memory processes.

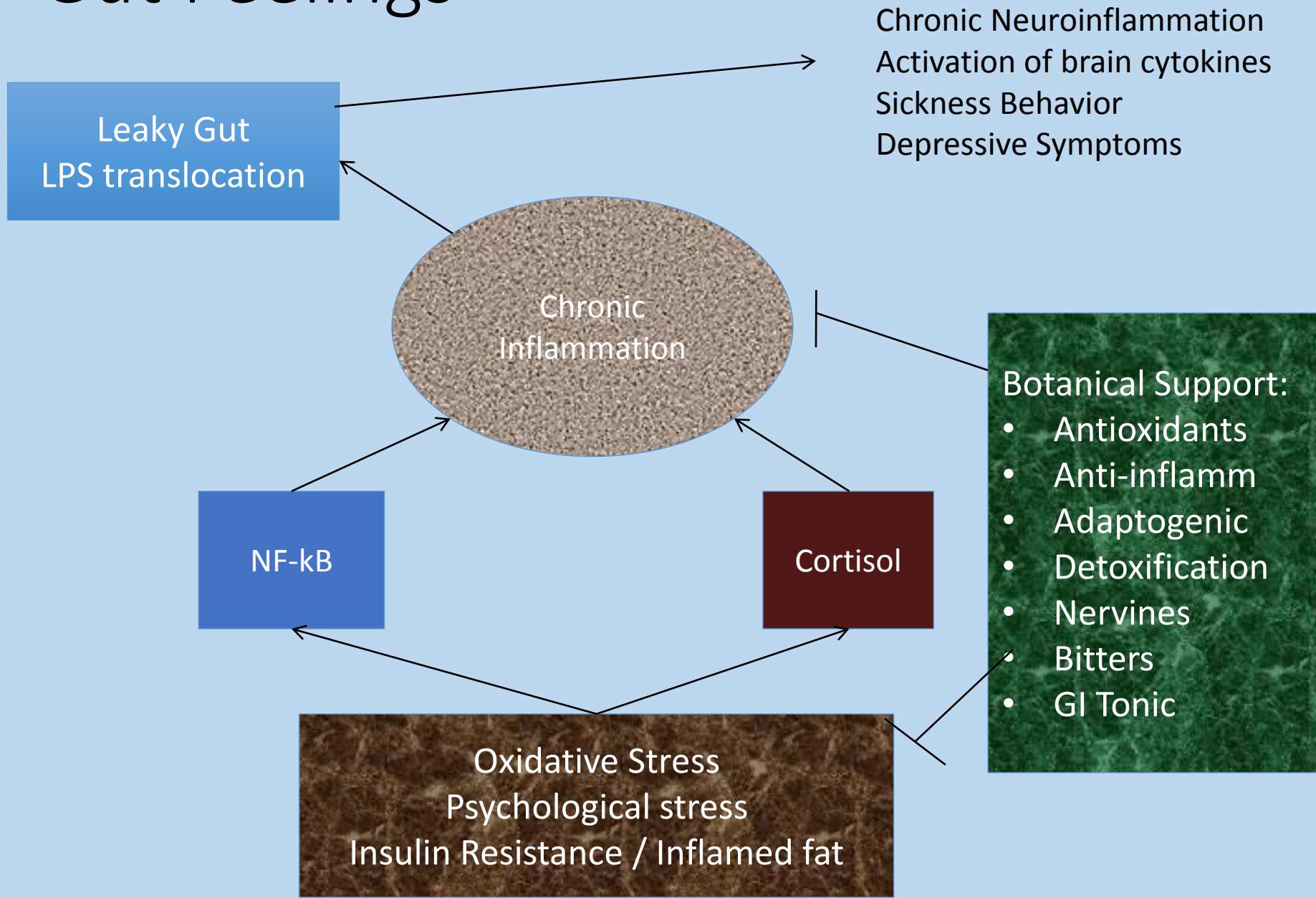
Role of Cortisol: Stress Adaptation

- When cortisol levels are chronically too low or too high, hippocampal transmission is impaired and therefore hippocampal outflow is reduced.
- This results in a myriad of symptoms related to energy, mood, memory and food cravings.
- It is at this point that cortisol ceases to be beneficial and begins instead to enhance vulnerability to damage.

Effects of Stress in the Body



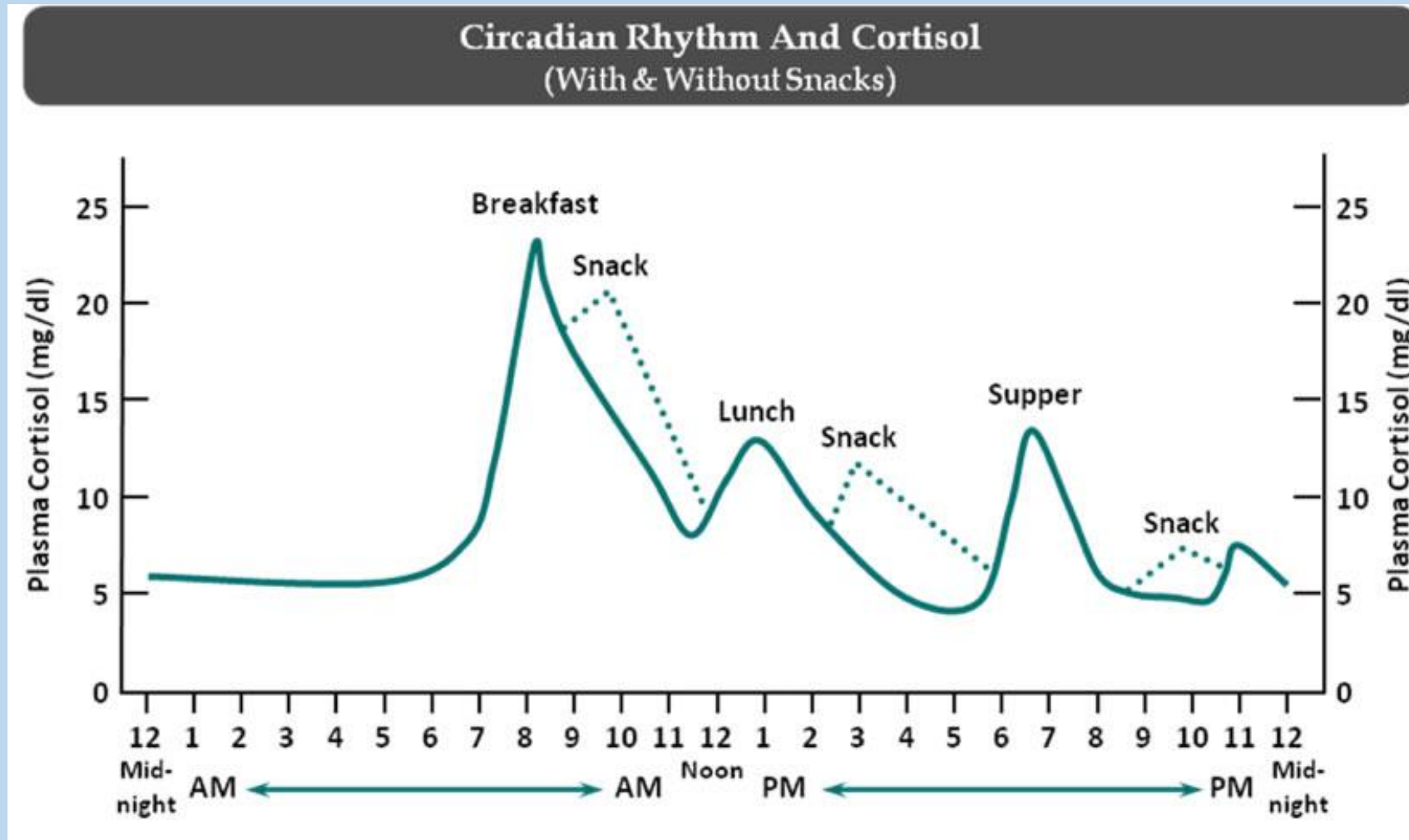
Gut Feelings



Hypoglycemia can be classified as fasting or reactive

- Fasting hypoglycemia is a more common finding with serious disease.
- Reactive hypoglycemia can also be called "functional hypoglycemia" since it is most often associated with functional disorders affecting blood glucose control mechanisms.

Glucose Dysregulation



What to Do?

- Lifestyle Shifts
- Diet
 - What is eaten
 - When it is eaten
 - How often one eats
- Herbal Medicines
 - Adaptogens
 - Glucose Regulating Agents
 - Microbiome Support Agents

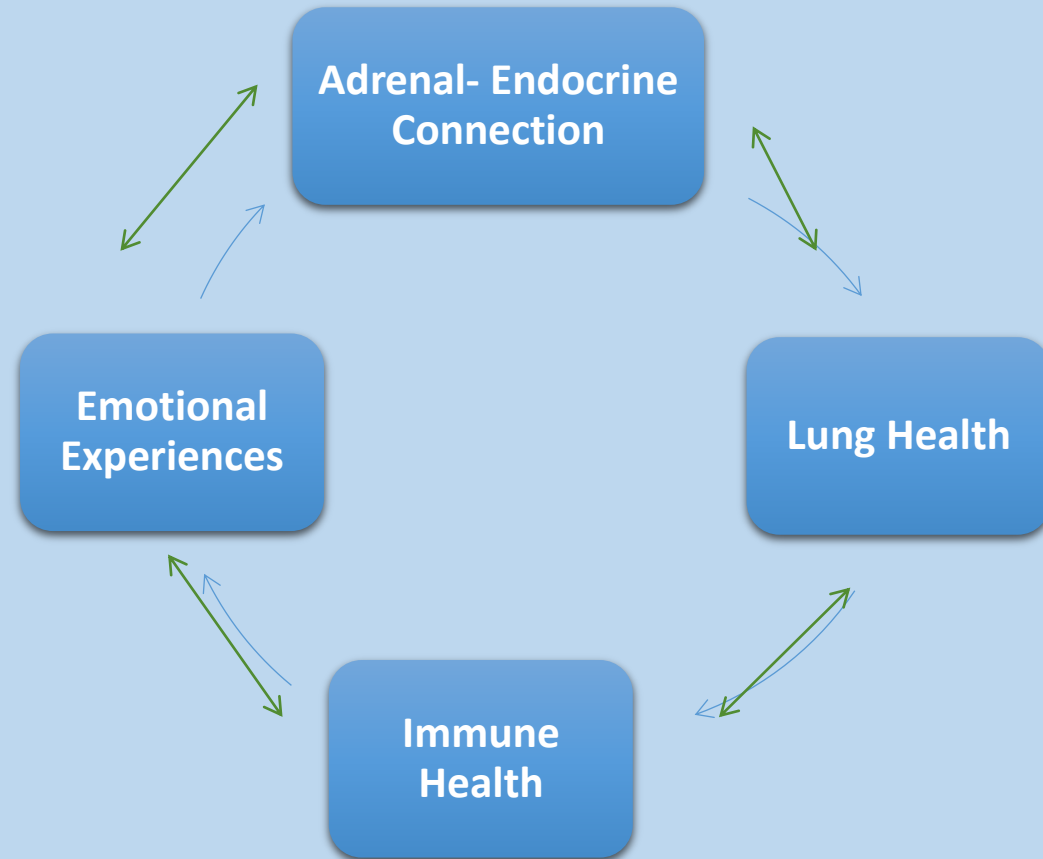
Glucose Regulating Herbs

- *Trigonella foenum-graecum* – fenugreek seed
- *Syzygium cumini* / *Eugenia jambolana*
- *Stevia rebaudiana*
- *Oplopanax horridum* - devil's club
- *Momordica charantia* - bitter melon
- *Gymnema sylvestre*
- *Galega officinalis* – goat's rue
- *Vaccinum* spp – blueberry, bilberry, huckleberry
- Cassia Cinnamon *Cinnamomum burmanii*, *Cinnamomum aromaticum*



Adrenal Immune Connection

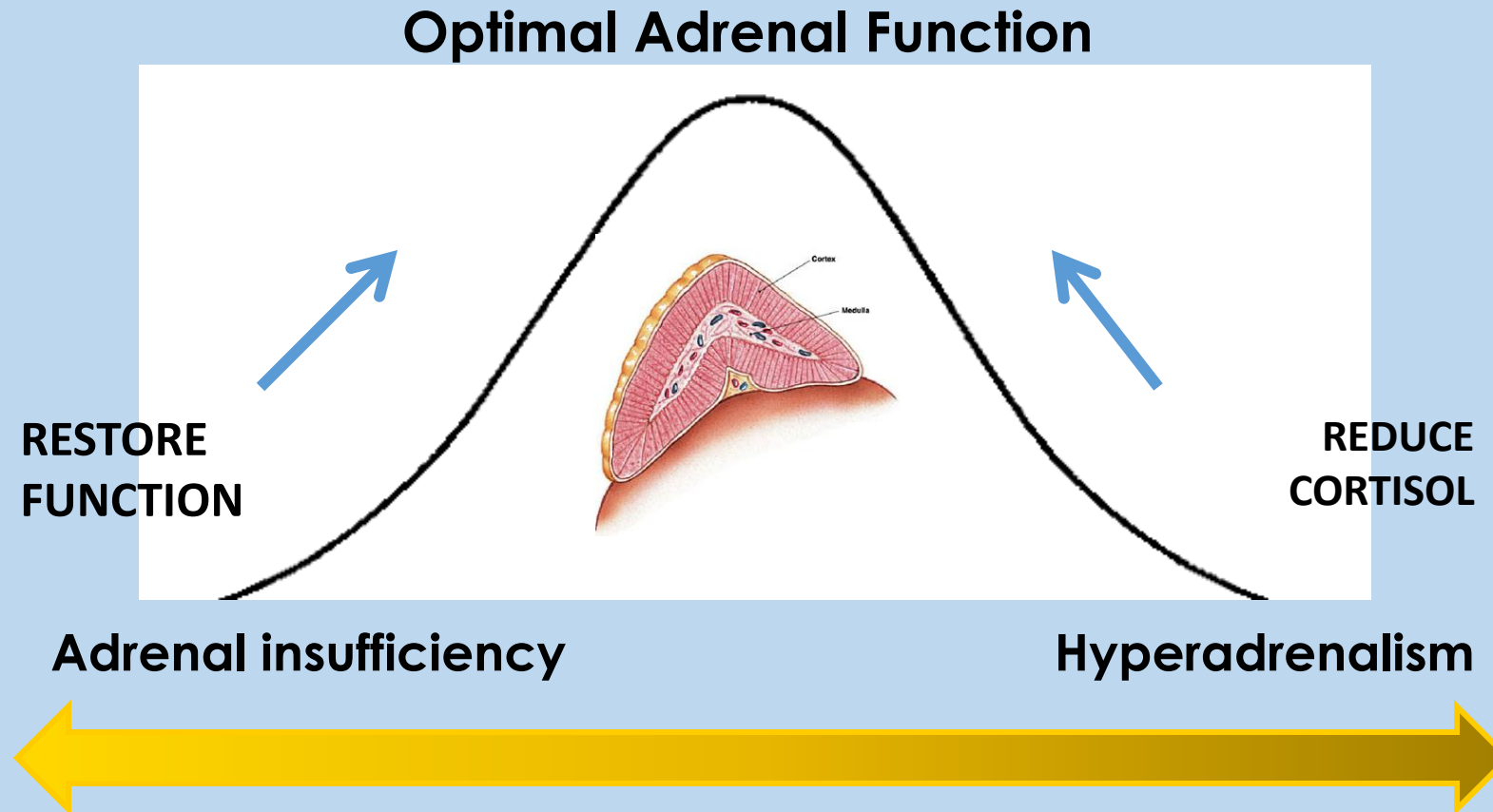
- HPA axis has direct effect on immune system health and function
- Disruption of the adrenal axis (HPA) and cytokine relationships lead to a predisposition and aggravation of allergies and autoimmune disorders.*



Stress and Inflammation

- Stress promotes inflammatory responses through effects on sympathetic and parasympathetic nervous system pathways.
- Proinflammatory cytokines have been found to interact with neurotransmitter metabolism, neuroendocrine function, synaptic plasticity and behavior.

Spectrum of Adrenal Dysregulation



Adrenal Compromise

Immune Signs

- Increase in allergies
- Increase in respiratory infection - chronic sinusitis
- Link to immune dysregulation diseases
- Gum inflammation
- Changes in microbiome health

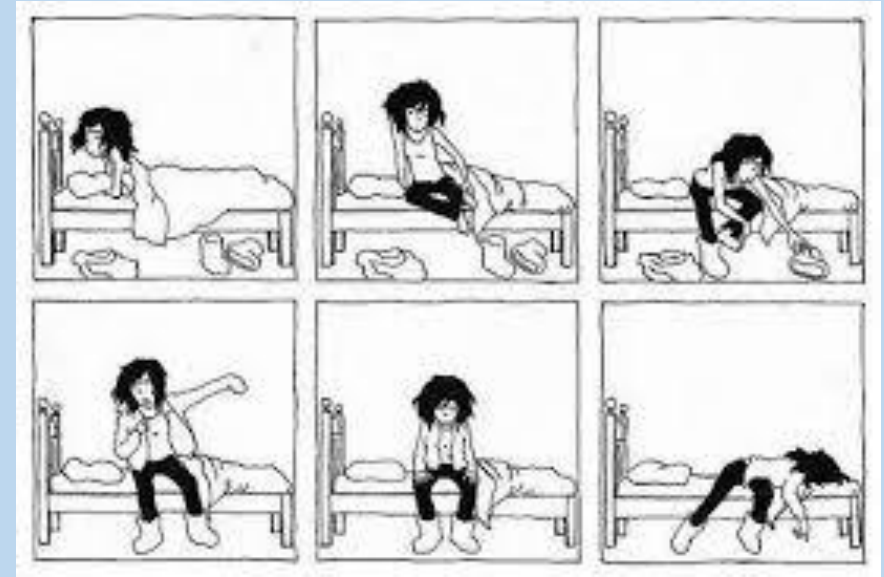
Disruption of the adrenal axis (HPA) and cytokine relationships lead to a predisposition and aggravation of allergies and autoimmune disorders.

Common Symptoms

- Stress
- Anxiety
- Irritability
- Mental fog
- Fatigue
- Hyperactivity
- Suppressed immune system
- Depression
- Insomnia
- Difficulty getting up in the morning
- Decreased stamina
- Sugar or salt cravings
- Headaches
- Low energy around 3-4pm, but after dinner energy increases. Winding down for bedtime is difficult

Adrenal Exhaustion

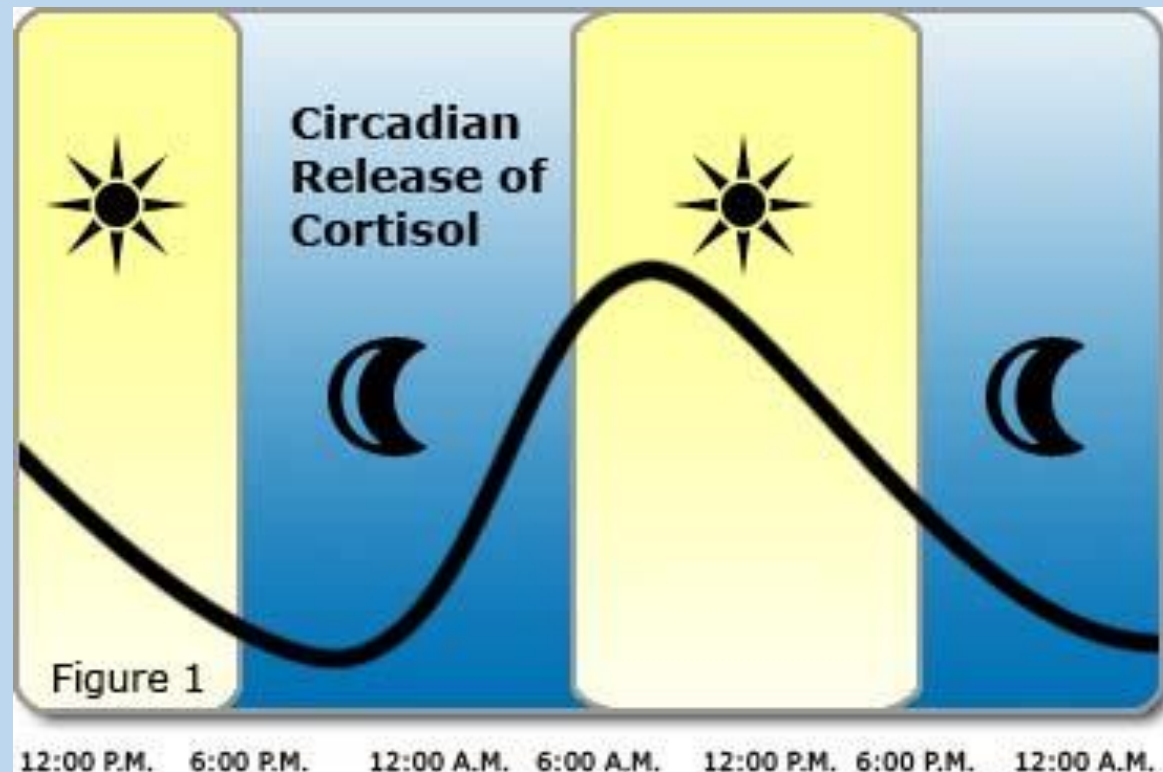
- HPA activity falters
- Cortisol level falls
- DHEA level falls
- Worsening organism response and ultimately death



Phases of Adrenal Gland Fatigue

Healthy Adrenal Response (Cortisol levels within range with desired rhythm)	Phase 0
Acute Fight or Flight (Increased HPA tone)	Phase 1
HPA Axis Dysfunction (Zig Zag patterns)	
Early Adrenal Fatigue (Elevated/high range AM with HPA blunting thereafter)	
Evolving Adrenal Fatigue (Suboptimal or low AM cortisol with HPA blunting thereafter)	Phase 2
Established Adrenal Fatigue/Hypoadrenia (Hypofunctioning HPA axis)	Phase 3

Cortisol Circadian Cycle

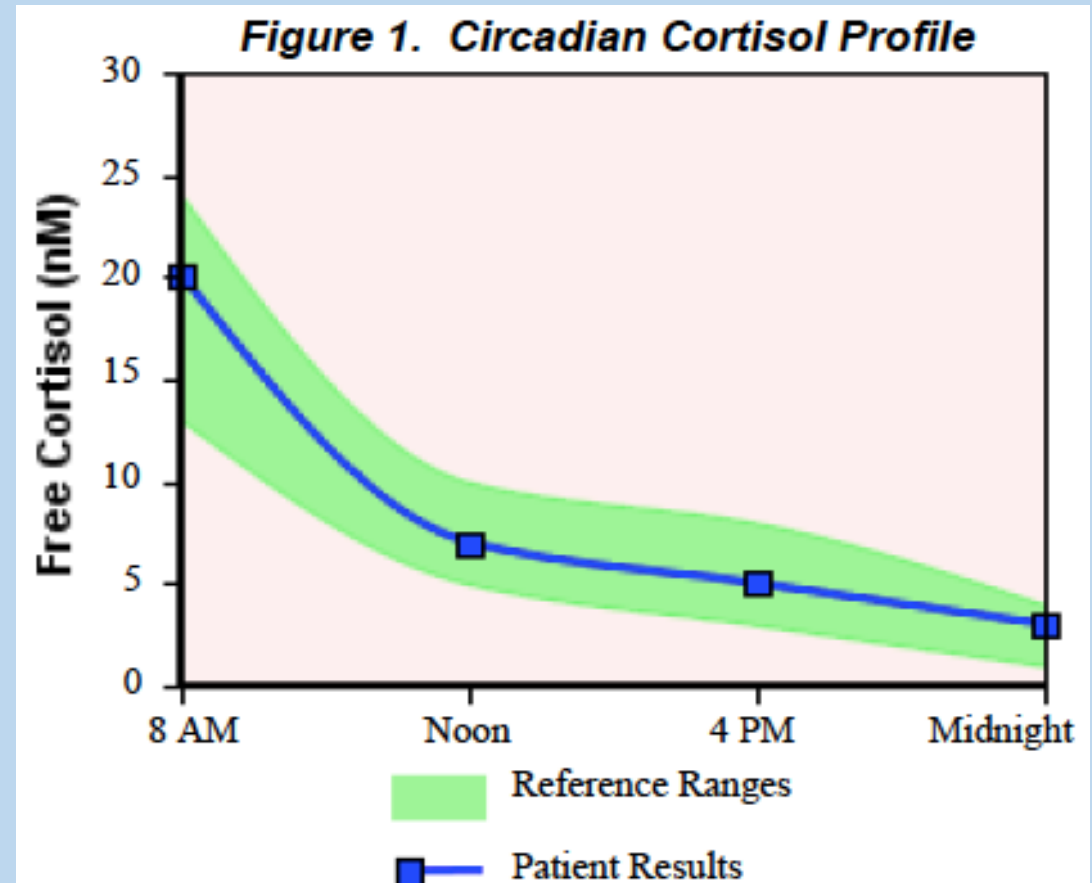


Normal 24 hour Circadian Cortisol Cycle

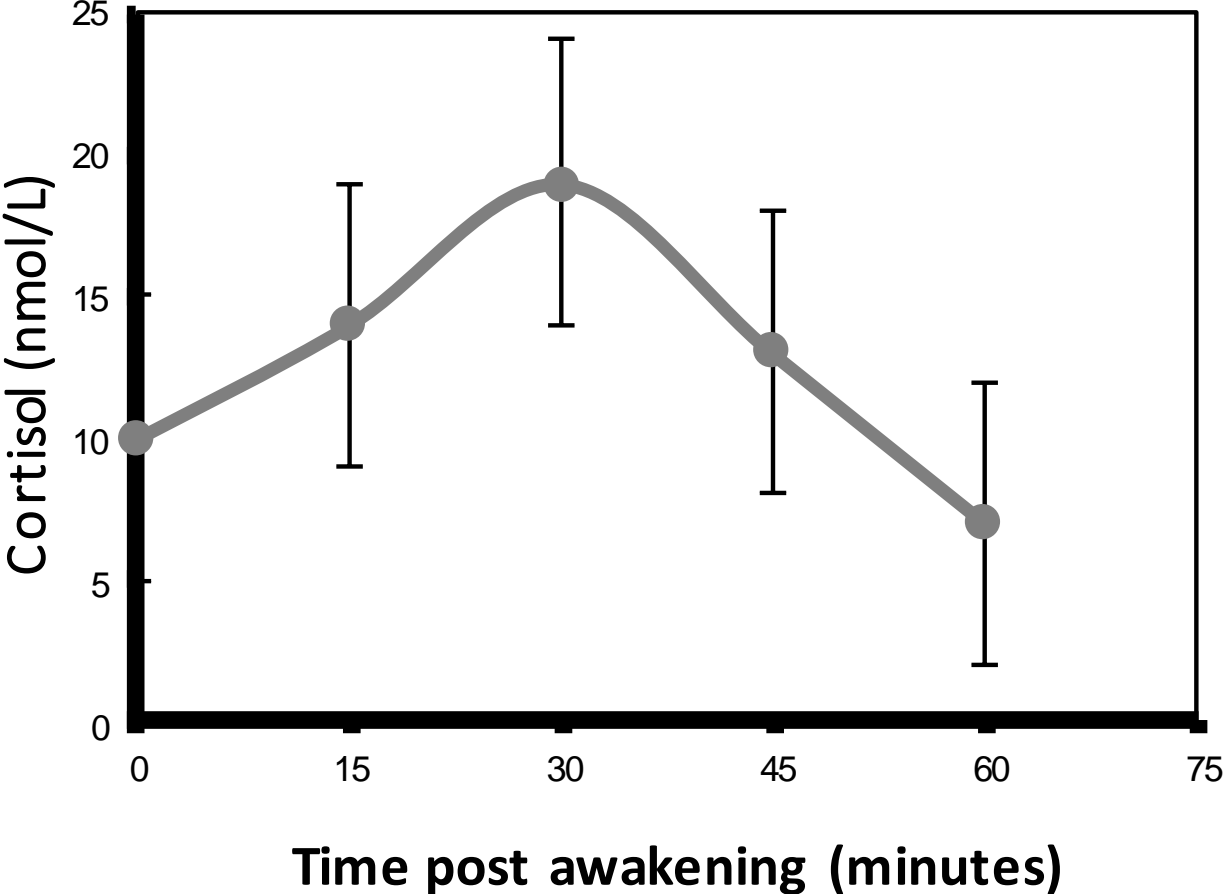
Cortisol is released in a circadian rhythm pattern. This means that the levels of cortisol change based on the time of day

Cortisol levels are highest in the morning, decline sharply by noon, flatten out in the afternoon, and slightly decline before bed

This type of pattern suggests a properly functioning Hypothalamic-Pituitary-Adrenal (HPA) Axis

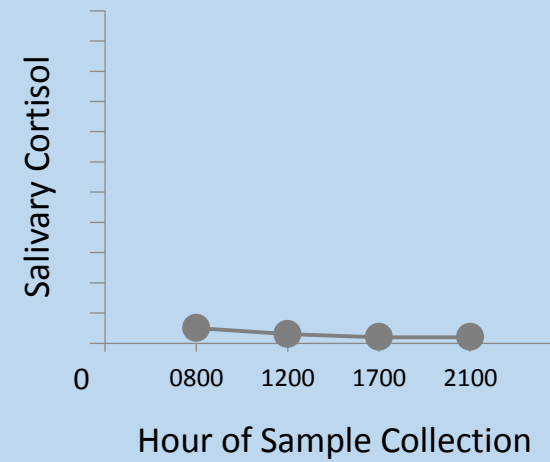
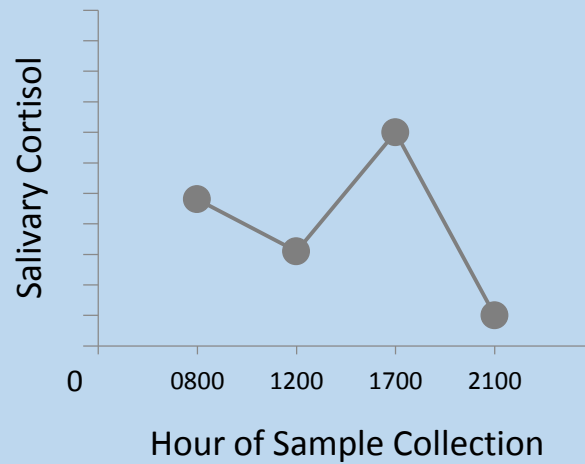
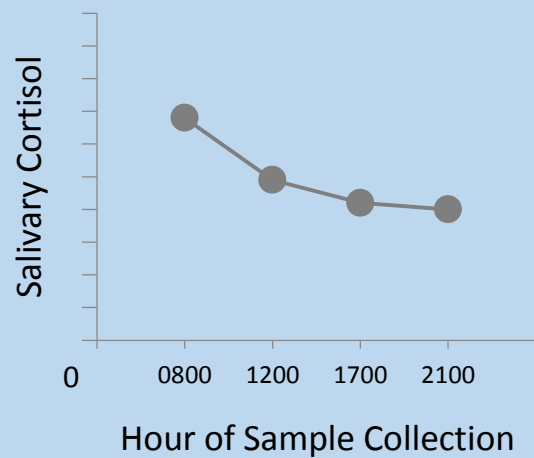
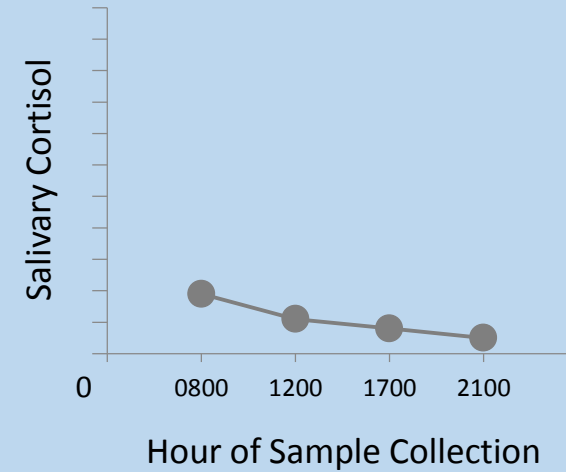
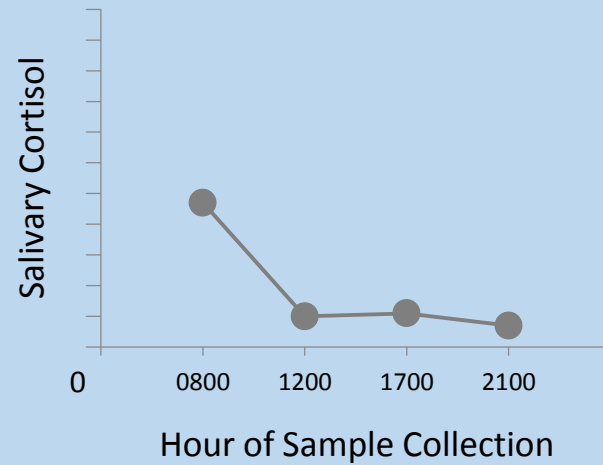
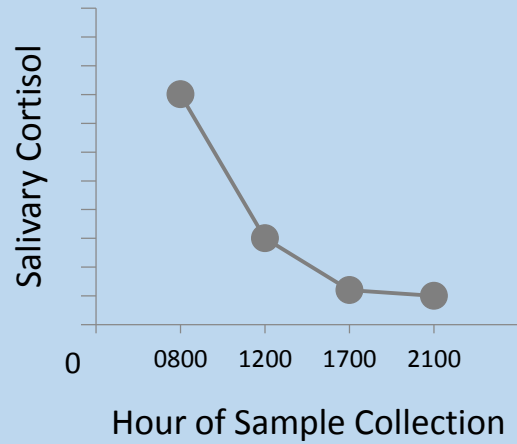


Cortisol Awakening Response



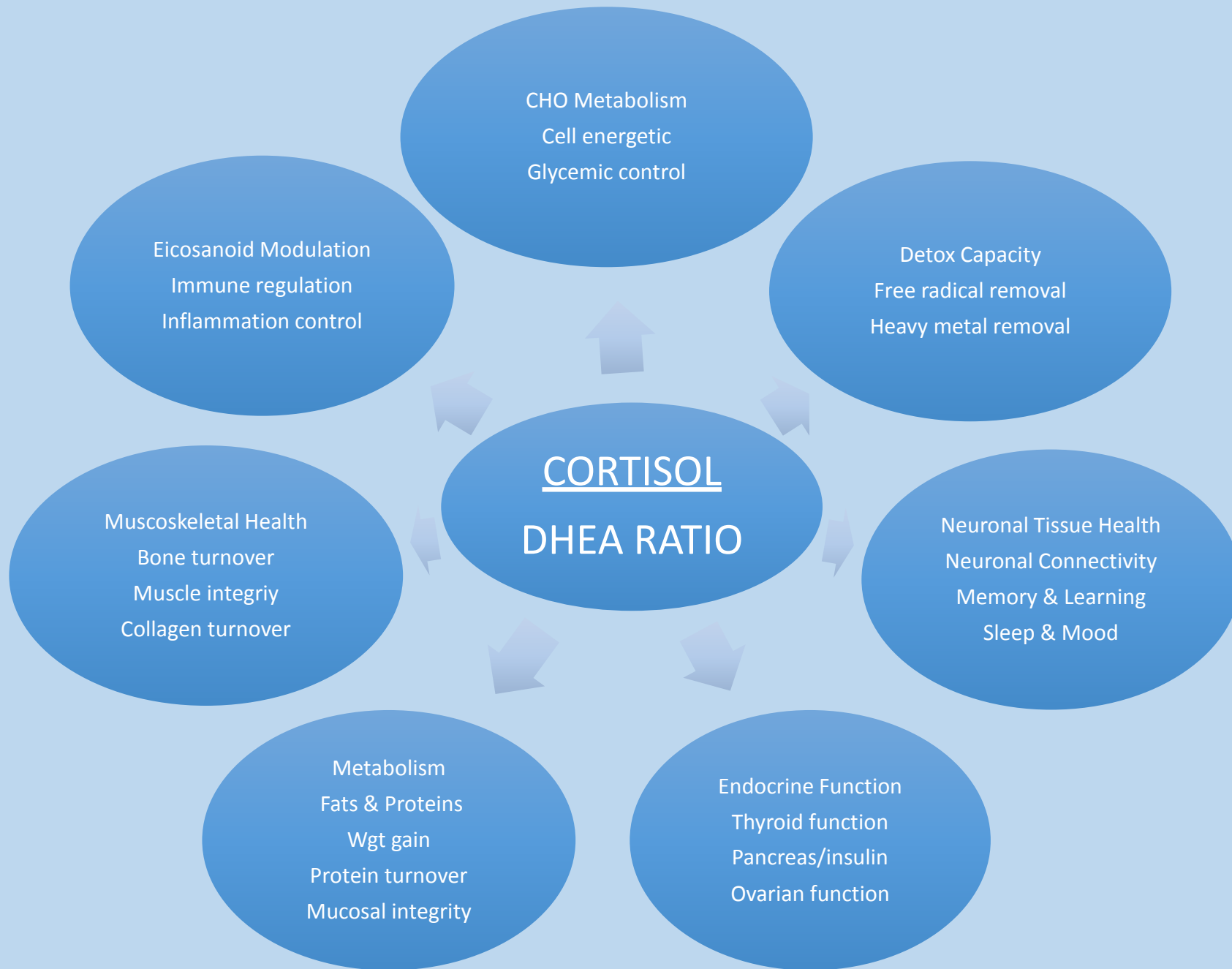
HPA Axis

DIURNAL CURVE



*Using Saliva Hormone Testing for
Evaluation and Treatment of
Adrenal Function*

A Stress Evaluation Index



Clinical Presentations of Adrenal Disturbances

- Chronic Pain/Fibromyalgia:
An adequate adrenal response can maintain a higher pain threshold. The impact of stress on chronic pain and inflammation in the joints and muscle tissue can accelerate breakdown of these tissues.

Clinical Presentations of Adrenal Disturbances

- Chronic Fatigue syndrome (CFS):
A common HPA axis defect in CFS is impaired corticotrophin release. As a result low cortisol and eventual adrenal atrophy may be observed. Depleted adrenals with flat rhythms are often seen.

Clinical Presentations of Adrenal Disturbances

- **Glycemic Dysregulation:**
Chronic hypoglycemia can impair normal adrenal function by repetitive overstimulation of cortisol. Recurring exposure to high cortisol will impair insulin activity & invariably lead to insulin resistance & hyperglycemia
- **Obesity and Weight Gain**
Cortisol imbalances stimulates fat deposits in the body- abdominal

Clinical Presentations of Adrenal Disturbances

- Allergies/Autoimmune Disorders:
Disruption of the adrenal axis and cytokine relationships lead to predisposition and aggravation of autoimmune diseases and allergies

Clinical Presentations of Adrenal Disturbances

- Depression/ADD:
Hyperactive HPA axis is common in depressed patients, mood swings
- Cortisol midnight elevation
- Cortisol elevations and rhythm disruptions throughout the day are typical of attention deficit disorders (ADD)

Clinical Presentations of Adrenal Disturbances

- Elevated midnight salivary cortisol is now considered one of the best tests in diagnosing endogenous depression.
- Other anomalies in cortisol rhythm usually accompany the midnight elevation.

55 year old women with anxiety,
hypoglycemia, fat intolerance,
sleep issues



Test	Description	Result	Ref Values
------	-------------	--------	------------

ASI Adrenal Stress Index

TAP	Free Cortisol Rhythm	Result	Ref Values
	07:00 - 08:00 AM	18 Normal	13-24 nM
	11:00 - Noon	63* Elevated	5-10 nM
	04:00 - 05:00 PM	9 Elevated	3-8 nM
	11:00 - Midnight	3 Normal	1-4 nM

Cortisol Burden: 93 **23 - 42**

The cortisol burden reflects the area under the cortisol curve. This is an indicator of overall cortisol exposure, where high values favor a catabolic state, and low values are sign of adrenal deterioration.

*** Further investigation is warranted**

Figure 2.

The Cortisol release inducers fall into 4 broad categories shown in the adjacent flowchart. Long term adrenal axis maintenance and restoration, require optimization of all the cortisol inducers.

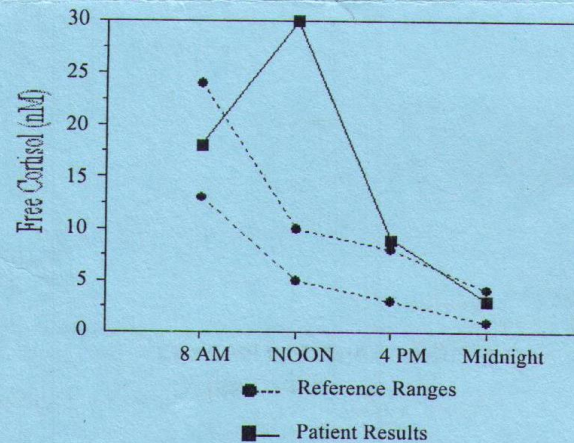
Remarks: An elevated noon/afternoon free cortisol value is caused by a stress response to an emotional or mental situation, hypoglycemia or chronic pain and overt/hidden inflammation.

What Next?

- Consider appropriate dietary modifications and glycemic control that include an insulin friendly carbohydrate-to-protein balance.
- Consider initiating a mild to moderate aerobic exercise program.
- The literature reports ACTH pulse height is attenuated by use of Phosphorylated serine supplement within 1 - 2 hours of time(s) of high cortisol.
- Consider the palliative use of a natural or pharmaceutical anti-histamine or anti-inflammatory.
- Consider balancing the sympathetic/parasympathetic systems using established techniques, examples: meditation and Tai Chi or heart rate variability coherence (Freeze Framing).
- If above changes do not yield the desired clinical and follow up test results, look for low grade or hidden inflammation and infections. Examples food intolerances, chronic gastrointestinal and other infections.

Patient shows a high cortisol output profile typical of day long exposure to

Figure 1. Circadian Cortisol Profile



The Inducers of Cortisol Release

Inducers below must be individually examined for successful restoration of adrenals.

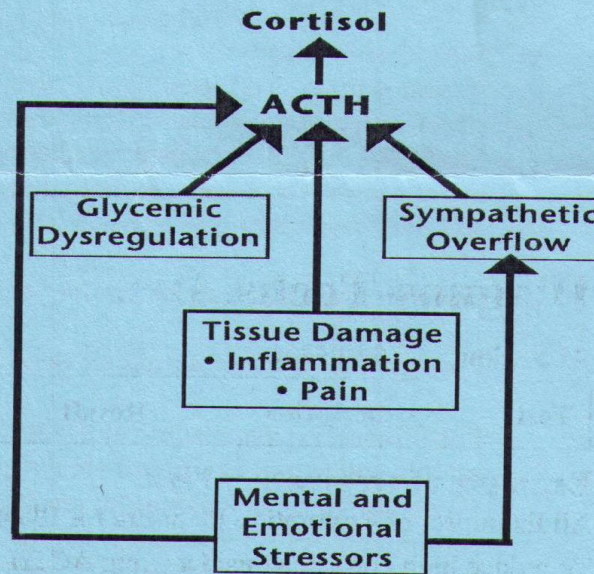
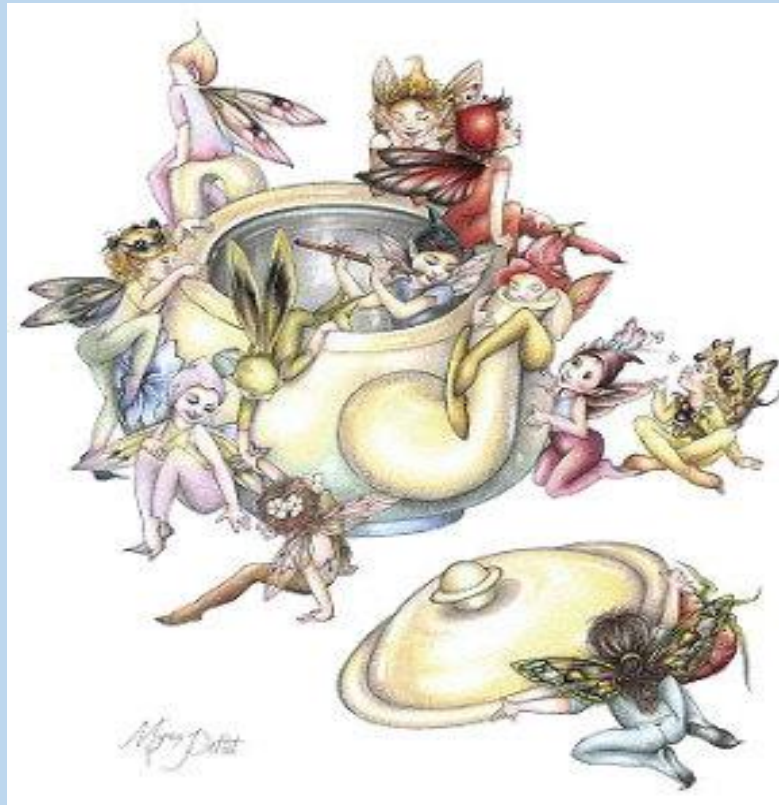


Figure 2.

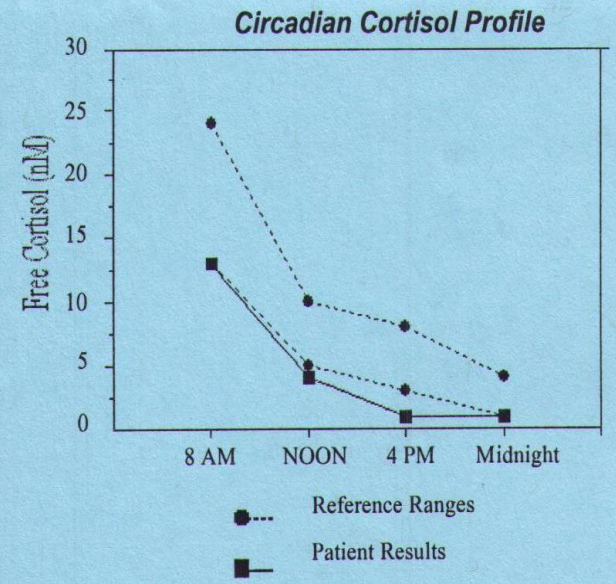
56 year old women with
depression, wgt gain and
menopausal complaints



Test	Description	Result	Ref Values
------	-------------	--------	------------

TAP Free Cortisol Rhythm

TAP	Free Cortisol Rhythm	Result	Ref Values
07:00 - 08:00 AM		13 Normal	13-24 nM
11:00 - Noon		4 Depressed	5-10 nM
04:00 - 05:00 PM		<1 Depressed	3-8 nM
11:00 - Midnight		<1 Depressed	1-4 nM
Cortisol Burden:		19	23 - 42



Diagnosis Code: 255.4

Please Note: All examples of patient treatment or therapy are for illustrative and/or educational purpose. Use this report in context of the clinical picture before initiating hormone or other therapies.

COURTESY INTERPRETATION of test and technical support are available upon request, to Physician Only

Code	Test Name	Result / Notes	Reference Values/Key
ISN	Insulin	Post-prandial: <3 Depressed	Optimal: 5-20 uIU/mL Low: < 5 uIU/mL High: > 20 uIU/mL

Depressed Post-prandial insulin within four hours after meal. This may be caused by a small carbohydrate load in the preceding challenge meal or a reduction in pancreatic insulin release or synthesis. Consider a closer examination of challenge meal composition to rule out pre-diabetic tendencies.

Why Test for Insulin?

Insulin activity is affected by the stress and cortisol responses. Chronic stress with cortisol elevation antagonizes insulin, and may cause functional insulin resistance. Furthermore, chronic hypercortisol causes hyperinsulin responses to carbohydrate intake. Chronic insulin resistance and overproduction lead to pancreatic exhaustion.

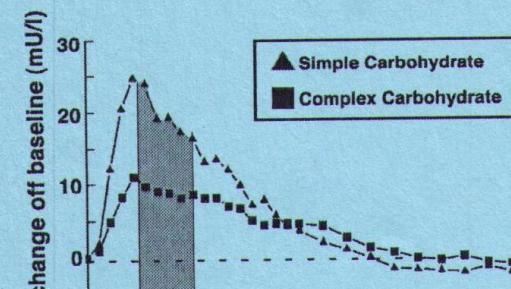
General information about insulin values.

Fasting: This insulin value is elevated in cases of insulin resistance.

Post Prandial: This insulin value varies with type of meal and time of sample collection. See figure 1b.

Adapted, Br. J. Nutr. 2003, 90:853

To obtain the most meaningful results, instruct patient to eat 50g of carbohydrate or what is equivalent to 200 calories about 45-90 minutes before noon sample collection. Examples: 2 slices of white bread and 1 cup of orange juice OR 1 cup of cooked oatmeal and 1 cup of orange juice OR 2 ounces of corn flakes snack.



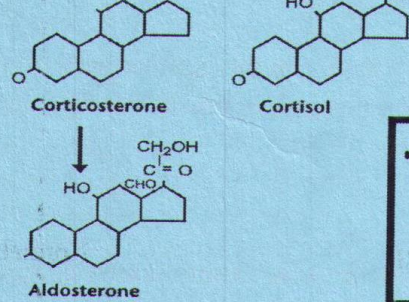


Figure 5.

→ The preferential pathway under stress shunts pregnenolone into cortisol at the expense of DHEA.

▼ 21-Hydroxylase enzyme, may be deficient with high 17-OHP.

MB2S Total Salivary SIgA 10 Depressed

A depressed mucosal SIgA may be attributed to one or more of the following reasons:

- 1- Excessive chronic cortisol output causes a reduction in the number of SIgA producing immunocytes. Appropriate restorative treatments have been shown to produce incremental improvements in SIgA.
- 2- Excessive sympathetic activity causes inhibition of SIgA release from the mucosal immunocytes.
- 3- Chronic deficits in cortisol and/or DHEA levels.
- 4- Possible systemic deficit in capacity to produce IgA - an inherited problem. Rule out possibility with a serum IgA test. A normal finding rules out this possibility.

Normal: 25-60 mg/dl
Borderline: 20-25 mg/dl

Basic Facts About SIgA

1. Secretory IgA (SIgA) is secreted by the various mucosal surfaces. It is mostly a dimeric molecule. Less than 2% of Saliva is of serum origin. The secretory component of SIgA stabilizes it against enzymatic and bacterial degradation.
2. The main functions of SIgA include Immune Exclusion, Viral and Toxin Neutralization, Plasmid Elimination, and Inhibition of Bacterial Colonization. SIgA immune complexes are not inflammatory to the mucosal surfaces.
3. Production of SIgA is adversely affected by stress which is mediated by increased cortisol and/or catecholamine levels.

FI4 Gliadin Ab, SIgA 12 Negative

There is an expected increase in the frequency of false-negatives to Gliadin with decreasing total secretory IgA levels that occurs in IgA suppressed individuals. Contextualize findings into overall clinical picture.

Borderline: 13-15 U/ml
Positive: >15 U/ml

Notes on Gliadin Ab Test

Gliadins are polypeptides found in wheat, rye, oat, barley, and other grain glutes, and are toxic to the intestinal mucosa in susceptible individuals. Healthy adults and children may have a positive antigliadin test because of subclinical gliadin intolerance. Some of their symptoms include mild enteritis, occasional loose stools, fat intolerance, marginal vitamin and mineral status, fatigue, or accelerated osteoporosis.

Scan. J. Gastroenterol. 29:248(1994).

52 year old women with
hypothyroidism, low blood
pressure, light-headedness



Test	Description	Result	Ref Values
------	-------------	--------	------------

ASI Adrenal Stress Index

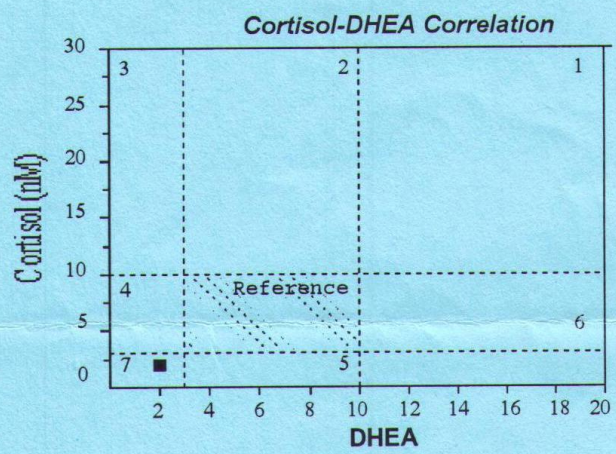
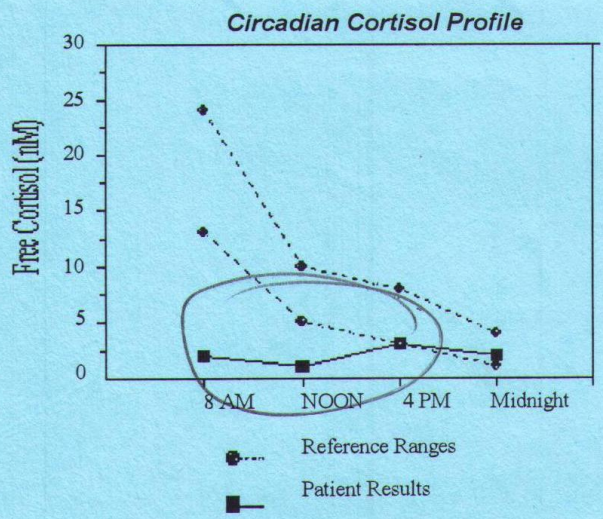
TAP	Free Cortisol Rhythm	Result	Ref Values
	07:00 - 08:00 AM	2 Depressed	13-24 nM
	11:00 - 12:00 PM	1 Depressed	5-10 nM
	04:00 - 05:00 PM	3 Normal	3-8 nM
	11:00 - 11:59 PM	2 Normal	1-4 nM
	Cortisol Burden:	8	23 - 42

DHEA	Dehydroepiandrosterone	Result	Ref Values
	Pooled Value	2 Depressed DHEA	Adults (M/F): 3-10

KEY: CORTISOL-DHEA CORRELATION

1. Stress adapted "Hyper" response; minimal change.
2. Stress adapted with a divergence in response to ACTH.
3. Maladaptation Phase I.
4. Maladaptation Phase II.
5. Adrenal fatigue, non-adapted.
6. Inappropriate DHEA(S) value.
7. Adrenal failure.

Addison



Patient Result Interpretations

Depressed morning cortisol, < 13 nM, is suggestive of marginal HPA performance.
 Normal rhythms exhibit highest cortisol value for the day at 7 - 8 AM.
 Morning cortisol augmentation, or 11 Beta HSD inhibitors, as in licorice, worth consideration.
 Minimal cortisol rhythm; cortisol augmentation and anabolic support suggested.

WB

Test	Description	Result	Ref Values
MB2S	Total Salivary SIgA	7 Depressed	Normal: 25-60 mg/dl Borderline: 20-25 mg/dl
FI4	Gliadin Ab, SIgA	3 Negative	Borderline: 13-15 U/ml Positive: >15 U/ml

Clinical Antigliadin SIgA (AGA) Interpretation

36 year old women
desiring to get pregnant



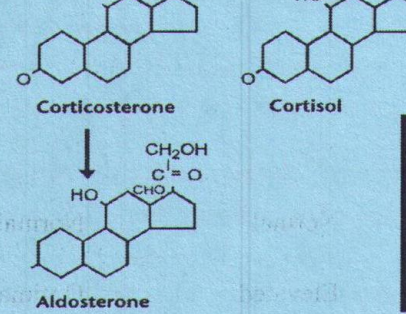


Figure 5.

➔ The preferential pathway under stress shunts pregnenolone into cortisol at the expense of DHEA.

▼ 21-Hydroxylase enzyme, may be deficient with high 17-OHP.

MB2S Total Salivary SIgA 7 Depressed

A depressed mucosal SIgA may be attributed to one or more of the following reasons:

- 1- Excessive chronic cortisol output causes a reduction in the number of SIgA producing immunocytes. Appropriate restorative treatments have been shown to produce incremental improvements in SIgA.
- 2- Excessive sympathetic activity causes inhibition of SIgA release from the mucosal immunocytes.
- 3- Chronic deficits in cortisol and/or DHEA levels.
- 4- Possible systemic deficit in capacity to produce IgA - an inherited problem. Rule out possibility with a serum IgA test. A normal finding rules out this possibility.

Normal: 25-60 mg/dl
Borderline: 20-25 mg/dl

Basic Facts About SIgA

1. Secretory IgA (SIgA) is secreted by the various mucosal surfaces. It is mostly a dimeric molecule. Less than 2% of Saliva is of serum origin. The secretory component of SIgA stabilizes it against enzymatic and bacterial degradation.
2. The main functions of SIgA include Immune Exclusion, Viral and Toxin Neutralization, Plasmid Elimination, and Inhibition of Bacterial Colonization. SIgA immune complexes are not inflammatory to the mucosal surfaces.
3. Production of SIgA is adversely affected by stress which is mediated by increased cortisol and/or catecholamine levels.

FI4 Gliadin Ab, SIgA 7 Negative

There is an expected increase in the frequency of false-negatives to Gliadin with decreasing total secretory IgA levels that occurs in IgA suppressed individuals. Contextualize findings into overall clinical picture.

Borderline: 13-15 U/ml
Positive: >15 U/ml

Notes on Gliadin Ab Test

Gliadins are polypeptides found in wheat, rye, oat, barley, and other grain glens, and are toxic to the intestinal mucosa in susceptible individuals. Healthy adults and children may have a positive antigliadin test because of subclinical gliadin intolerance. Some of their symptoms include mild enteritis, occasional loose stools, fat intolerance, marginal vitamin and mineral status, fatigue, or accelerated osteoporosis.
Scan. J. Gastroenterol. 29:248(1994).

Restoring the Adrenal 24 Hour Cycle

- Regulating Adrenal and HPA axis communication
- Homeostasis of cortisol patterns & influences
- Glycemic Regulation and Stability
- Healthy Sleep Wake Cycle
- Application of Specific Adaptogen agents in the 24 hour cycle
 - Morning
 - Night
 - Daytime

Adaptogens

What are they?

Coined in 1947 by the Soviet Union's Ministry of Health, to define a narrow class of botanical medicines and must fulfill 3 categories:

1. It must be non-toxic to the body's physiological functions;
2. It must increase the body's resistance to adverse influences, not by a specific action but by a wide range of physical, chemical, and biochemical factors;
3. It must have an overall normalizing effect, improving all kinds of conditions and aggravating none.

A pharmacotherapeutic group defined as:

“Herbal preparations that increased attention and endurance in fatigue, and reduced stress-induced impairments and disorders related to the neuro-endocrine and immune systems.”

Sources: 1. Nikolai Vasilyevich Lazarev;

2. Panossian, A.; Wikman, G. Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity.

Current Clin.Pharmacol. 2009, 4, 198– 219

Adaptogens

- Regulation of key mediators of stress response, such as molecular chaperons (HSP70), stress-activated protein kinases, transcription factors, cortisol, and nitric oxide*
- The paradigm of one drug for one disease is not appropriate for adaptogens as they have numerous pharmacological effects and indications
- Adaptogen acts to prolong the phase of resistance
- General Stimulatory Effect
- Stress Protective Activity

*Panossian A and Wikman G, Effects of Adaptogens on the CNS and the Molecular Mechanisms Associated with Their Stress-Protective Activity, *Pharmaceuticals* 2010, 3,188-224; doi:10.3390/ph3010188

Adaptogens

- Metabolic Regulators
- Improves carbohydrate metabolism
- Counter catabolic processes associated with any form of stress on the body
- Stimulating effect more pronounced with a background of fatigue and stress.



Winston, D.; Maimes, S. *Adaptogens. Herbs for Strength, Stamina and Stress Relief*, Healing Arts Press: Rochester, Vermont, USA, 2007; pp. 1-324.

General Stimulatory Effect

- High quality of arousal
- No energy depletion
- No addiction potential
- Increased performance in stress
- Rarely side effects
- Increased DNA/RNA & protein synthesis

- Salidroside - the active principles of *R. rosea* stimulating effect lasts 4 hr or more



Adaptogens

- Adaptogens reduce stress-induced generation of nitric oxide → preventing a shortage in ATP production in stress, resulting in increased performance and endurance
- Decreases metabolic markers associated with anaerobic metabolism such as lactic acid
- Protective activity to CNS, CVS, Endocrine, Immune systems



Role of Adaptogens in Endocrine Dysfunction



Improves the quality of life of patients when implemented as adjuvant therapy for many chronic diseases and pathological conditions

Anti-fatigue agents that induces increased attention and endurance in situations of decreased performance caused by fatigue and/or sensation of weakness

To reduce stress-induced impairments and disorders related to the function of the neuro- endocrine and immune systems

Role of Adaptogens in Endocrine Dysfunction

- Immunomodulating
- Neuro-protective
- Antioxidant/ Free Radical Scavenging
- Improve cognitive function
- Anti-depressive activity
- Anti-anxiety
- To reduce state of cell apoptosis



Not All Adaptogens are Created Equal

While all adaptogens share some basic characteristics, adaptogens work on the body in different ways. Gaia is using different adaptogenic actions in each HPA Axis formula to reach specific results.

Physically & emotionally supporting: Such as Rhodiola, Holy Basil & Schisandra. Support your body's ability to naturally protect against daily stressors, supporting your daily circadian rhythm.*

Regulating, calming & restoring: Such as Magnolia Bark, Ashwgandha, Mimosa Bark & Cordyceps. Work on the body to balance adrenal function, restoring the body's nighttime circadian rhythm.

Physically & emotionally motivating: Such as Eleuthero, Korean Ginseng, Rhaponticum & Licorice Root. While not stimulating like caffeine, they awaken the body and set in motion internal activity that can help people power through their day.*



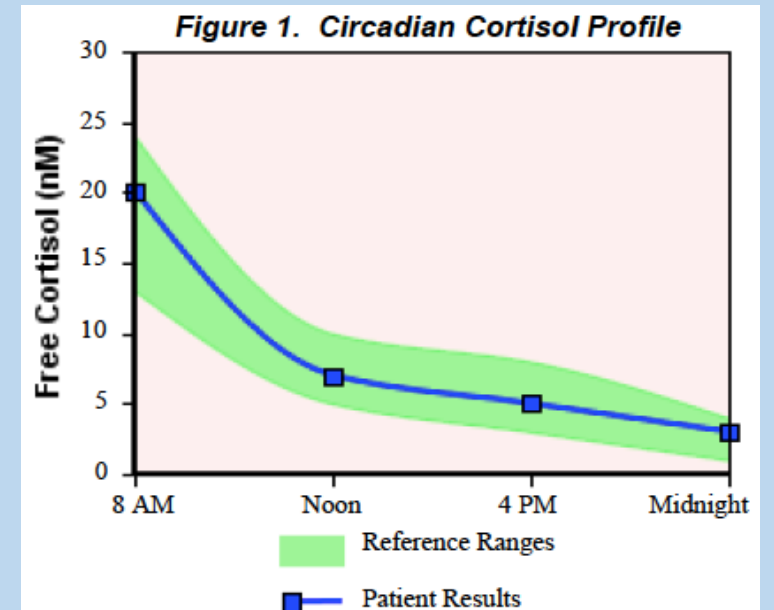
Adaptogens with Cytokine Lowering Action

- Ashwagandha/*Withania somnifera*
- Astragalus root/*Astragalus membranaceus*
- Holy Basil/*Ocimum sanctum*
- Maitake mushroom/*Grifola frondosa*



Chronic Acute Stress Mode

- 42 yr old man, with a family and a busy work schedule with lots of stress and responsibility. He often feels uptight and experiences a racing heart much like he drank too much coffee.
- He has trouble falling to sleep, sometimes it takes hours, he sleeps 4-5 hours/night, wakes with a start and a sense of dread sometimes. He has headaches more than ever and tends to be anxious and worrisome as of late. He finds himself more irritable at home and with the kids. No sexual energy.



Phase 1

Adaptogens & Nervine Botanicals

- Ashwagandha
 - Rhodiola
 - Maca
 - Schisandra Berry
 - Holy Basil
- Lemon Balm
 - Blue Vervain
 - Skullcap
 - Chamomile Flowers
 - Avena

Ashwagandha

Withania somnifera



- Root, Solanaceae
- Indian ginseng, Winter cherry
- Somnifera means “sleepmaking”
- Improves and conserves adaptive energy
- Tonic

Withania somnifera Ashwagandha



Actions;

- Adaptogen, amphoteric, anti-inflammatory, anti-oxidant, anti-anemic, anti-tumor, hypoglycemic agent, immune supportive, neuroendocrine tonic, regulates HPA axis, general tonic

Withania somnifera (Ashwagandha)

Effecting the neuroendocrine system

- Thyroid modulating
- Supports blood sugar metabolism
- Enhances conception, fertility issues
- Regulates HPA axis
- Neuro-protective effects



Withania and Thyroid

In vitro studies suggest;

- Decrease oxidative stress load
- Reduces lipid peroxidation
- Increases SOD and catalase
- Regulates serum T3 & T4 levels
- Regulates thyroid hormone conversion

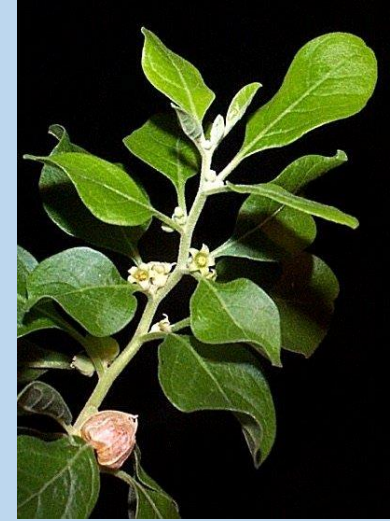
Autoimmune Thyroid Disease



Withania somnifera (Ashwagandha)

- Improves and conserves adaptive energy
- Increases stamina
- Immune modulator, anti-inflammatory
- Promoter of learning and memory retrieval; cognitive enhancer
- Tonic- debility, chronic exhaustion, low WBC, increases hemoglobin*, convalescence
- Failure to thrive in children*
- Post-partum, post miscarriage

Dosage for Withania



- 3-6 grams daily of the dried root
 - 6-15ml of a 1:2 fluid extract per day
 - 300-500 mg of an extract standardized to contain 1.5 percent withanolides
 - 125mg-250mg/d WSE- CVS/ Glucose regulation*
 - 125mg-500mg/d WSE for stress reducing effects*
-
- Generally safe. Large doses have been shown to cause gastrointestinal upset, diarrhea, and vomiting

Holy Basil

Ocimum sanctum



- Mental cloudiness from use of drugs and marijuana
- Uplifting
- Enhancing mental clarity and meditation
- 4-10mls/day 1:5LE
- 250-1000mg/d dry herb

Holy Basil

- Adaptogen, antiviral, galactogogue, radioprotective, hypoglycemic, anti-inflammatory, Cortisol regulator
- Enhancing metabolic functions and natural resistance
- Modulates innate stress response
- Reduces generalized anxiety
- Enhanced endurance
- Cortisol reducing compounds
- Ursolic acid, a constituent in Holy Basil, reveals it's activity as an anti-inflammatory and COX-2 inhibitor.
- Enhances the activity of glutathione S-transferase, a key enzyme in detoxification.

Anti-Depresso Pesto (Compliments Gaia Herbs)

- ½ cup fresh holy basil
- 1 ½ cup fresh sweet basil
- 1 cup Italian parsley
- 2-5 cloves fresh garlic
- 2 tsp lemon juice
- 3 to 3 ½ cups of Olive oil –
- Pine nut or other nut optional
- Puree well food processor



Holy Basil Butter

- ¼ to ½ cup fresh holy basil leaves
- 1/2 lb soft butter
- 1Tbsp olive oil or hemp oil
- Blend well in a blender or food processor until petals are specks in the soft butter
- Serve on rolls, toast, pancakes, corn bread, crackers, scones, crepes, rice and grains, sauces, veges, bake potato.....



Nootrophic Herbs

- **Improving memory** (spatial, long term, speed);
- **Keeping feelings of depression and anxiety under control**
- **Speeding-up the learning process**
- **Stimulating concentration and focus for sports performance**
- **Delaying onset of age-related cognitive decrease**
- **Enhancing dreams and sleep recovery**
- **Developing self-confidence**
- **Maintaining high mood and sharp social skills**

Holy Basil as a nootropic

- Increases mental clarity and focus
- Facilitates a shift in perspective
- Reduces mental inertia and even depression
- Restores hope and optimism
- Holy Basil increased motivation to make lifestyle changes and facilitated the ability to change perception of current circumstances.

Bhattacharyya D. Nepal Med Coll J. 2008;10(3):176-9



Siberian Asiatic Rose

Rhodiola rosea



- Rhizome,
- Crassulaceae family
- Cooling, dry
- Spicy bitter
- Enhances resistance to high altitude sickness
- Anemia
- Fertility enhancer

Rhodiola rosea

Active Constituents:

- Rosavin, rosin, rosarin, salidroside, rhodioloside, tyrosol, flavonoids (rodiolin, rodionin), phenolic antioxidants, including proanthocyanidins, quercetin, gallic acid, chlorogenic acid and kaempferol

Actions:

- Adaptogen, anti-depressant, antioxidant, anti-viral, immunomodulating, nervine, cardioprotective, neuroprotective, tonic
- Cardiovascular system – prevents stress-induced heart damage, arrhythmia, improves cardiac output

Rhodiola Clinical Indications



- Fatigue
- Anxiety
- Depression – mild to moderate, stress induced
- Moodiness
- Physical and mental performance
- Protects against the effects of stress, hypoxia, extreme temperatures, intense physical activity
- Neuroprotective

Winston, D.; Maimes, S. *Adaptogens. Herbs for Strength, Stamina and Stress Relief*, Healing Arts Press: Rochester, Vermont, USA, 2007.

Rhodiola rosea

- Increases memory, endurance, and productivity
- Improves mental capacity and accuracy
- Improves male sexual erectile dysfunction
- Anemia of pregnancy
- Insomnia, sleep disturbances
- Male and Female Fertility



Rhodiola rosea: Actions in the Brain

Brain Stem: Reticular Activating System

Cognitive Stimulation:

Improves: Norepinephrine
& 5-HT (Serotonin)



Cerebral Cortex

Improves: Cognitive Functions

Prefrontal & Frontal Cortex

Improves: Attention
Memory
Learning

Emotional Calming:

Improves: Norepinephrine
5-HT (Serotonin)
Dopamine
Acetylcholine



Limbic System Pathways

(Regulates Emotional Tone & Mood)



Hippocampus

Emotion
Memory
Vigilance



Amygdala

Emotion
Memory



Hypothalamus

decreases: CRF



Pituitary

decreases: corticotrophin



Adrenal Gland

decreases: Release of
Cortisol, Norepinephrine,
and Epinephrine



Forebrain Reward System

Pleasure, Satiety
Energy & Drive



Brain & Heart

Rhodiola Dosage



- 4-8 ml/d liquid extract
- 200-600mg/d dried root
- 100 mg of extract standardized to 3 percent rosavins and 0.8-1 percent salidroside, as the naturally occurring ratio of these compounds is approximately 3:1.
- A high dose-daily intakes of 1,000 mg

Rhodiola Dosage



- Mild – Moderate Depression-170 mg or 340 mg twice daily)/placebo for 6 weeks*
- Anti-fatigue - 200 mg three times a day
- Insomnia - 600mg dose**

*Darbinyan, V. et al; A. Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression. Nord. J. Psychiatry 2007, 61, 2343–2348

**Panossian A and Wikman G, Effects of Adaptogens on the CNS and the Molecular Mechanisms Associated with Their Stress-Protective Activity, Pharmaceuticals 2010, 3,188-224; doi:10.3390/ph3010188

Schisandra chinensis



- Fruit and Seed
- Schisandraceae Family
- Warming, dry
- Sour, sweet, bitter, salty, pungent
- Liver, kidney, heart, lungs, spleen
- Calming nerve tonic
- Dries excess fluids

Schisandra chinensis

Dosing

- 3-10 mls/day 1:3 liquid extract
- 2-6g/day dry fruit
- Avoid in pregnancy
- *No negative effects were observed on the somatic state of patients*

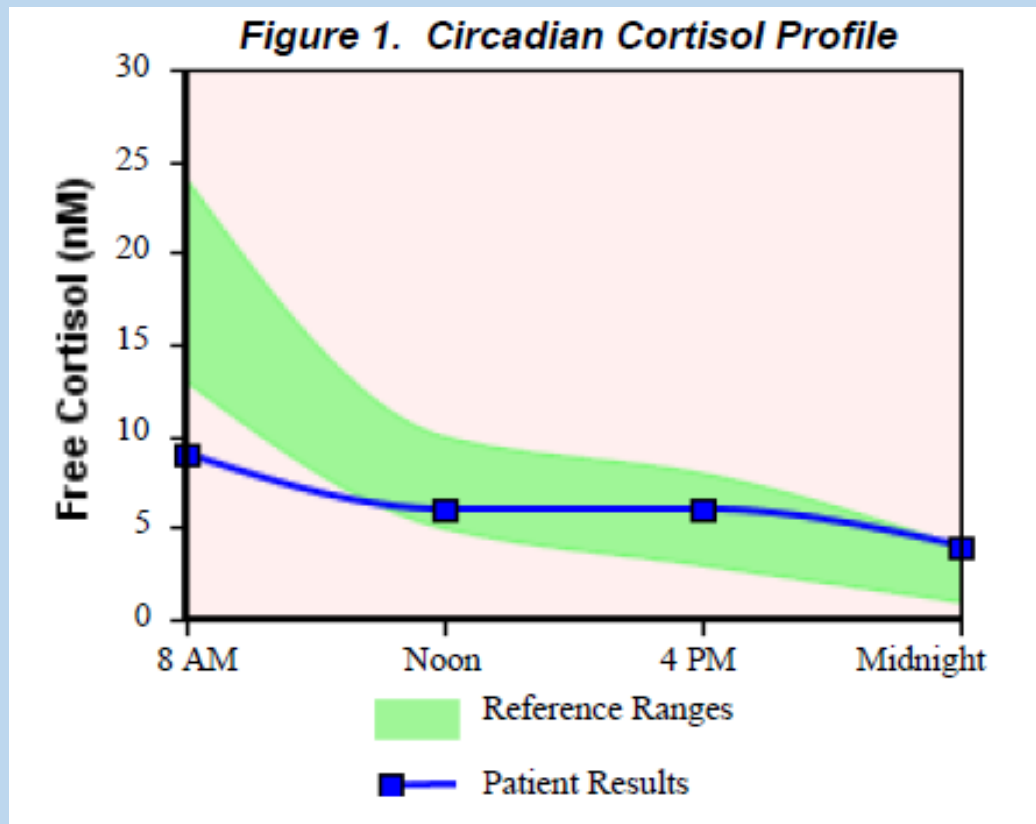


HPA Imbalance

Super Mom

- 36 year old with 2 young children under the age of 6, just weaned youngest child.
- Works full time as manager in large company, describes her job as high stress and her life very busy.
- Sleep is disrupted due to kids, often feels tired upon waking and gets anxious easily which can lead to heart palpitations.
- Not able to put on a little needed weight, vegetarian, and finds herself to startle easy and worry more.

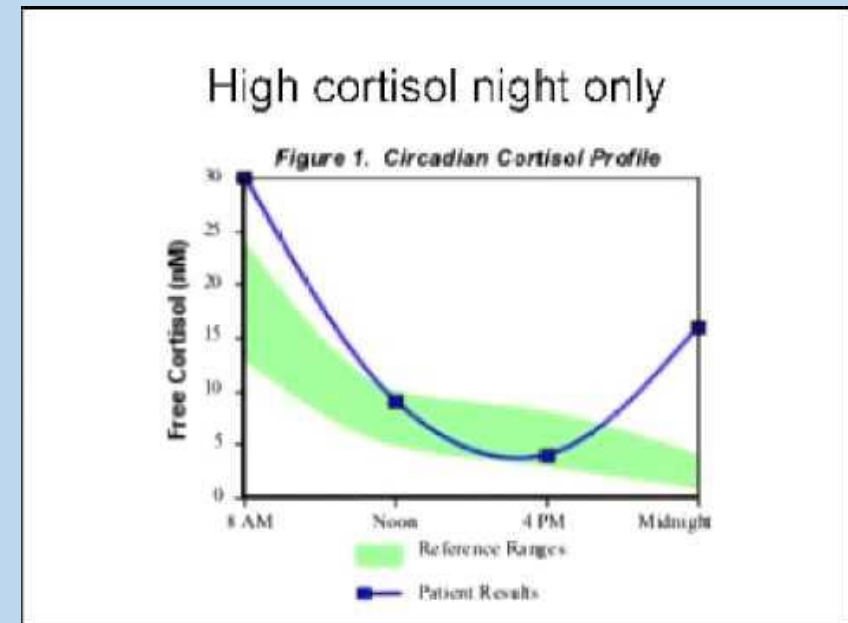
Chronic Acute Stress Mode



- Allostatic Load is Heavy
- More than the NeuroEndocrine Stress Response can handle in a healthy way.
- System is over taxed
- Stress maladaptation response
- Breakdown of Healthy & Wellness

Night Owl

- Never seems to get enough sleep, wakes up tired but able to get up and going.
- Always has a low time midafternoon looking for a sweet or caffeine to boost their energy.
- Notes that they feel tired soon after they evening meal or may even fall asleep for a short time while putting the kids to bed.
- After that she gets a second wind and may stay up to 1-2am doing things as the house is quiet and this is “her time.”
- Struggles with weight issues even though she exercises regularly.



Phase 2

Adaptogens & Supportive Botanicals



Adaptogens

- Ashwagandha
- Rhodiola
- Holy Basil
- Schisandra Berry
- Cordyceps
- Elethrococcus

Nervines

- Passionflower
- Valerian
- St John'swort
- Magnolia
- Mimosa Flowers

Night Cycle Adaptogen Formula



Ashwagandha:

Promotes a healthy sleep cycle by supporting the nervous system during nightly restoration.*



Cinnamon Bark:

Promotes healthy blood sugar function, which in turn supports the adrenals.*



Magnolia Bark:

Supports the HPA axis, healthy cortisol production and restful sleep.*



Vervain:

Supports a healthy fight-or-flight response, as well as a healthy and calm mood.*



Albizia Bark:

Promotes a healthy balance of the parasympathetic and sympathetic nervous systems.*



Reishi:

Tonifies while promoting healthy energy levels, healthy breakdown of hormones by the liver and normal sleep cycles.*



Lemon Balm:

Supports the body's natural state of calm & restoration*



Cordyceps:

Supports healthy stamina and physical energy levels while providing immune support.*

Eleutherococcus senticosus



- Root, Araliaceae
- Expels wind dampness
- Sweet, slightly warming, slightly bitter
- Moves obstructions causing swellings
- Increases alertness, cognitive function and energy

Eleutherococcus senticosus

- Immunotonic, adaptogen, neuro-protective, hepato-protective, gastro-protective, anti-oxidant, anxiolytic
- Regulates blood sugar levels for hypo & hyper
- Improves use of glycogen and high energy phosphorus compounds
- Improves metabolism of lactic and pyruvic acids leading to better energy production

Farnsworth, N. et al; Siberian Ginseng (*Eleutherococcus senticosus*): Current status as an adaptogen. In *Economic and Medicinal Plant Research*; Wagner, H., Hikino, H., Farnsworth, N.R., Eds.; Academic Press: London, UK, 1985; Volume 1, pp.156–209.

Eleutherococcus senticosus

- Effects of prolonged stress, fatigue, insomnia, depression, post surgery/ trauma/ chemotherapy
- Normalizes leukocyte levels
- Improves reproductive capacity and uterine health (rhodiola and astragalus)
- Counteracts hypertrophy and atrophy of the thyroid and adrenal glands

Eleutherococcus Dosage

- 3-10mls/day 1:3 liquid extract daily
- 10-15 mls 1:5 tincture daily
- 1-4 gr/day dry root
- Standardized preparations of Eleutheroside E
- 2gr/day reduces frequency of recurrent herpes simplex outbreaks*
- Combines well with Rhodiola and Schisandra

Cordyceps



Scientific names: *Cordyceps sinensis* & *militaris*

Aka Caterpillar mushroom

In nature, this parasitic fungus grows on the caterpillar larvae of a moth.

Grows in the highlands (10,000 feet) of China, Tibet and Nepal

Recently, cultivated varieties (*Cordyceps militaris*) have been developed. These Cordyceps fruiting bodies are cultivated on nutritious barley substrate, and they are therefore vegan. Research has shown that *C. militaris* and *C. sinensis* provide similar support, and they are used interchangeably in TCM and other branches of herbalism.* Our Cordyceps (*C. militaris*) are processed by hot water extraction into a fine powder.

Cordyceps

Bioactive compounds:

Cordycepic acid (aka D-mannitol)

Many polysaccharides demonstrating lipid-lowering ability, blood sugar-lowering effect, immunostimulating and radioprotective activity

18 amino acids, many micronutrients

Saponin compounds researched for their tumor-inhibiting effects



Cordyceps

Action:

Anti-inflammatory, antioxidant, anti-tumor, adaptogen, immunomodulatory, endocrine modulator, hypolipidemic, tonic

Promotes restoration and regeneration



Cordyceps in nature

Sourcing:

We use only fruiting bodies not substrate.

Cordyceps

- Decreases fatigue and increases physical endurance, vigor, and energy
- Enhances athletic performance and training
- Builds vitality when recovering from stress
- Oxygen free-radical scavenger
- Regulates testosterone and cortisol



- Supports liver function and acts to protect the liver from stressors, aids regeneration
- Immune regulating, building, and supporting to normal cell growth and development

Safety: Research on this mushroom shows complete safety when consumed in recommended doses

Magnolia

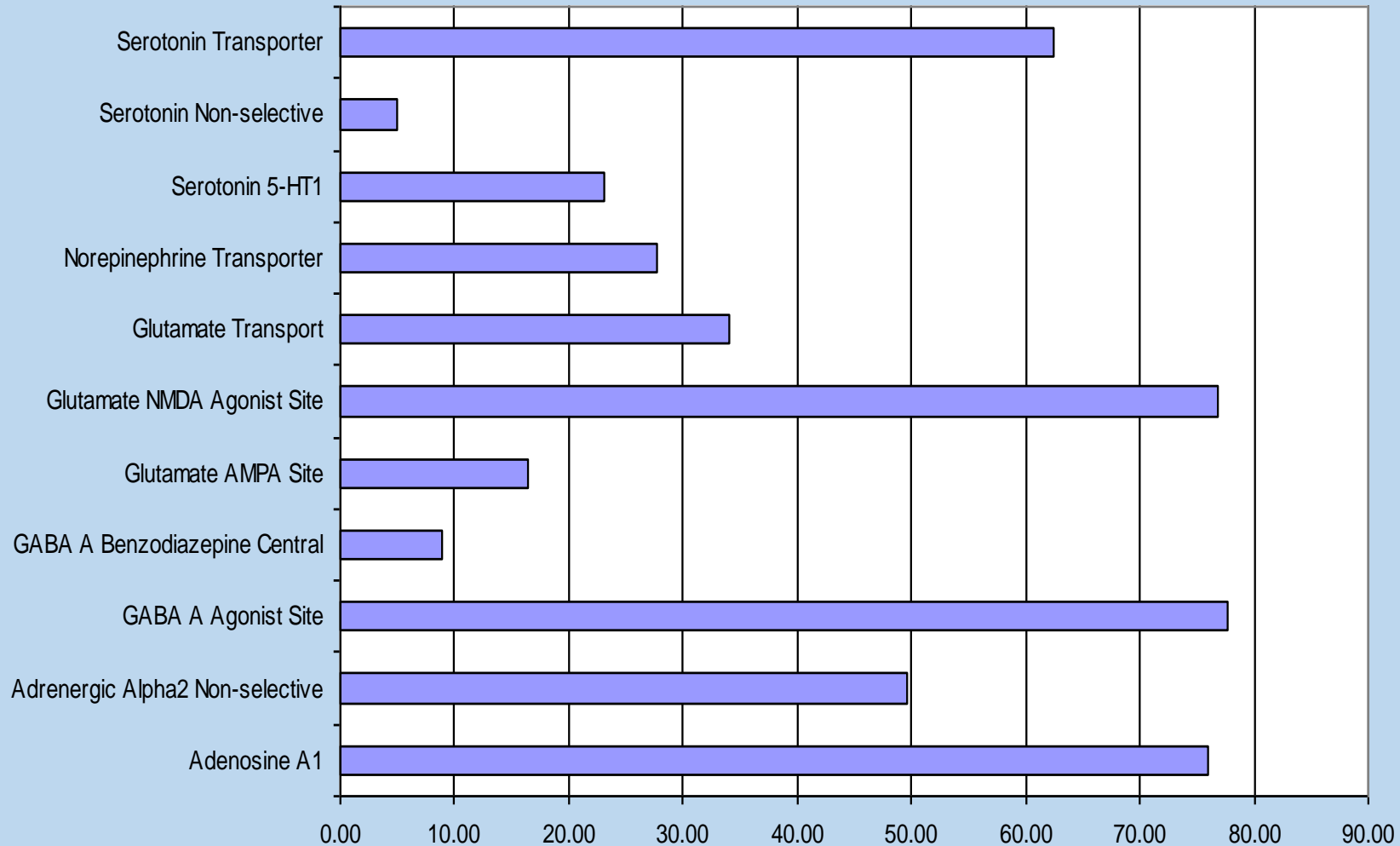
Magnolia officinalis
Bark



Anxiety and Adrenals

- Magnolia (*Magnolia officinalis*),
- Overweight premenopausal women
- A decrease in transitory anxiety, although salivary cortisol levels were not significantly reduced.
- Magnolia has been demonstrated to improve mood, increase relaxation, induce a restful sleep and enhance stress reduction.

Magnolia Binds to Several Important Targets Associated With Drowsiness:



Magnolia References

- Cortisol and Mood

<http://www.ncbi.nlm.nih.gov/pubmed/23924268>

- Anti-inflammatory Suppresses NF-kB

<http://www.ncbi.nlm.nih.gov/pubmed/24893579>

- Honokiol, a Multifunctional Antiangiogenic and Antitumor Agent <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2842137/>

- Enhanced GABAergic Neurotransmission in Hippocampal Neurons

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3652012/>

Magnolia

Dose: 160 mg to 500 mg depending on weight/condition of patient

- Refers to total neolignans (usually magnolol plus honokiol), which are usually at 1-10% of a basic bark extract
- Centuries of Traditional Use

Caution : Safety data is not substantial. Avoid in pregnancy due to possible oxitocic effects

Mimosa

Albizia julibrissin

Scientific name: Tree of Happiness

“Calms the spirit”

“Relieves constrained emotions”

Parts used: Bark and flower

Has an acrid taste

Actions: Anxiolytic,
anti-microbial, anti-oxidant, anti-inflammatory, anti-asthma, nervine,
hepatoprotective and lipid-lowering



Mimosa Tree



Bioactive Compounds:

- High in saponins in many forms: triterpenes, monoterpenes, flavone saponins, alkaloids and flavonoids
- Flowers high in Quercetin and Isoquercetin

Mimosa Bark

Nervine with immune-regulating and cancer-inhibiting effects.

5-HT receptor binding – depression, anxiety, irritability

Neurotransmitter mechanisms via GABA, dopamine and serotonin

Supports:

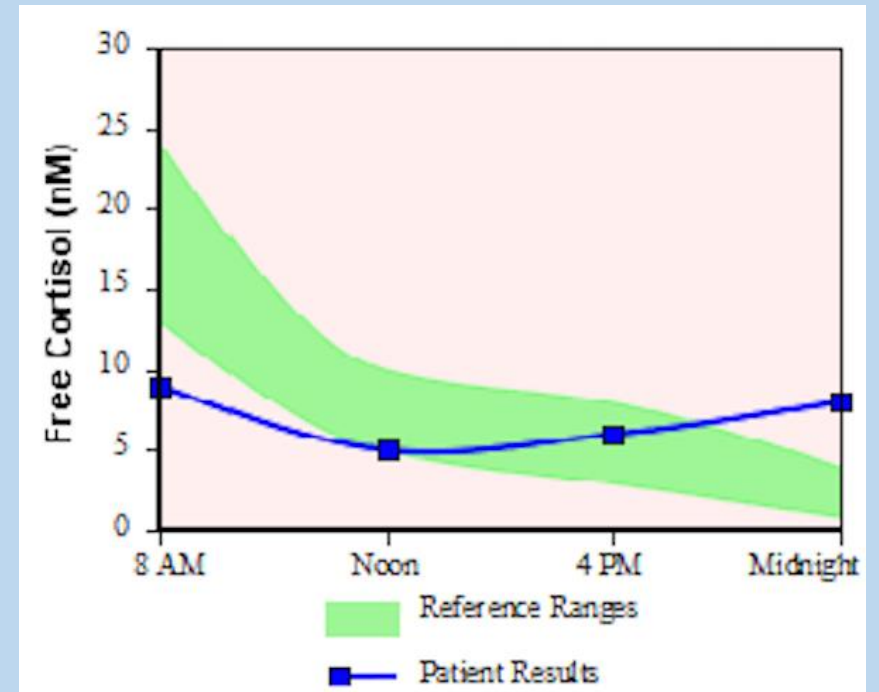
- Person with low blood pressure, low mood, low thyroid, anxiety and poor energy
- Parasympathetic-dominant person
- Low thyroid function with female hormonal aggravation and low mood
- Linking endocrine system to the nervous system via the pituitary gland
- Decreases sleep latency
- Poor memory, mind chatter

Who Might That Be

- Adrenal Exhaustion, Fatigue, Maladaptation
- At this point the adrenal system is failing, they may have dizziness with bending over or getting up too fast, may have anxiety or panic attacks for no specific reason, sleep disruption often waking a number of times in the night with the best sleep coming in the morning hours, difficult waking in the morning, Deals with anxiety, fatigue, brain fog, depression and forgetfulness. Chronic pain and discomfort get in the way of activities and exercise.

Wired and Tired

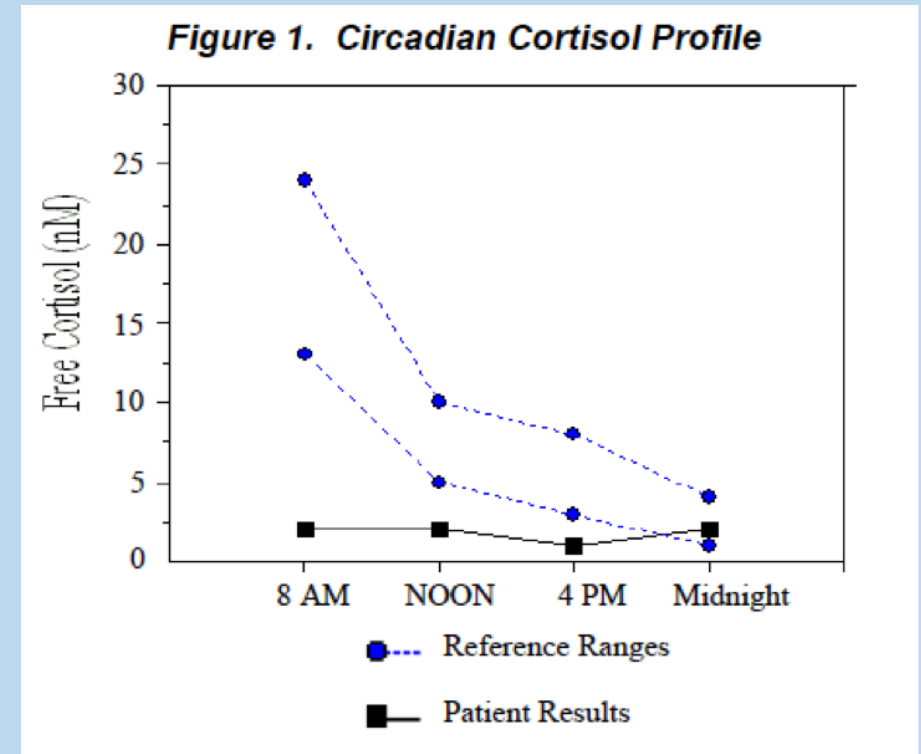
- This person wakes in a fog, takes a long time to wake up “has to have their caffeine fix”, feels draggy most of the day, finding hard to focus and concentrate until later in the day.
- They get more energized as the day goes and finds the evening a high energy time.
- They have difficulty winding down from the day and though they may feel tired at 11pm they don't fall asleep until 1am most nights.
- Has a very active mind that goes into overdrive once in bed



Who Might That Be

Adrenal Burnout

This person has had life challenging situations for several years. Examples of this could be graduate student, very stressful job, several pregnancies with breastfeeding periods close together, PTSD, chronic fatigue issues, super athlete for several years coupled with acute injury to body over that time and a very busy life



Phase 3

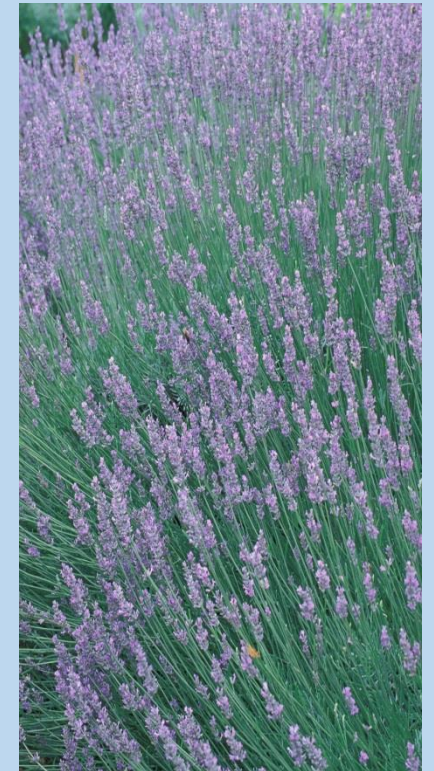
Adaptogens & Supportive Botanicals



- Licorice
- Rhaponticum
- Cordysep
- Ashwagandha
- Rhodiola
- Holy Basil
- Korean Ginseng

Nervines

- Lavender flowers
- Mimosa
- Blue Vervain
- Magnolia Bark
- Tonic Nervines
Scutellaria, Avena, etc



Day Cycle Reinforcing Adaptogen Formula



Rhodiola:

Supports the body's natural resistance and adaptation to both physical and emotional influences.*



Rhaponticum:

Supports physical and mental endurance and natural resilience, in conjunction with the body's normal stress response.*



Eleuthero:

Enhances the body's natural ability to adapt to stress, while supporting mental endurance and metabolic efficiency.*



Schisandra:

A traditionally harmonizing tonic that promotes natural balance within the endocrine system by supporting the liver.*



Licorice Root:

Supports healthy adrenal function and promotes vitality while maintaining efficient use of normal cortisol levels.*



Korean Ginseng:

Assists the body in adapting to stress and supports normal levels of stamina and endurance.*



Prickly Ash:

Tonifying herb that promotes healthy flow of energy and healthy circulation*



Cordyceps:

Supports healthy stamina and physical energy levels as well as overall endocrine health while offering antioxidant support.*

Licorice

Glycyrrhiza glabra



Root, leguminosae

Clears heat, moistens membranes

Balances and harmonizes herbal
formulas

Adrenal Gland Tonic

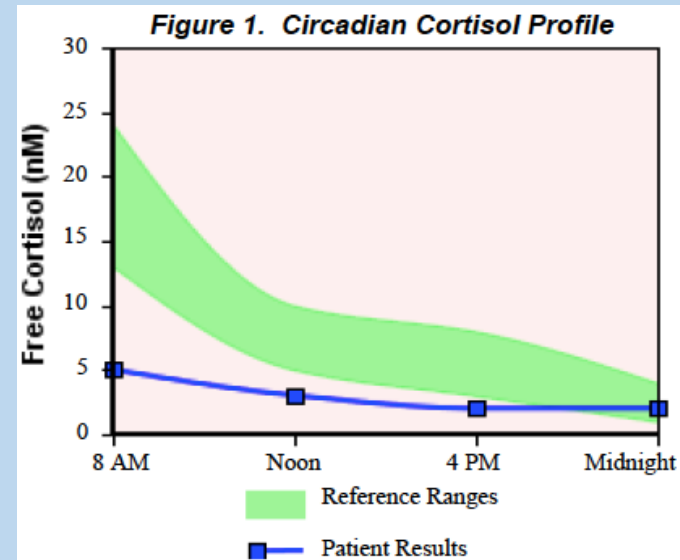
Tones qi

5-10 mls/day 1:5 liquid extract

1-4g/day dry root

Support the cortisol cycle

- Licorice Root – helps decrease the breakdown of cortisol thereby effectively increasing cortisol levels. If your cortisol levels are very low then you may benefit from licorice root supplementation at the appropriate times of the day
- Adaptogens to support anabolic metabolism



Glycyrrhiza glabra

Adrenal restorative

Anti-inflammatory, mucoprotective,

Moves mucus from the respiratory system

PCOS- regulate testosterone levels,

Reduces irritation of the body's mucus membranes

Can raise the blood pressure if pre hypertensive

Rhaponticum



Rhaponticum carthamoides

Common name: Leuzea or Maral Root, derived from the fact that the Maral deer fed on this plant.

Root

Herbaceous plant native to the sub-alpine and alpine meadows of Siberia. Traditionally used as an energizing or tonic remedy after long Siberian winters

This plant was often combined with *Rhodiola rosea* in traditional Siberian folk medicine and is still used by modern Russian athletes.

Rhaponticum

Active Constituents:

Levseins (over 10 different ecdysterones), which increase activity of the cellular compartments where protein synthesis takes place, thus enhancing muscle protein synthesis

25 years of research and clinical study has gained this plant entry to the *Official Russian Pharmacopoeia*.

Recommended for: increasing work efficiency, athletic performance and recovery after muscular workloads. Stimulates muscle growth by increasing protein synthesis in the muscle.



The Real Deal: A synthetic version was manufactured in Russia and the US, but the Rhaponticum extract proved superior to both synthetic versions.

Rhaponticum

How does Rhaponticum affect the physiology?

- Promotes anabolic metabolism, preserves mitochondria
- Increases working capacity of skeletal muscle and their content of glycogen for fuel and increases ATP
- Increases glycogen to the brain, liver and muscles; has mental and physical anti-fatigue effects



- Increases oxidative enzyme systems, decreases lipid peroxidation acting as a free-radical scavenger
- Enhances protein synthesis in muscle tissue, builds lean muscle mass
- Increases muscle recovery, supports structural integrity of muscle
- Decreases fat deposition
- Restoration of lowered IgG, IgA and C3 concentrations, improving humoral immunity

Reishi

Active constituents:

- Polysaccharides
- Immunomodulating proteins
- Steroidal saponin glycosides

Influences:

- Adrenal-hypothalamic-pituitary axis
- Regulates inflammation
- Circadian rhythm
- Sleep cycles
- Reduces stress

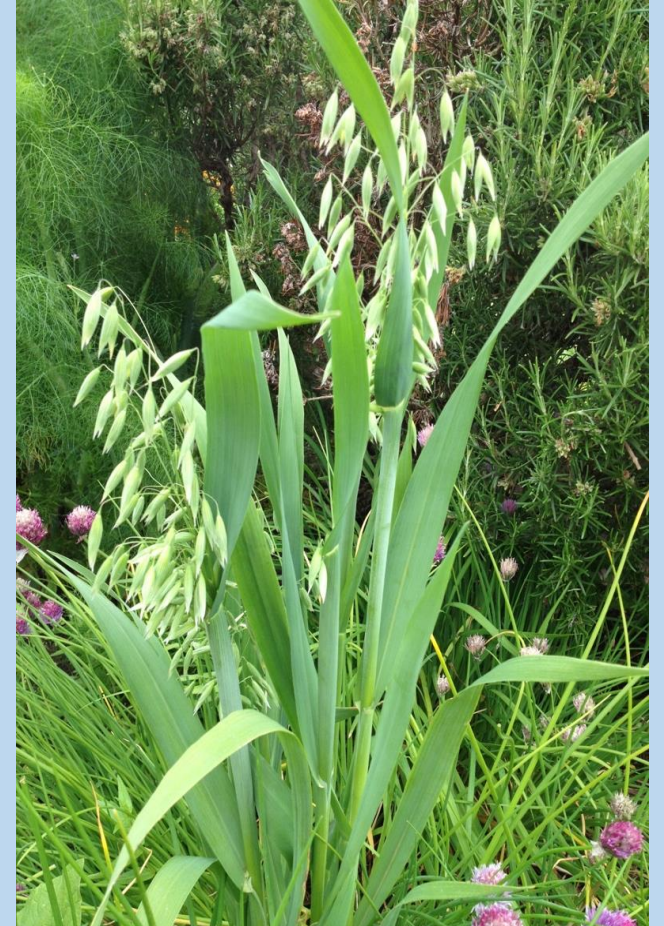


Herbal Protocol for 24 Hour Support

	Recover & Rebalance	Daily Support	Sleep Support
Possible Botanicals of Relevance	Asian Ginseng, Cordyceps, Eleuthero, Licorice, Prickly Ash, Rhaponticum, Rhodiola, Schisandra	Ashwagandha, Holy Basil, Oats, Rhodiola, Schisandra	Ashwagandha, Cordyceps, Lemon Balm, Magnolia, Mimosa, Reishi, Vervain
Mechanism/Intention	Deep support of the HPA Axis, for those in state of adrenal fatigue/exhaustion.	Adaptogens to help the HPA Axis deal with and adapt to everyday stressors; Foundational and supports adrenal function;	Restores HPA Axis function at night promoting a healthy sleep cycle, repair, growth and restoration
Dosage/Usage	Short term use, 8-12 weeks until HPA Axis achieves a state of homeostasis. Then move to a daily support formula.	Daily dose, in the morning or before noon intended for long-term use	Daily dose, in the evening after dinner. Take in conjunction with a daytime formula.

Botanical Nervines

- CNS relaxant (mild)
 - Anti-epileptic
 - Analgesic
 - Anxiolytic
- Hypnotic (mild)
- Sleep architecture improver
- Anti-spasmodic
- Balance autonomic nervous system
- Influence neurotransmitter production
- Not sedating
- Anti-addiction (maybe)



Botanical Nervine Summary

- Lemon Balm
 - Attention, focus, cognitive function, memory
 - Insomnia, restlessness, hyperactivity
 - Mood elevation, anxiety
- Passion Flower
 - Insomnia
 - Generalized anxiety
 - Hyperactivity, nervousness
- American Skullcap
 - Nervous irritation, fear, anxiety
 - Depression
 - Substance withdrawal
- Chamomile Flowers
 - Agitation, worry, nervousness, anxiety
 - Insomnia, restlessness
 - Mood elevation



Botanical Nervines

- *Avena Sativa*/ Milky Oats
- *Centella asiatica*/ Gotu Kola
- *Ginkgo biloba*/ Gingko
- *Humulus lupulus*/ Hops
- *Lavedula spp*/ Lavender Flowers
- *Nepeta cateria*/ Catnip
- *Piper methysticum*/ Kava kava Root
- *Tillia odorata*/ Linden Flowers



Thank you
and have a
lovely Herbal
Conference

Questions ?

