THE

integrative
women's health

INSTITUTE

presents

Fitness, Lifestyle, and Nutrition to Address Common Perimenopausal Concerns PRESUMMIT PROGRAM

Jessica Drummond, DCN, CCN, PT

PART 1: The Scope of the Problem

“I’m exhausted, brain foggy, and have no desire for sex? I’m 40, not 80. How did I get here?”

What is Menopause/ Perimenopause?

- **Menopause** is the permanent cessation of menstruation resulting in the loss of ovarian follicle development.

- When does menopause occur?

- Genetically determined
- Not affected by race
- Not affected by socioeconomic status
- Not affected by age at menarche
- Not affected by number of prior ovulations

Dalal, P. K., & Agarwal, M. (2015). Postmenopausal syndrome. Indian Journal of Psychiatry, 57(Suppl 2), S222–S232. http://doi.org/10.4103/0019-5545.161483

What is Menopause/ Perimenopause?

- Factors that are **toxic to the ovary** often result in an earlier age of menopause:
- Smoking
- Ovarian surgery
- Hysterectomy (even with ovary retention)

- **Premature ovarian failure** is defined as menopause before the age of 40 years.
- Idiopathic or associated with toxic exposure, chromosomal abnormality, or autoimmune disorder *(I have seen cases of reversal with healing of autoimmunity/ decreasing toxic load.)*

Dalal, P. K., & Agarwal, M. (2015). Postmenopausal syndrome. Indian Journal of Psychiatry, 57(Suppl 2), S222–S232. http://doi.org/10.4103/0019-5545.161483

The Most Common Concerns Reported in The Perimenopausal Years…

- The menopause transition is experienced by **1.5 million women each year** in the US.
- Common symptoms, including vasomotor symptoms (hot flashes and night sweats), vaginal dryness, decreased libido, insomnia, fatigue, and joint pain.

Santoro, N., Epperson, C. N., & Mathews, S. B. (2015). Menopausal Symptoms and Their Management. Endocrinology and Metabolism Clinics of North America, 44(3), 497–515. http://doi.org/10.1016/j.ecl.2015.05.001

The Most Common Concerns Reported in The Perimenopausal Years…

- In one population-based assessment of **386 Australian women…**
- ***86% consulted a clinician at least once to discuss menopausal symptoms***

- During menopause, women may develop depressive symptoms and cognitive difficulties, which are more subtly and inconsistently linked to hormones.
- Postmenopausal women are also at increased risk for osteoporosis and cardiovascular disease.

Santoro, N., Epperson, C. N., & Mathews, S. B. (2015). Menopausal Symptoms and Their Management. Endocrinology and Metabolism Clinics of North America, 44(3), 497–515. http://doi.org/10.1016/j.ecl.2015.05.001

The Most Common Concerns Reported in The Perimenopausal Years…

- 60% of perimenopausal women report brain fog, memory loss, and reduced cognitive endurance

- Anecdotally, 40% of women in their 30's and 40's experience lack of desire.
- 12% meet the clinical criteria for low sexual desire.

The Perimenopause Transition

- An average of 4 years, but can be up to 10-15 years.
- Usually starts in the 40’s, but can naturally begin in the 30’s.
- Estrogen fluctuations, and cycle length variations.
- ***These changes are normal in most cases, but how can we soothe the transition to be less symptomatic and gentler?***

http://www.webmd.com/menopause/guide/guide-perimenopause#1
https://my.clevelandclinic.org/health/articles/what-is-perimenopause-menopause-postmenopause

How prevalent is perimenopausal brain fog, memory impairment, and reduced cognitive endurance for 40-55 year old women?

How Common is Reduced Cognitive Function in Perimenopause?

- The Seattle Midlife Women's Health Study: of 230 women aged 33 to 55 years who were interviewed about their perceived cognitive function, **60% noticed an unfavorable memory change "over the past few years."**
- The Study of Women's Health Across the Nation (SWAN): Forgetfulness was common in middle age: in this sample of 12,425 women aged 40–55 years, 44% of early or late perimenopausal women endorsed forgetfulness.
  - **Perimenopausal women were 1.4 times more likely to report forgetfulness than were premenopausal women.**

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of cognitive impairments and low libido common in or related to perimenopause.

Mechanisms of Cognitive and Libido Impairments in Perimenopause

- **Decline in Estrogen:** Estrogens have neurophysiologic effects, thus it could be the case that a drop in estrogen (which occurs during perimenopause) would be detrimental to cognition.
  - The hippocampus and prefrontal cortex, which serve episodic and working memory, are rich in estrogen receptors.
  - Low estrogen—> decreased vaginal and joint lubrication.
  - Estrogen modulates serotonin receptors in the brain.

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive Impairments in Perimenopause

- **Decline in Estrogen:** Estrogens have neurophysiologic effects, thus it could be the case that a drop in estrogen (which occurs during perimenopause) would be detrimental to cognition.
  - In animal and in vitro models:
    - Estrogens elevate levels of neurotransmitters such as serotonin and acetylcholine
    - Estrogens promote neuronal growth and formation of synapses
    - Estrogens act as antioxidants

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive Impairments in Perimenopause

- **Estrogen's effect on distinct brain regions in perimenopause:**
- In a series of neuroimaging studies, healthy premenopausal women underwent pharmacological ovarian hormone suppression with leuprolide acetate (*Lupron - think endometriosis!), and given a verbal memory task.
- Hormone suppression produced decreased activation in the left prefrontal cortex, anterior cingulate, and medial frontal gyrus.
- A subsequent study demonstrated that brain function returned to baseline when ovarian hormone levels returned to normal.

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive Impairments in Perimenopause

- **Estrogen's effect on distinct brain regions in perimenopause:**
- The combination of estrogen suppression and cholinergic suppression led to dramatic decreases in activity in the left inferior frontal gyrus during verbal encoding.
- The left inferior frontal gyrus is involved in processing of the meaning of verbal material.
- These data suggest that estrogen withdrawal might negatively affect the extent to which verbal information is meaningfully processed.

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive Impairments in Perimenopause

- **Estrogen's effect on distinct brain regions in perimenopause:**
- A recent fMRI study investigated brain function in two groups of women, one that initiated hormone therapy beginning in perimenopause and continuing to older age, and the other that used no menopausal hormone therapy.
- The neuroimaging task was a delayed word list task (verbal memory) that included an encoding phase, a 15-minute delay, and a retrieval phase to parallel clinical neuropsychological measures of verbal memory.
- **Early continued use of estrogen was associated with enhanced verbal memory and enhanced function in the hippocampus during memory retrieval.**

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive and Libido Impairments in Perimenopause

- **HPA Axis Dysregulation:**
  - Women with high cortisol levels or greater cortisol reactivity, have correlated symptoms of hot flashes, depressive or anxiety symptoms, and declines in cognitive performance.
  - Experimental administration of corticosteroids produces verbal memory impairment, and higher endogenous cortisol levels are associated with poorer performance on memory tasks.

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Do perimenopausal brain fog, memory issues, and reduced cognitive endurance, increase a woman's risk for Alzheimer's, dementia, or other disabling brain health issues that we normally associate with the elderly?

YES! Risk for Alzheimer's and Other Dementias can be Increased

- Because of the impact of dysglycemia and inflammation on neuronal health that often begins or worsens in perimenopause…
- A reduction in brain glucose metabolism (associated with altered insulin signaling) has been shown to be a preclinical symptom of AD.
- Increased adiposity (especially abdominal adiposity) elevates neuroinflammation, which has been implicated as a pathologic mechanism in AD.

Christensen, A., & Pike, C. J. (2015). Menopause, obesity and inflammation: interactive risk factors for Alzheimer's disease. Frontiers in Aging Neuroscience, 7, 130. http://doi.org/10.3389/fnagi.2015.00130

YES! Risk for Alzheimer's and Other Dementias can be Increased

- Perimenopausal women with Mild Cognitive Impairment (MCI), episodic memory loss without dementia, are more likely to progress to dementia (including Alzheimer'd disease.)
- **Over half of those with MCI will develop dementia within 5 years**, especially AD - BUT, that also means that lots of people with MCI will not develop dementia. (*good news!)
- **MCI can be regarded as preclinical dementia, and the prevention of it is very important clinically.**

Kim, S. A., & Jung, H. (2015). Prevention of Cognitive Impairment in the Midlife Women. Journal of Menopausal Medicine, 21(1), 19–23. http://doi.org/10.6118/jmm.2015.21.1.19

CLINICAL GOAL: Reduce MCI in Perimenopausal Women

- **HOW?**
- Address stress (cortisol quantity and rhythm)
- Right size estrogen
- Balance blood sugar
- Feed the brain necessary nutrients, such as iron, vitamin D, and omega-3 fats
- Absorb nutrients
- Calm inflammation
- Optimize mitochondrial function —> quench oxidative stress

Why are the Risks of Cardiovascular Disease and Stroke increased in Perimenopause —> Menopause?

How Does the Menopausal Shift Affect Cardiovascular Disease?

- Indian study:

- A cross-sectional comparative study on 100 women who were either postmenopausal or premenopausal and were between the **age group of 40 to 55 years** was carried out over a period of ten months. at our hospital.

- Women with premature/surgical menopause, renal disease, liver disease, endocrine disorders including diabetes mellitus, alcohol consumption, smokers and those with collagen vascular disease as well as women taking any form of hormone replacement therapy were excluded.

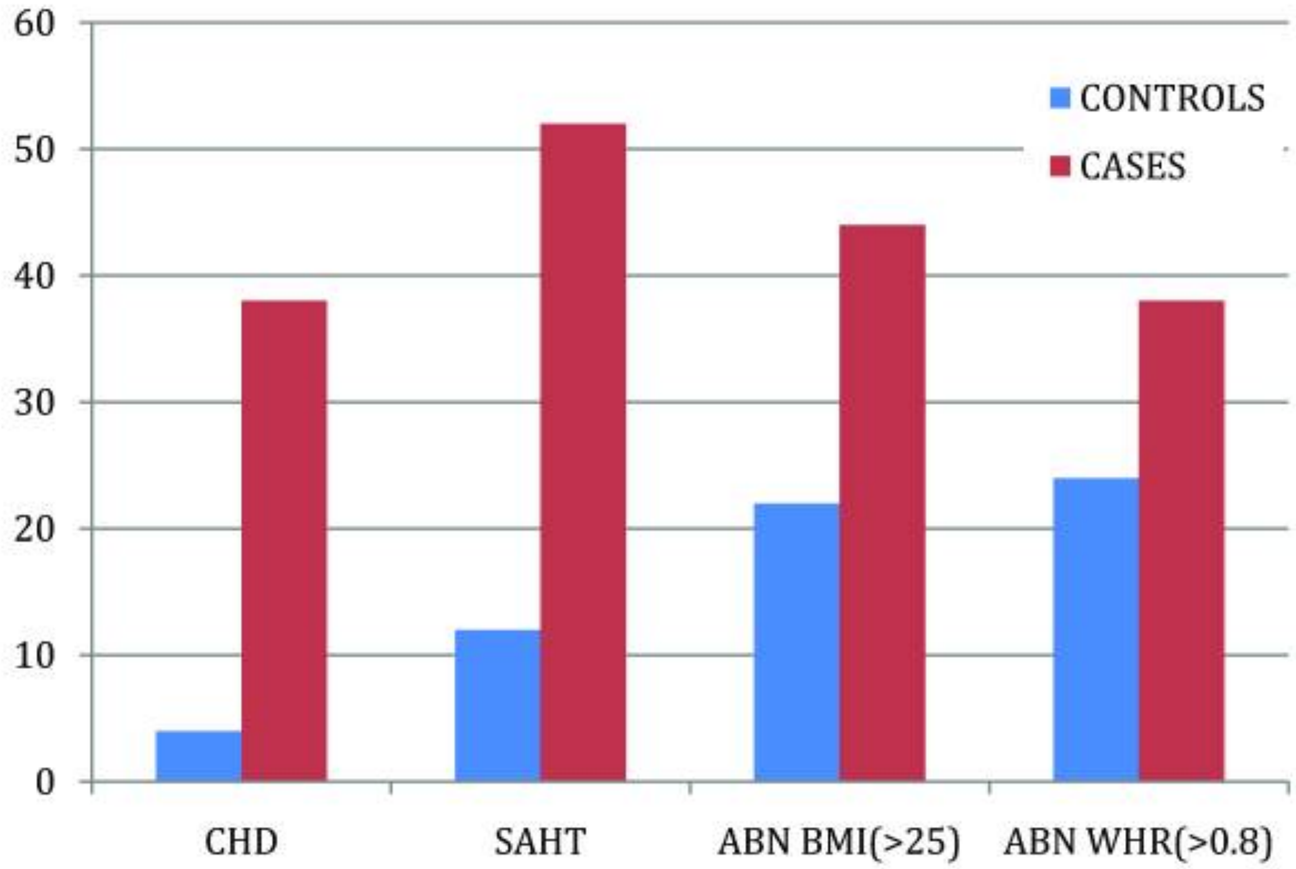
Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009

Does the Menopausal Shift Affect Cardiovascular Disease RISK?

- **YES!** The CAD prevalence was 38% (19/50) among postmenopausal women and 4% (2/50) in the control population ($p<0.001$).
- Hypertension was present in 52% (26/50) of the cases and 12% (6/50) of the controls ($p <0.001$).

Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009

How Does the Menopausal Shift Affect Cardiovascular Disease?



Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009

How Does the Menopausal Shift Affect Cardiovascular Disease?

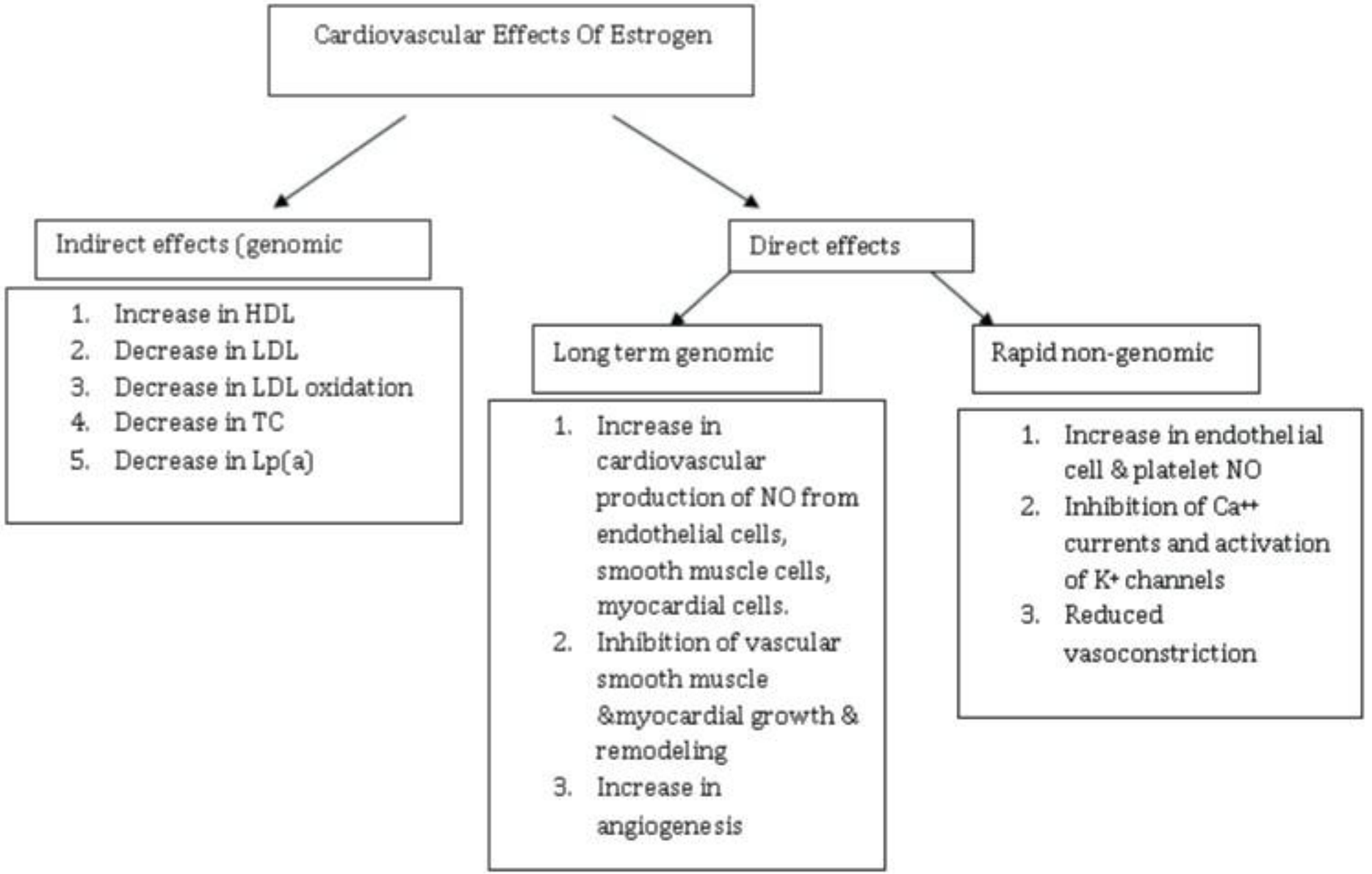
- Coronary Artery Disease (CAD)
- Hypertension (high blood pressure)
- Abnormal Body Mass Index (BMI) - modifiable!
- Abnormal Waist Hip Ratio (WHR) - modifiable!
- Abnormal Lipid Profiles were significantly higher in the postmenopausal group as compared to the premenopausal group. - modifiable!

Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009

How Does the Menopausal Shift Affect Cardiovascular Disease?

- **The postmenopausal women with a normal lipid profile also had increased prevalence of CAD and SAHT, which emphasizes the non-lipid cardiovascular benefits of estrogen. -** not modifiable? (enough peripheral and adrenal estrogen/ early HRT?)

Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009



Dosi, R., Bhatt, N., Shah, P., & Patell, R. (2014). Cardiovascular Disease and Menopause. Journal of Clinical and Diagnostic Research : JCDR, 8(2), 62–64. http://doi.org/10.7860/JCDR/2014/6457.4009

Brain Effects of Estrogen

- Enhances synaptic plasticity, neural growth, hippocampal neurogenesis, and long-term potentiation.
- Estrogen protects against apoptosis and against neural injury in a variety of experimental settings—> including toxicity induced by excitatory neurotransmitters, β-amyloid, oxidative stress, and ischemia.

Henderson, V. W. (2008). Cognitive Changes After Menopause: Influence of Estrogen. Clinical Obstetrics and Gynecology, 51(3), 618–626. http://doi.org/10.1097/GRF.0b013e318180ba10

Brain Effects of Estrogen

- Estrogen influences several neurotransmitter systems, including acetylcholine, serotonin, noradrenalin, and glutamate.

- Acetylcholine is important in memory processes.

- Prothrombotic properties of some estrogens may contribute to cerebrovascular disease, and vascular pathology increases dementia severity in the presence of Alzheimer pathology.

Bottom Line: Estrogens are both good and bad for brain and heart health. Right sized estrogen levels in the context of healthy adrenal and thyroid hormones are key.

Henderson, V. W. (2008). Cognitive Changes After Menopause: Influence of Estrogen. Clinical Obstetrics and Gynecology, 51(3), 618–626. http://doi.org/10.1097/GRF.0b013e318180ba10

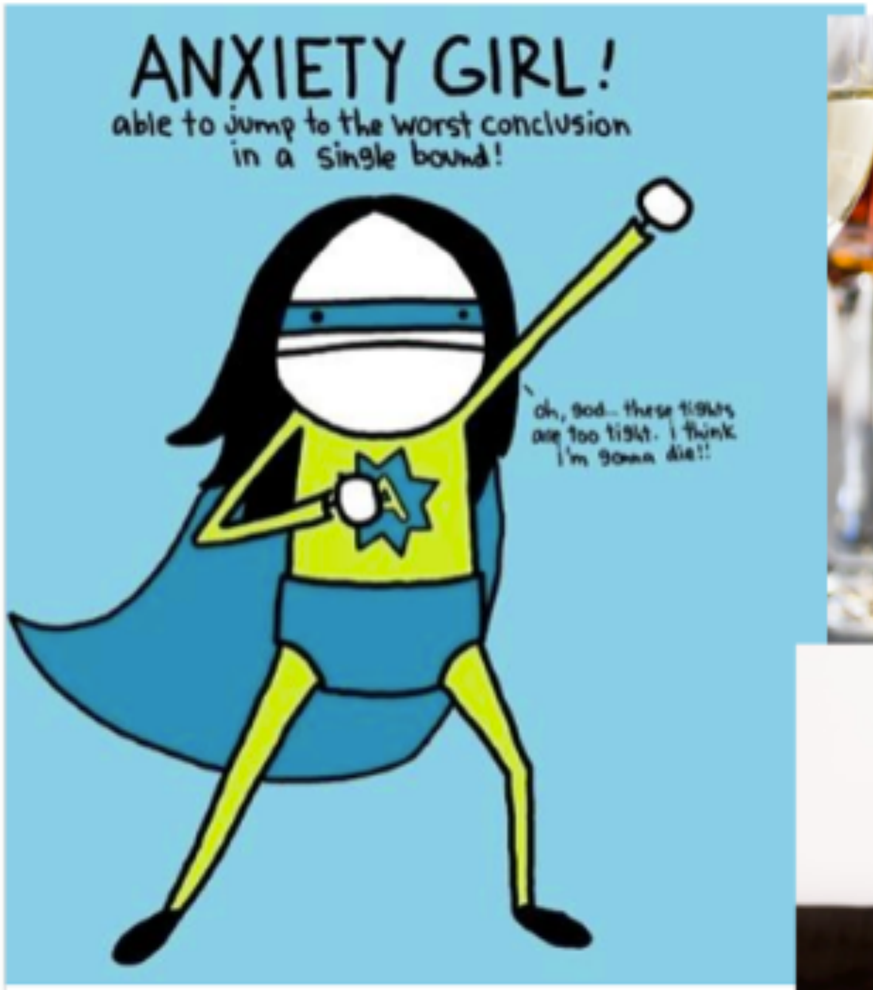
CLINICAL GOAL: Reduce CAD in Perimenopausal —> Menopausal Women

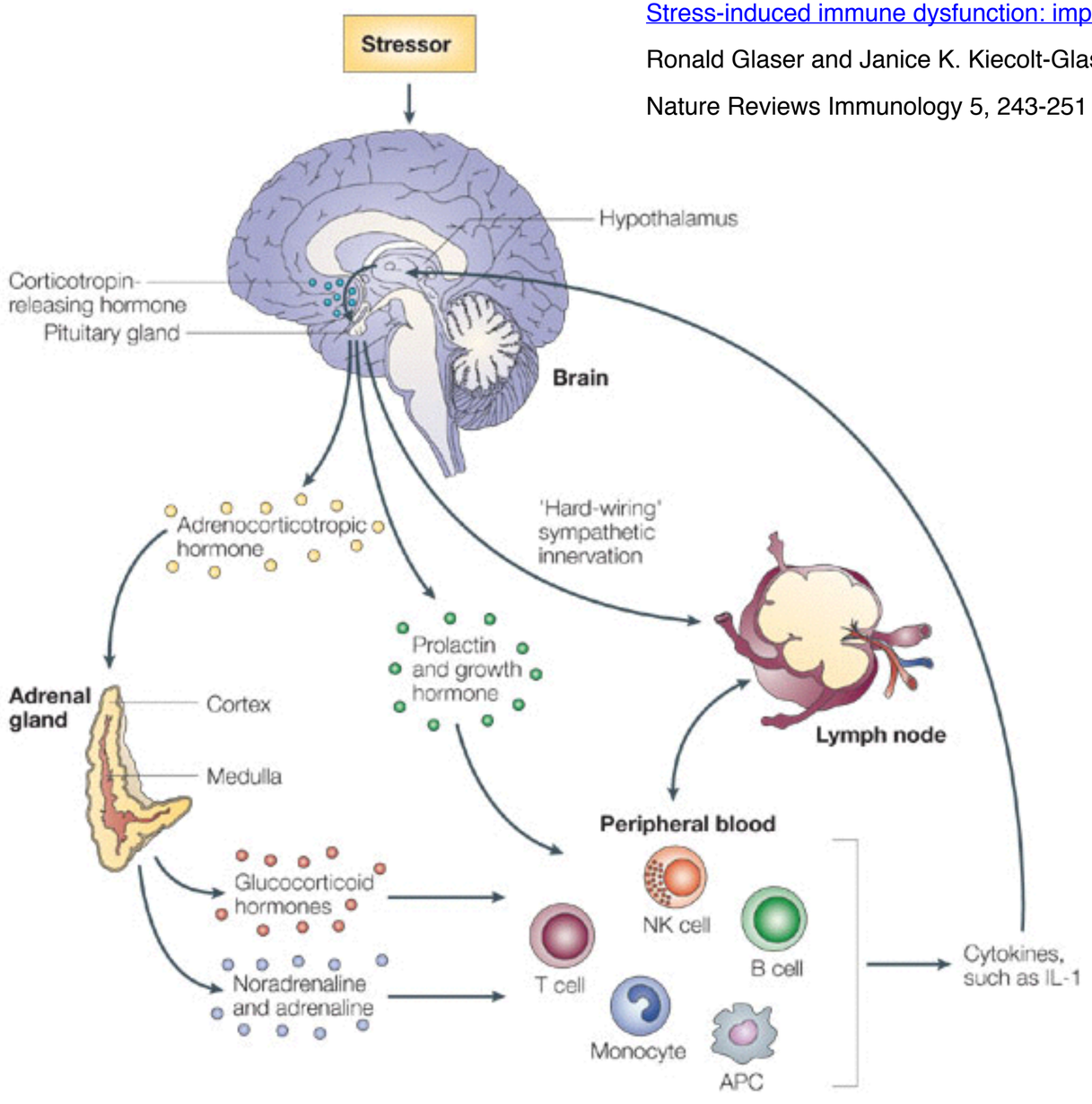
- **HOW?**
- Address stress (cortisol quantity and rhythm)
- Right size estrogen
- Balance blood sugar
- Feed the heart necessary nutrients, such as iron, vitamin D, and CoQ10
- Absorb nutrients/ digestive FUNCTION
- Calm inflammation
- Optimize mitochondrial function —> quench oxidative stress


Don't chase symptoms.
Optimize systems.
DR. JESSICA DRUMMOND

PART 2: Stress and Sex Hormone Balance

The Stress Response and Long Term Risk of Brain and Heart Diseases


ANXIETY GIRL!
able to jump to the worst conclusion in a single bound!
oh, god... these tights are too tight. i think i'm gonna die!!



Stress-induced immune dysfunction: implications for health

Ronald Glaser and Janice K. Kiecolt-Glaser

Nature Reviews Immunology 5, 243-251 (March 2005)

Mechanisms of Cognitive Impairments in Perimenopause

- **HPA Axis Dysregulation:**
  - **Estrogen may also buffer the stress response.**
  - Young women show less cortisol responsiveness to a laboratory stressor compared to men.
  - A meta-analysis of results from 34 laboratory stress studies concluded that the effect of aging on cortisol responsiveness is three times greater in women than in men.

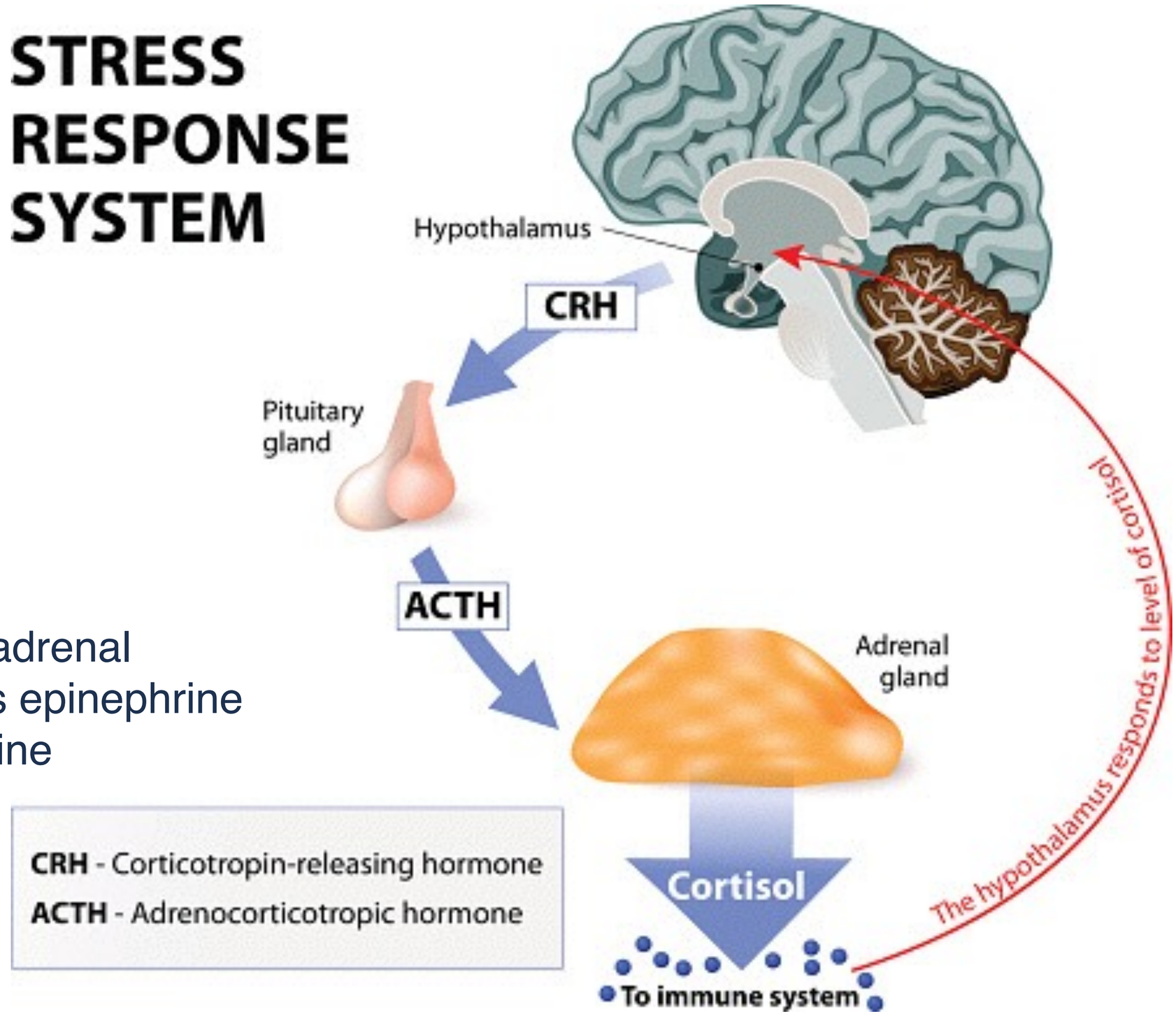
Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

Mechanisms of Cognitive Impairments in Perimenopause

- **HPA Axis Dysregulation:**
- The Seattle Midlife Women's Health Study examined longitudinal changes in HPA activation.
- An increase in overnight urinary cortisol levels during late perimenopause was observed; **cortisol levels returned to lower levels when women reached postmenopause.** *(*good news!)*

Greendale, G. A., Derby, C. A., & Maki, P. M. (2011). Perimenopause and Cognition. Obstetrics and Gynecology Clinics of North America, 38(3), 519–535. http://doi.org/10.1016/j.ogc.2011.05.007

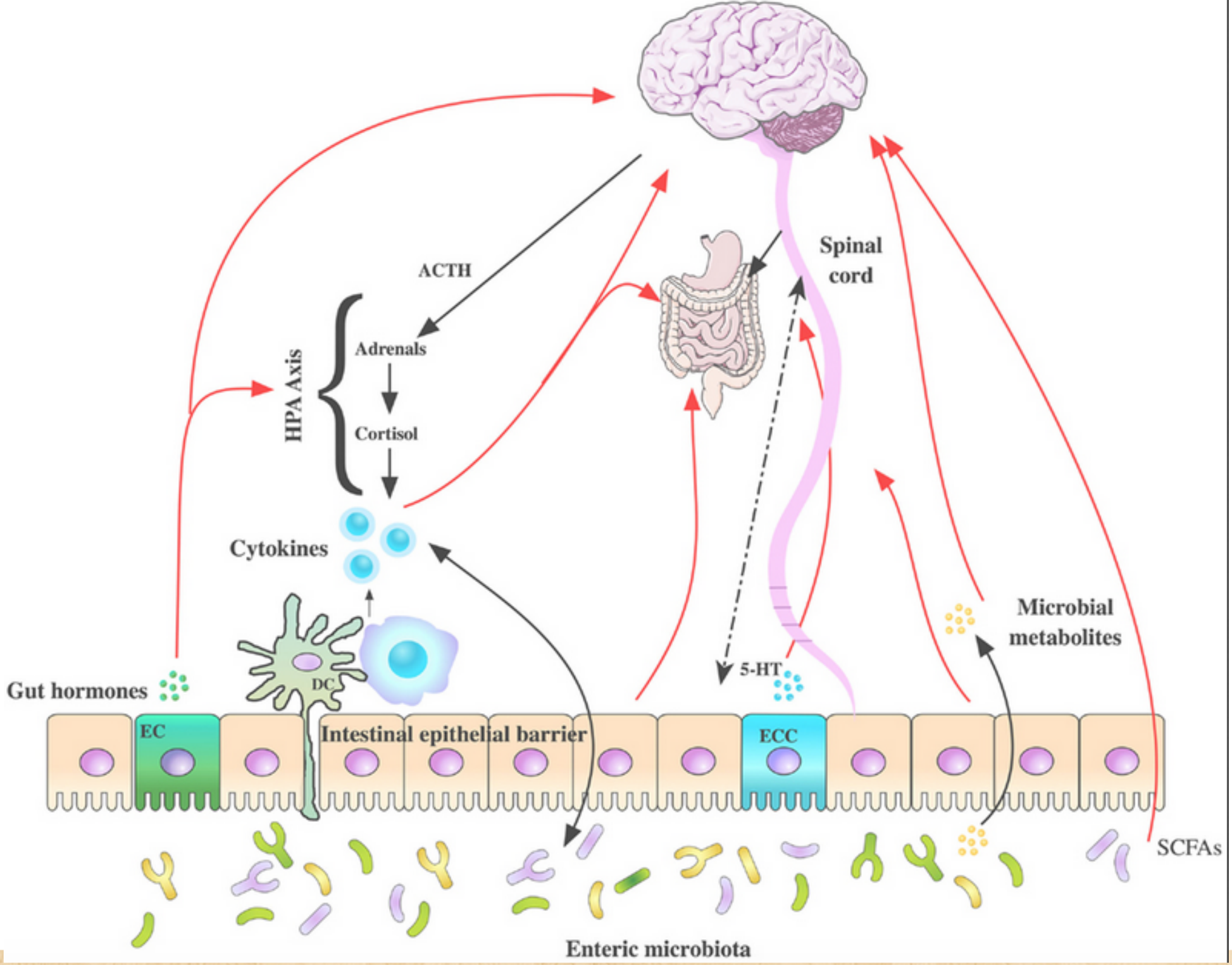
STRESS RESPONSE SYSTEM



Don’t forget the adrenal medulla secretes epinephrine and norepinephrine

CRH - Corticotropin-releasing hormone

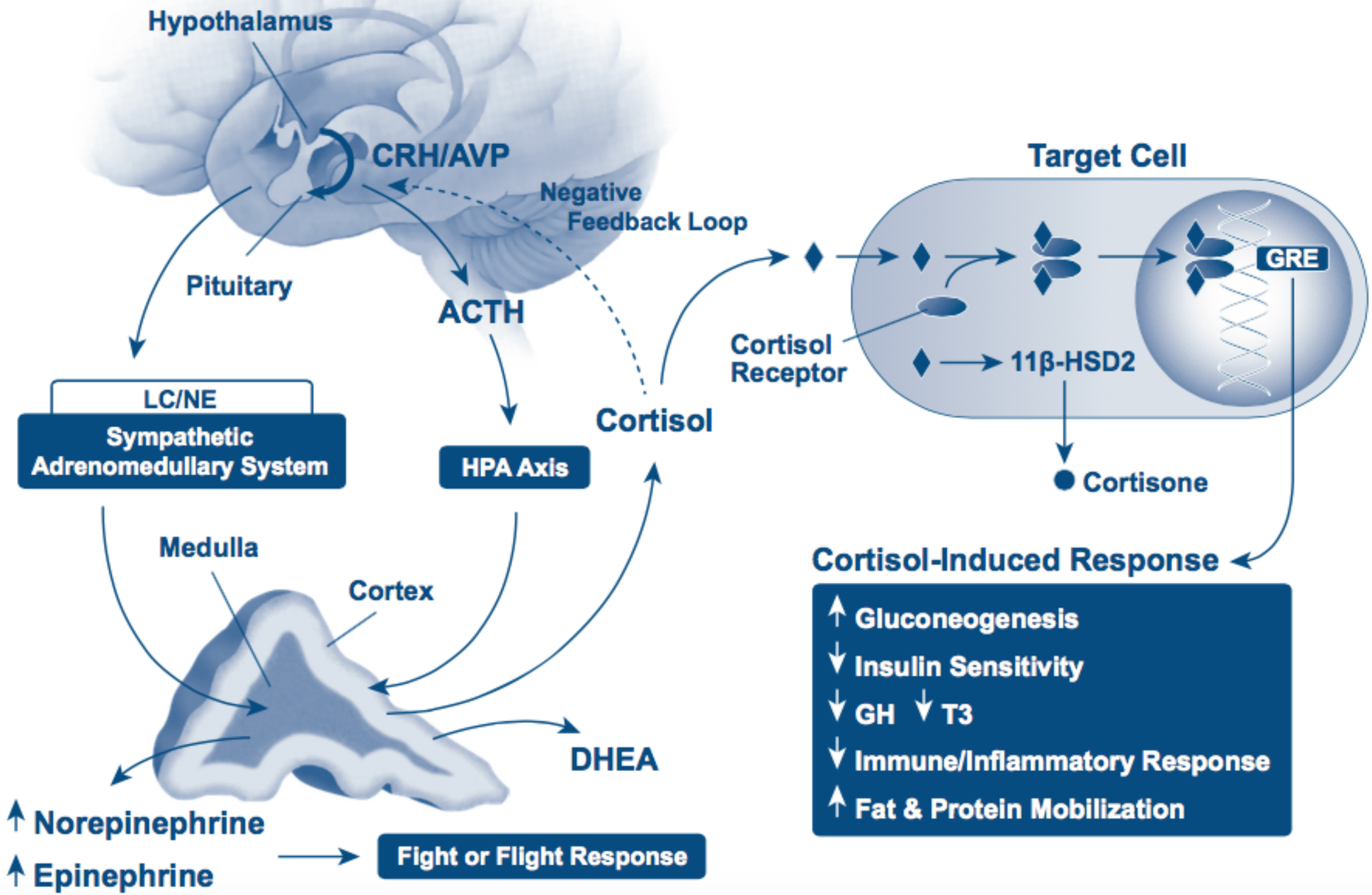
ACTH - Adrenocorticotropic hormone



Front. Psychiatry, 16 February 2015 I http://dx.doi.org/10.3389/fpsyt.2015.00015

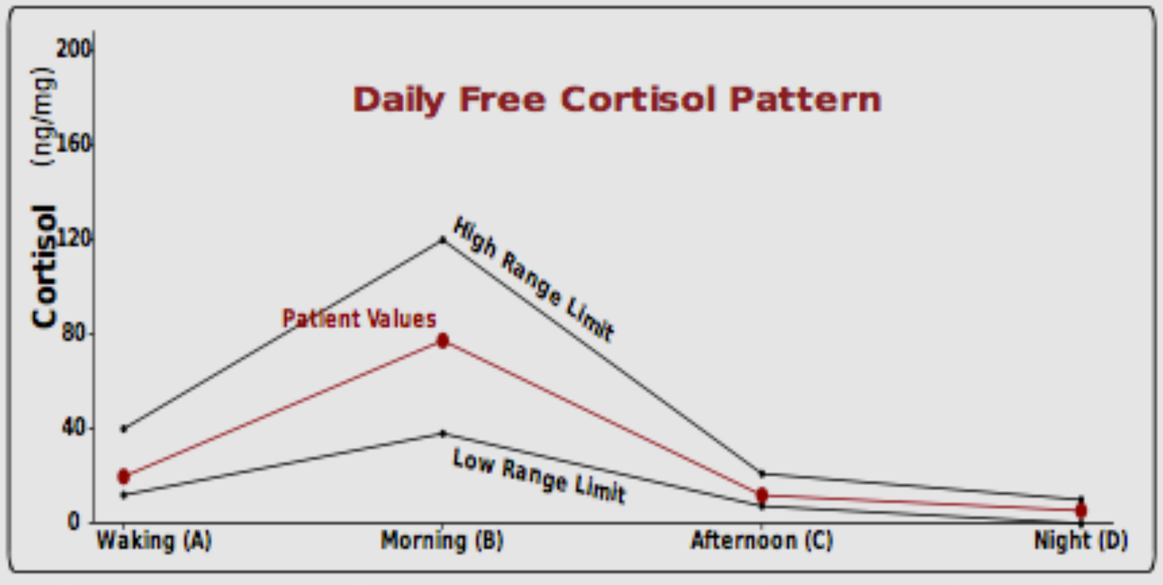
Figure 1

The HPA Axis and Stress Response System



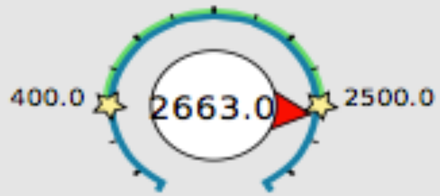
Guilliams, TG & Edwards, L (2010) Chronic Stress and The HPA Axis: Clinical Assessment and Therapeutic Considerations

Adrenal Hormones See pages 4 and 5 for a more complete breakdown of adrenal hormones

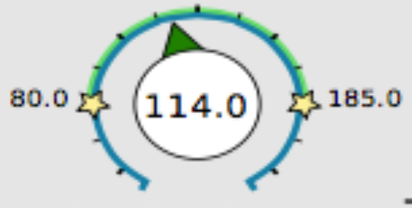


Total DHEA Production

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350

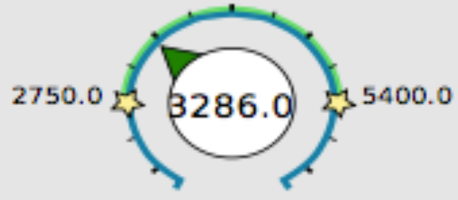


Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)



24hr Free Cortisol
(A+B+C+D)

cortisol metabolism



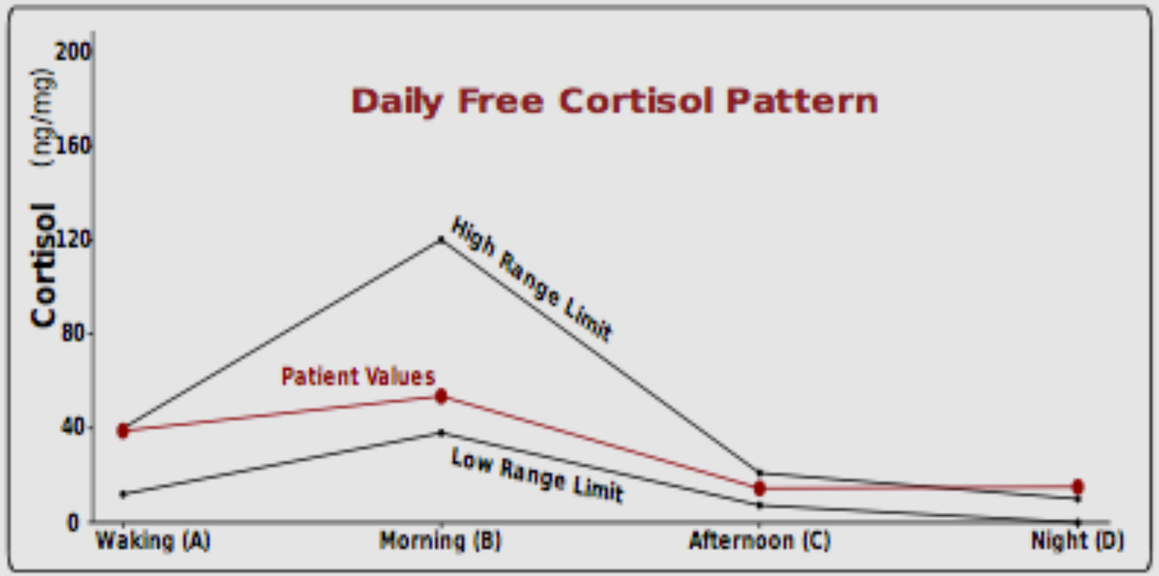
Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

- Reports afternoon and evening fatigue
- Painful sex/dryness very low estrogen and progesterone
- High DHEA
- Low-normal cortisol in afternoon and evening
- Depleted, but difficulty maintaining nourishing food plan

Adrenal Hormones

See pages 4 and 5 for a more complete breakdown of adrenal hormones



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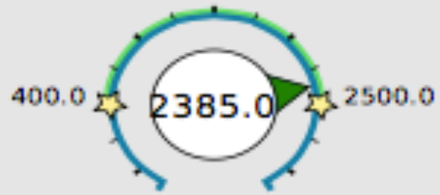
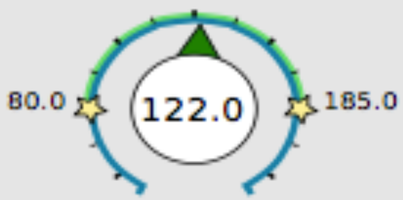


Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)



24hr Free Cortisol
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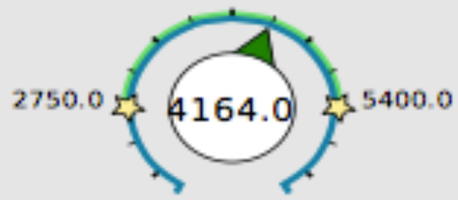


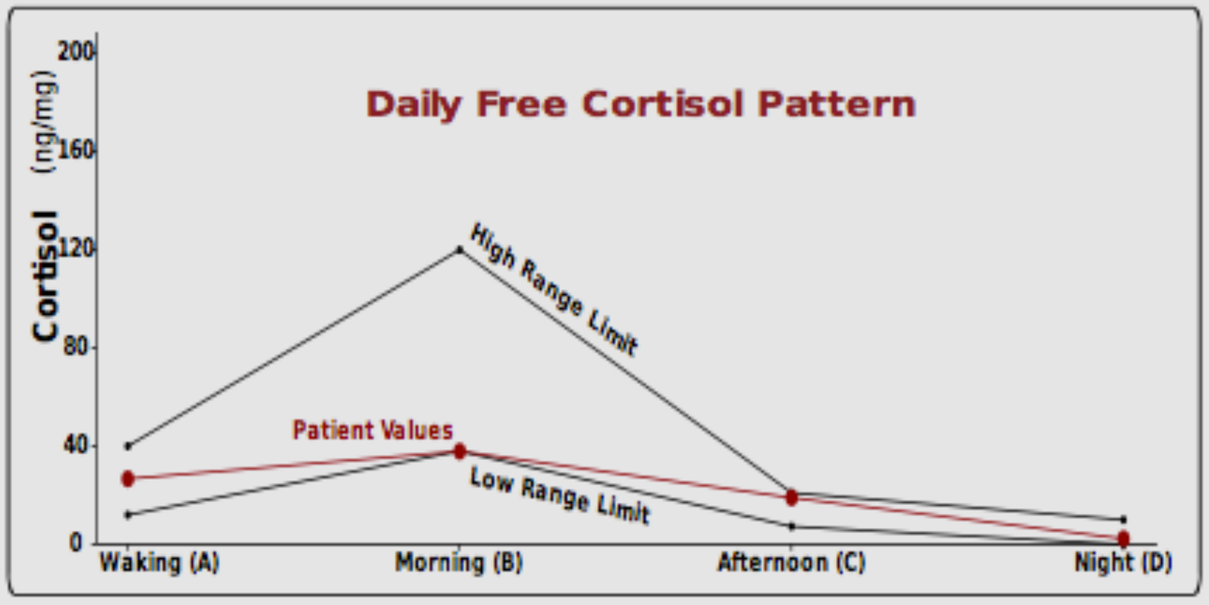
Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

- Flipped cortisol curve
- Good DHEA
- Normal total cortisol
- Pelvic pain/ fatigue

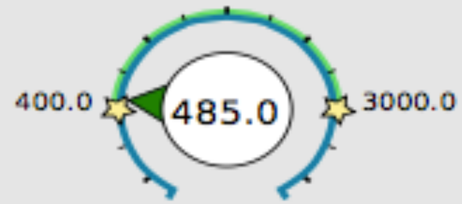
Adrenal Hormones

See pages 4 and 5 for a more complete breakdown of adrenal hormones

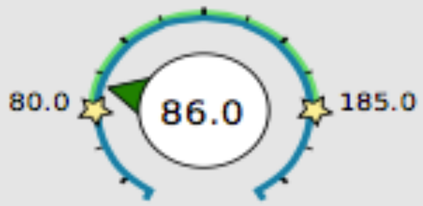


Total DHEA Production

Age	Range
20-30	1000-3000
30-40	800-2000
40-60	530-1550
>60	400-1350

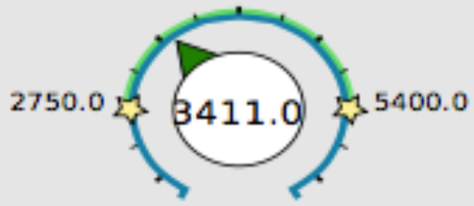


Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)



24hr Free Cortisol
(A+B+C+D)

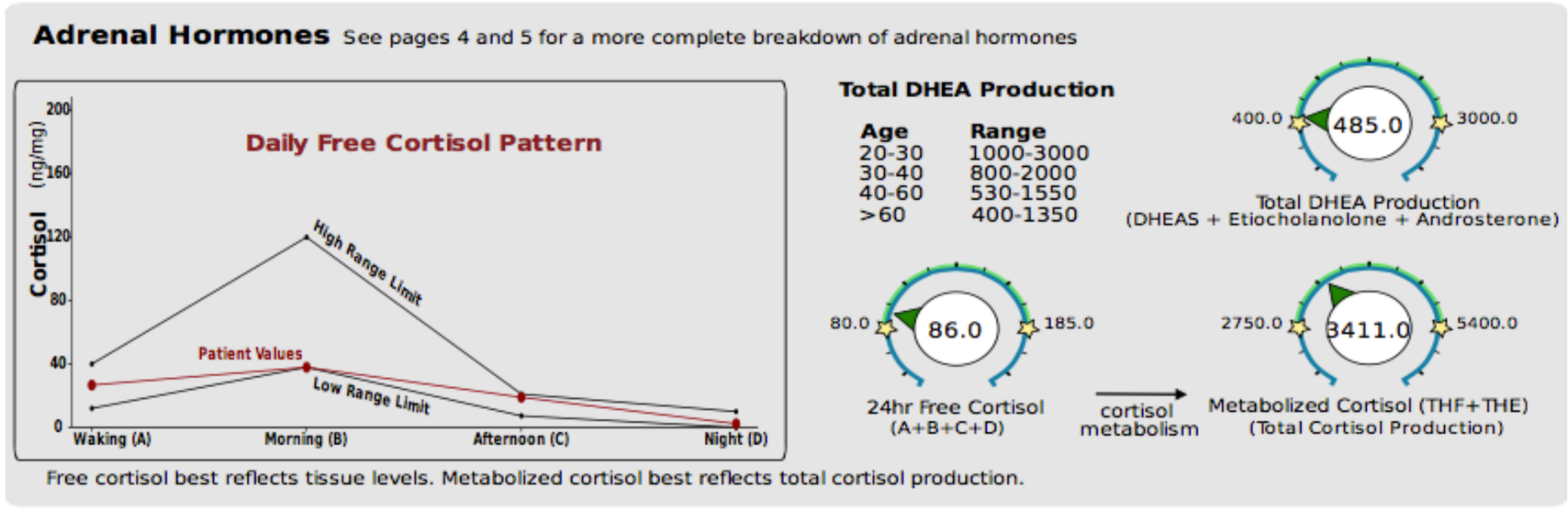
cortisol metabolism



Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

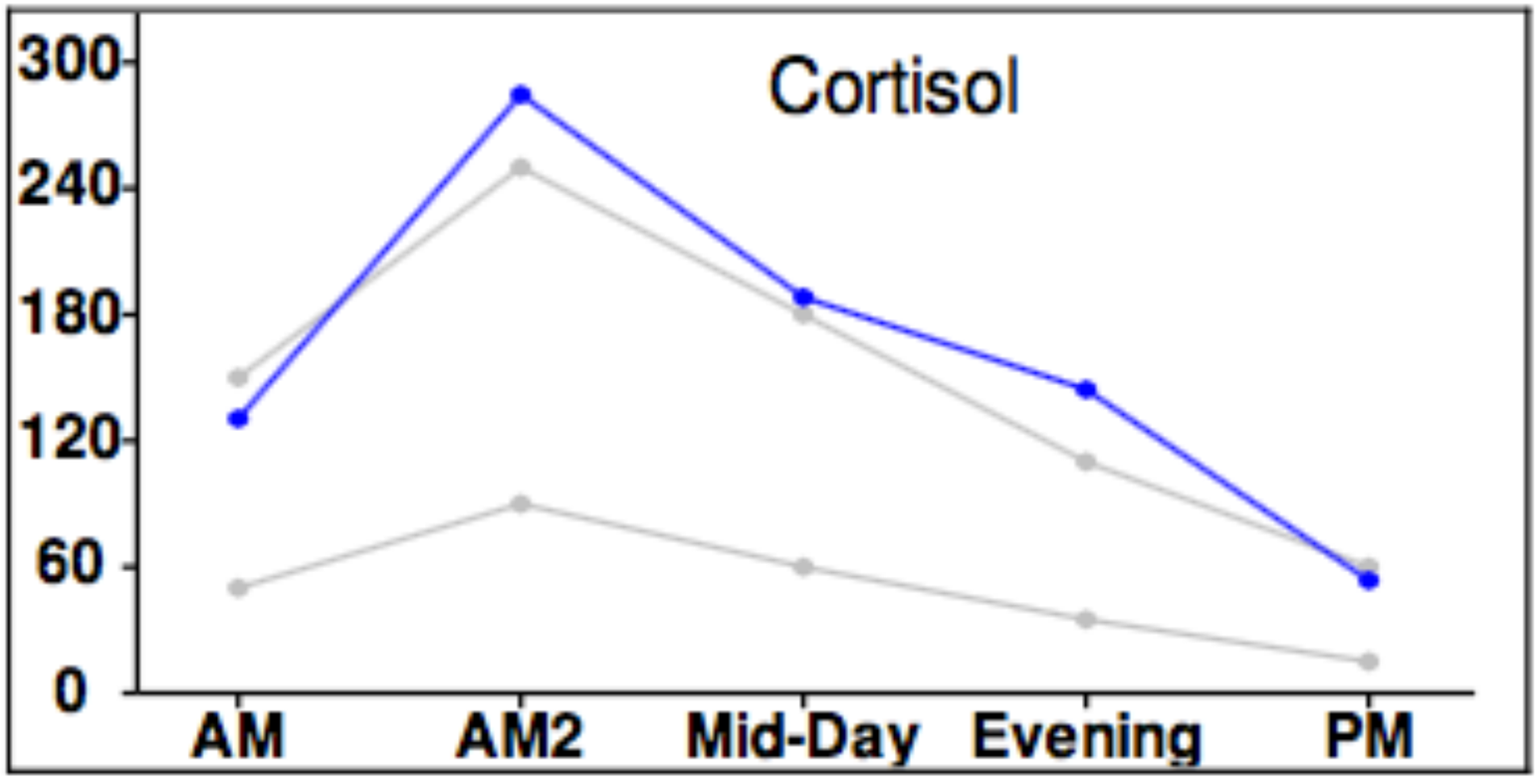
Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

- Low AM/ PM, spikes in afternoon
- Low DHEA
- Low-normal total cortisol
- Long term chronic pain managed with opioids



- Acute and chronic pain —> increased secretion of adrenocorticotrophic hormone (ACTH) and cortisol.
- BUT, the **chronic use of exogenous opioids** has been found in several studies to **decrease ACTH and cortisol levels and cortisol responses to adrenocorticotropin challenges**.
- **Opioids also affect the circadian rhythms of cortisol secretion**, resulting in persistently raised levels of ACTH and cortisol and eventually blunting the stress response.
- Levels of dehydroepiandrosterone sulphate (DHEAS), a precursor of adrenal androgens, have also been markedly reduced in both male and female chronic opioid users.

Seyfried, O., & Hester, J. (2012). Opioids and endocrine dysfunction. British Journal of Pain, 6(1), 17–24. http://doi.org/10.1177/2049463712438299



- High
- Anxiety, jittery
- In recovery, often transition from low —> high

Supplement Support of HIGH Cortisol

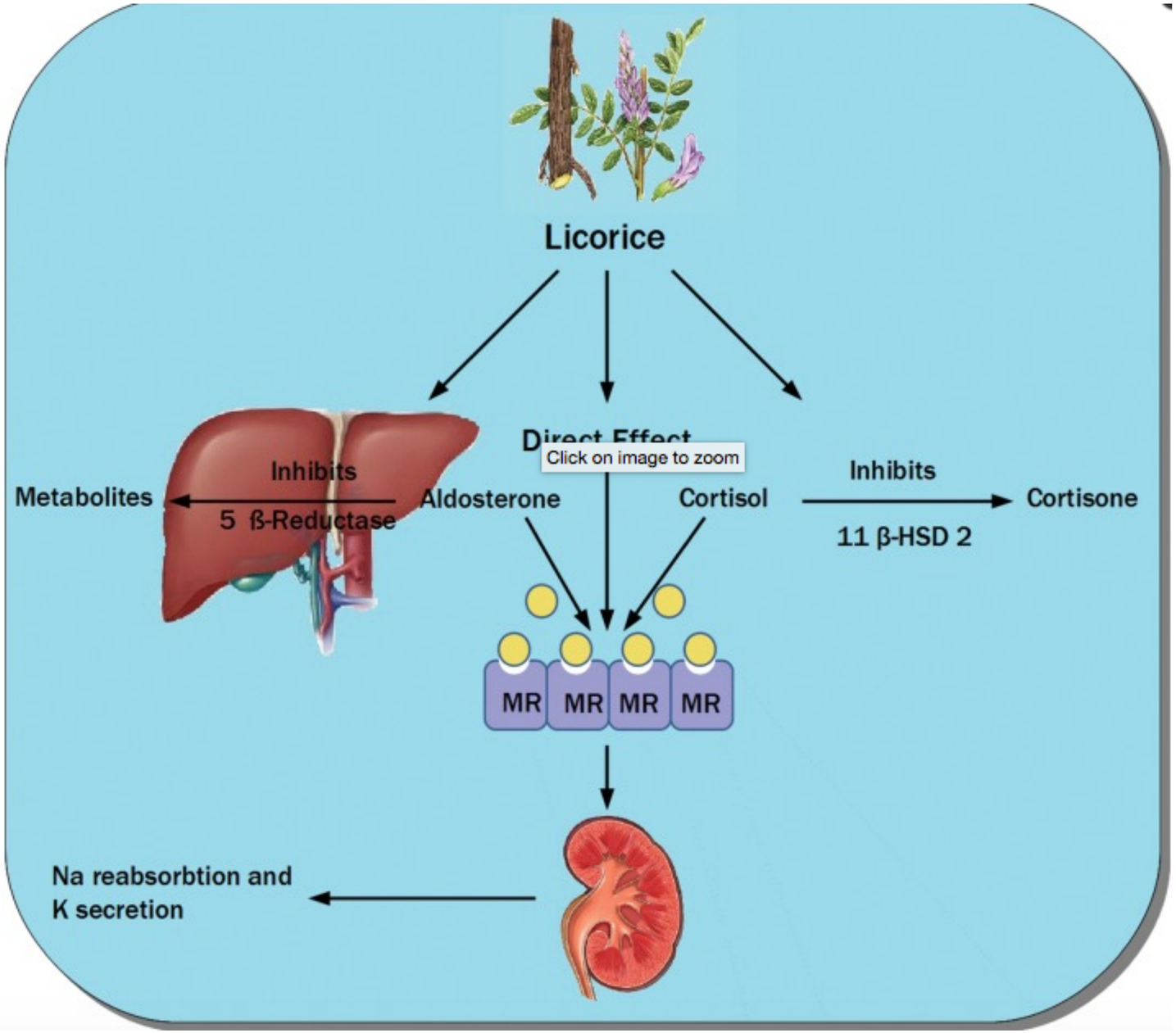
- **HPA Axis Dysregulation:**
- With cortisol elevation - catabolic, can breakdown gut mucosa.
- Dose phosphatidyl serine (~ 1 hour prior to high points on pattern, lasts 2-3 hours, cream may be absorbed better.)
- 100-800mg per day (lower doses for improved cognitive function, and higher doses to reduce the effects of overtraining)
- Be careful if total cortisol is low, but free cortisol is high (and metabolites very low) - may not want to suppress as much, can be a problem with cortisol clearance. Need to get to the root cause.
- Excess cortisol clearance can be due to hypothyroidism.

Supplement Support of LOW Cortisol

- **HPA Axis Dysregulation:**
- With LOW total cortisol
- Licorice root inhibits cortisol breakdown - again, what are the metabolites doing? (upper limit for regular ingestion of 100 mg of glycyrrhizin a day is safe for the majority of the population, but there are risks even at lower doses… unexplained metabolic alkalosis, HTN, or hypokalaemia)

- Risk factors: essential hypertension, salt sensitivity, old age, malnutrition, use of diuretics, chronic inflammatory conditions and mutations in the 11-beta-HDS2 gene.

De Putter, R., & Donck, J. (2014). Low-dose liquorice ingestion resulting in severe hypokalaemic paraparesis, rhabdomyolysis and nephrogenic diabetes insipidus. Clinical Kidney Journal, 7(1), 73–75. http://doi.org/10.1093/ckj/sft159



- Increase risk of HTN
- Increases 1/2 life of cortisol

Omar, H. R., Komarova, I., El-Ghonemi, M., Fathy, A., Rashad, R., Abdelmalak, H. D., … Camporesi, E. M. (2012). Licorice abuse: time to send a warning message. Therapeutic Advances in Endocrinology and Metabolism, 3(4), 125–138. http://doi.org/10.1177/2042018812454322

Mechanisms of Cognitive Impairments in Perimenopause

- **HPA Axis Dysregulation:**
- With LOW total cortisol

- Low cortisol metabolites are an issue of lack of clearance (hypothyroid?)
- High cortisol metabolites are an issue of increased clearance (obesity? inflammation?)

Adaptogenic Herbs

- Rhodiola
- Ashwagandha
- Ginseng
- Gotu Kola
- Licorice Root
- Eleutherococcus
- Reishi Mushroom
- Cordyceps
- Maca
- Schizandra
- Shatavari
- Holy Basil
- Eleuthero

Consider the Symptoms

- **HPA axis** - quantitative - total cortisol output from a quantitative perspective.

Stay tuned for part 4, where we'll also address BRAIN HEALTH

- **Hippocampus** - qualitative - consider the pattern, energy, and sleep rhythms, poor learning and memory too? Rx to consider: adaptogens, acetylcholine (alpha GPC is the most bioavailable form of choline. And, does she have enough pantothenic acid (B5) to convert choline > acetylcholine.
- **Mesencephalon** (watch for maladaptive plasticity!) - amplitude of sympathetic response. Small stimulation —> stress response (jumpy, doesn't like loud noises, lots of light stim.) Address inflammation and support GABA.

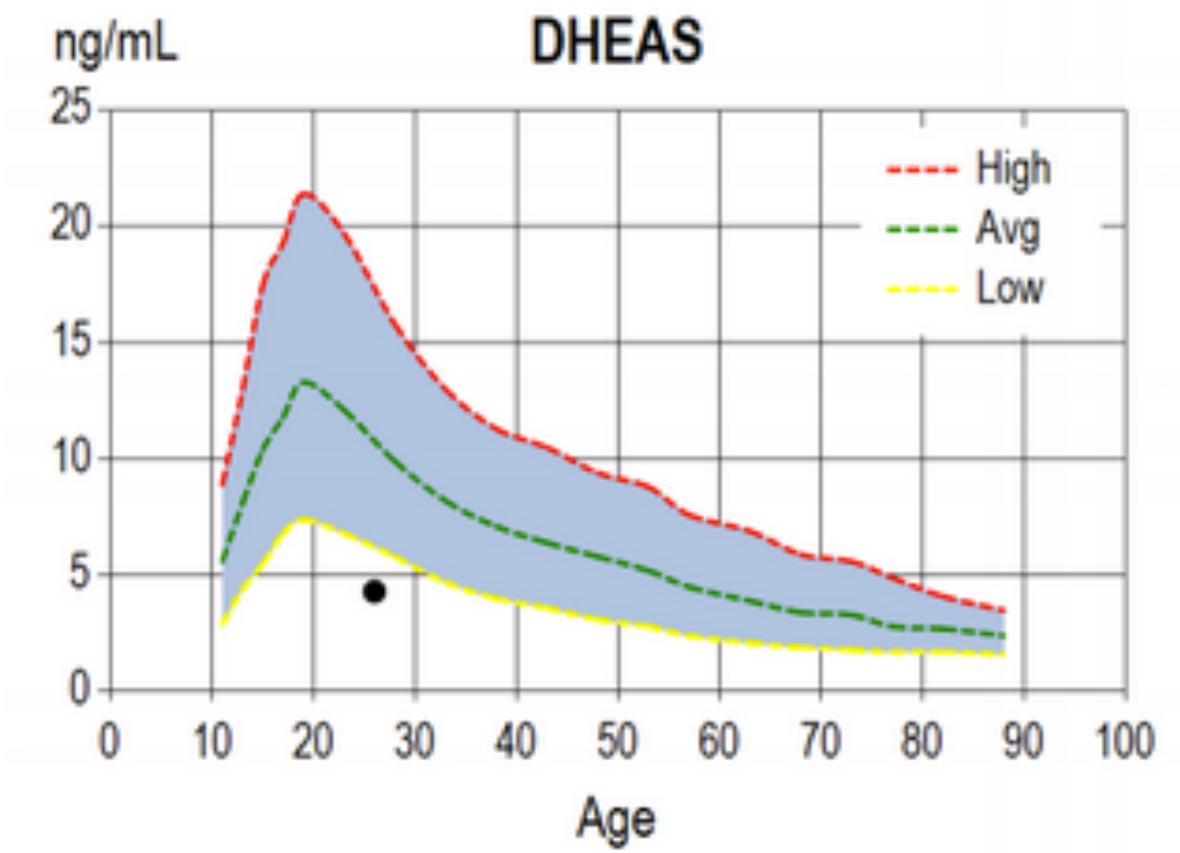
From neuro lecture, Dr. Noseworthy, MUIH, 2016

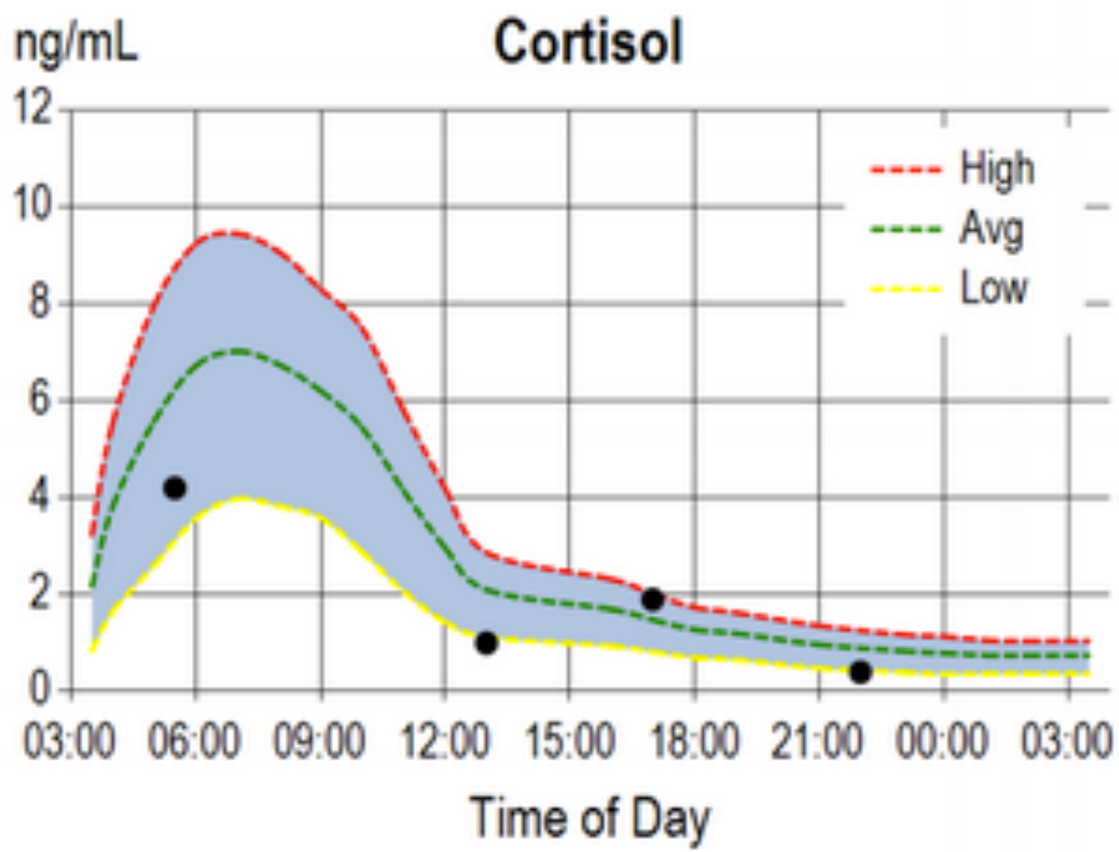
HOW To Balance THE HPA Axis in Perimenopause

- **HPA axis** - quantitative- total cortisol output from a quantitative perspective.
- **Consider cortisol curve shape.**
- **If high cortisol… what are her stressors? What is the timing?**
  - Phosphatidyl serine
- **If low cortisol… what does she need to do to RESTORE? REJUVENATE? PLEASURE?**
  - Licorice

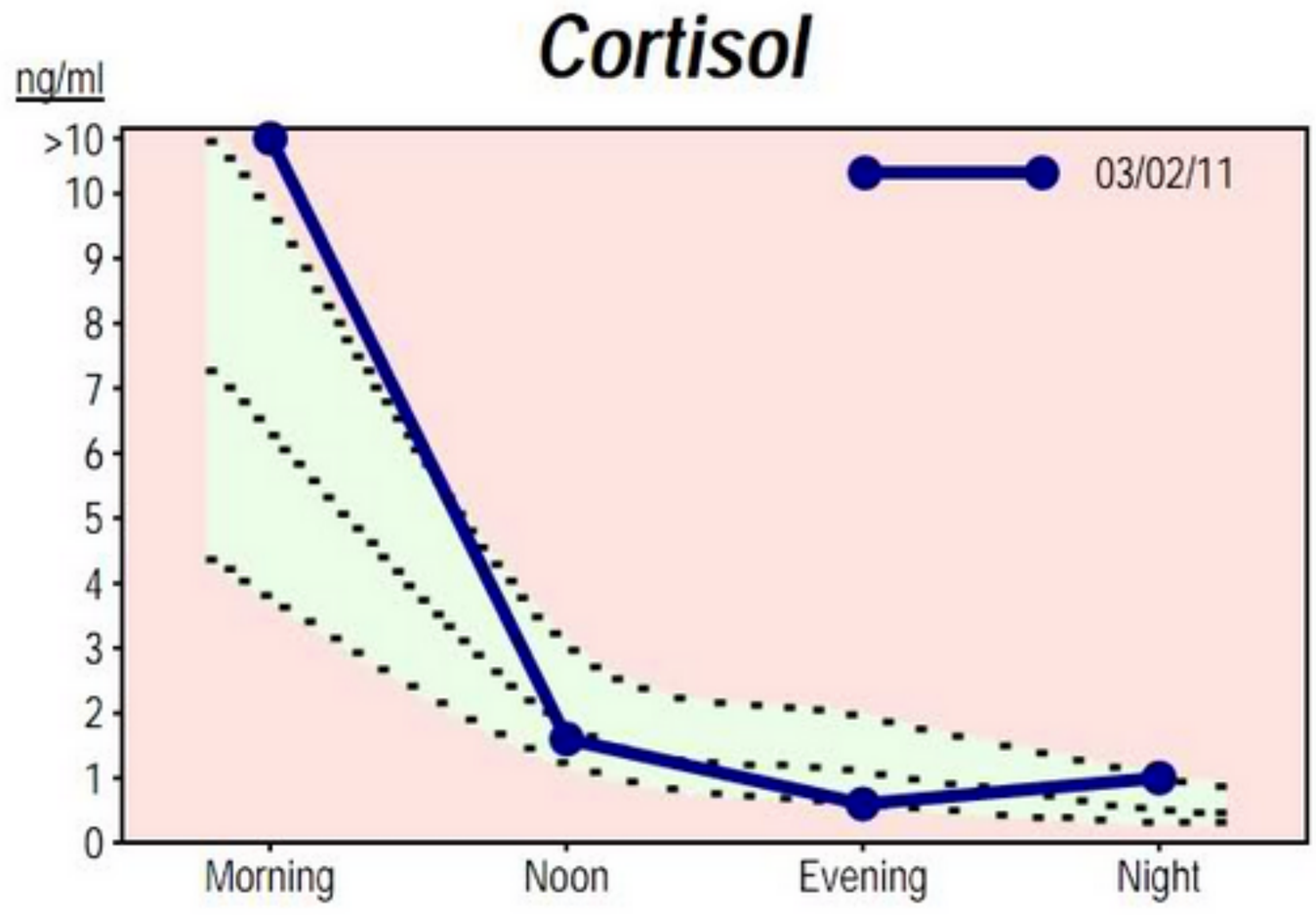
From neuro lecture, Dr. Noseworthy, MUIH, 2016

Let's Discuss… What is the curve shape? Quantity and quality of cortisol curve rhythm?

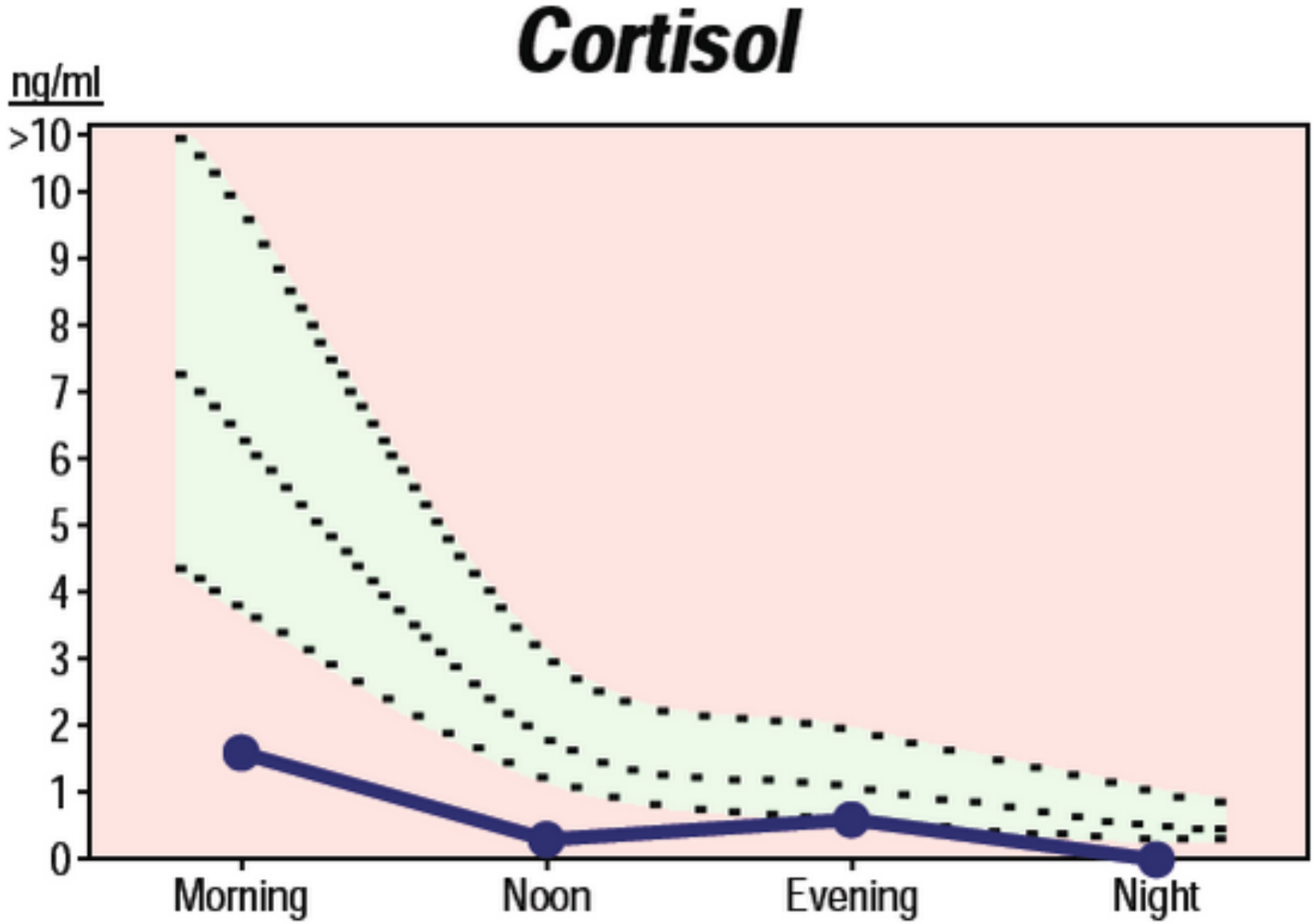


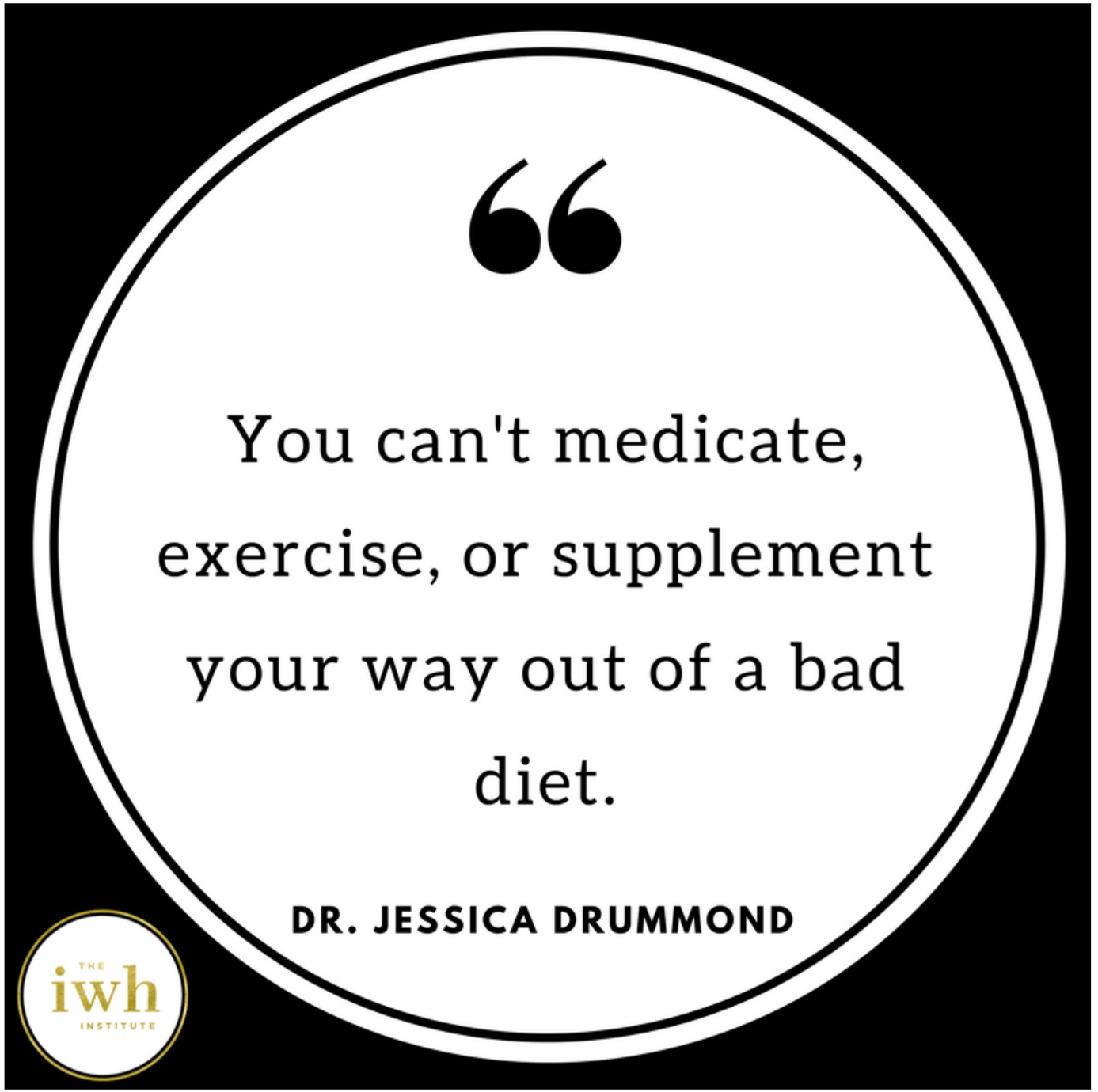


Let's Discuss…



Let's Discuss…




“
You can't medicate, exercise, or supplement your way out of a bad diet.
DR. JESSICA DRUMMOND

Cashmere Blanket Therapy + Healing Nutrition

- Puberty
- Perimenopause
- Postpartum
- After surgery
- After intense or prolonged stressor
- Do your clients have access to cashmere blanket therapy?
- Do you?
- **Do they (you) feel comfortable asking for that depth of support?**

STRESSFUL LIFESTYLE

- 4 categories of chronic HPA-axis stress to evaluate in each patient…
  - Mental/ emotional stress
  - Sleep disorders
  - Metabolic/ glycemic dysregulation
  - Chronic inflammation

Guilliams, TG & Edwards, L (2010) Chronic Stress and The HPA Axis: Clinical Assessment and Therapeutic Considerations

STRESSFUL LIFESTYLE

- **What is the root cause of her STRESS?**
  - Work/ finances
  - Close relationships
  - Need to control/ perfectionism —> often grounded in a lack safety/ security
  - Poor sleep
  - Sugar/ Inflammatory diet
  - Overexercise
  - Toxic exposure
  - Infection reactivation

- **Is it modifiable?**

Is Stress Harmful?

- Not necessarily.
- It is adaptive in the short term.
- **Stress is a helpful and powerful response and your belief about stress impacts it's effect on your physiology.**
- (For more read: The Upside of Stress from Kelly McGonigal, PhD)

- Current thinking is nuanced - we're in the midst of a shift from thinking "adrenal fatigue" —> HPA axis maladaptation.

- Consider how your client can better adapt her stress response to her modern situation.

Mental/ Emotional

- Grief, excitement, fear, anxiety, guilt, embarrassment, etc.
- Public speaking, clinical appointments, performance evaluations, etc.

- The magnitude will be based on…
  - novelty to the individual
  - unpredictable?
  - threat to their person or ego?
  - sense of loss of control

- Being female can amplify the experience.

Guilliams, TG & Edwards, L (2010) Chronic Stress and The HPA Axis: Clinical Assessment and Therapeutic Considerations

The Stress Response Varies Between the Sexes Biochemically

- The response to glucocorticoids varies between the sexes.

- When activation of glucocorticoid receptor (GR) was examined in response to administration of Dexamethasone, a synthetic glucocorticoid (GC), whole genome wide microarray analysis revealed a list of **sexually dimorphic genes** that were expanded, indicating GCs differentially regulate hepatic gene expression based on sex.

- GCs act to mainly repress hepatic gene expression in males, whereas GR activation seemed to generally induce gene expression in the female rat liver.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

The Stress Response Varies Between the Sexes Biochemically

- Functionally, **GCs do not work as potently as anti-inflammatory molecules in females versus males in response to a global inflammatory challenge.**

- This was demonstrated by injecting male and female Sprague Dawley rats with a lethal dose of lipopolysaccharide (LPS) and co-administering Dexamethasone.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

The Stress Response Varies Between the Sexes Biochemically

- "Male rats could be rescued from the global inflammatory challenge by several different doses of Dexamethasone, whereas female rats only survived when administered the highest dose of Dexamethasone."

- "In female rats, estrogens appeared to partially play a role in inhibiting the anti-inflammatory effects of Dexamethasone since ovariectomy allowed for the rescue by lower doses of glucocorticoids, however, still not to the same efficiency as in males."

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

The Stress Response Varies Between the Sexes Biochemically

- Several glucocorticoid sensitive pathways that are regulated in a sexually dimorphic manner utilize Hepatic Nuclear Factor 4alpha (HNF4α) as an upstream regulator.

- Besides HNF4α, there are several other transcription factors and co-activators that are enriched in males versus females and vice versa (e.g. Med12, HDAC4, STAT3).

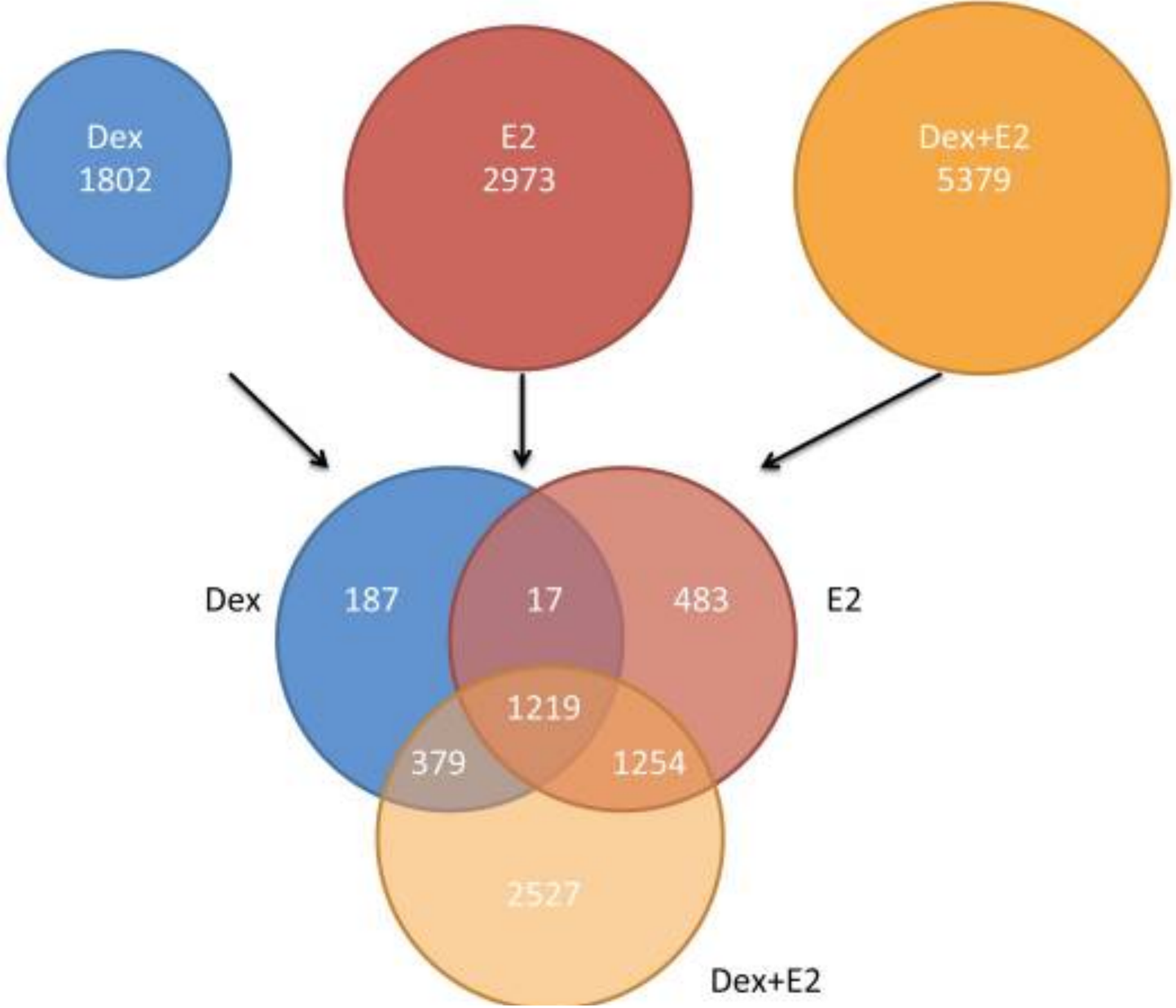
- There is still a lot to learn about how these pathways are regulated in males vs. females.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

The Stress Response Varies Between the Sexes Biochemically

- GCs can interfere with a number of genes regulated by estradiol.
- While glucocorticoids and estradiol regulate unique genes when administered alone, a common set of genes appears to be co-regulated by both hormones.
- **Very few of these common genes are antagonistically regulated, indicating a partial overlap in function of these two hormones in human uterine epithelial cells.**

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

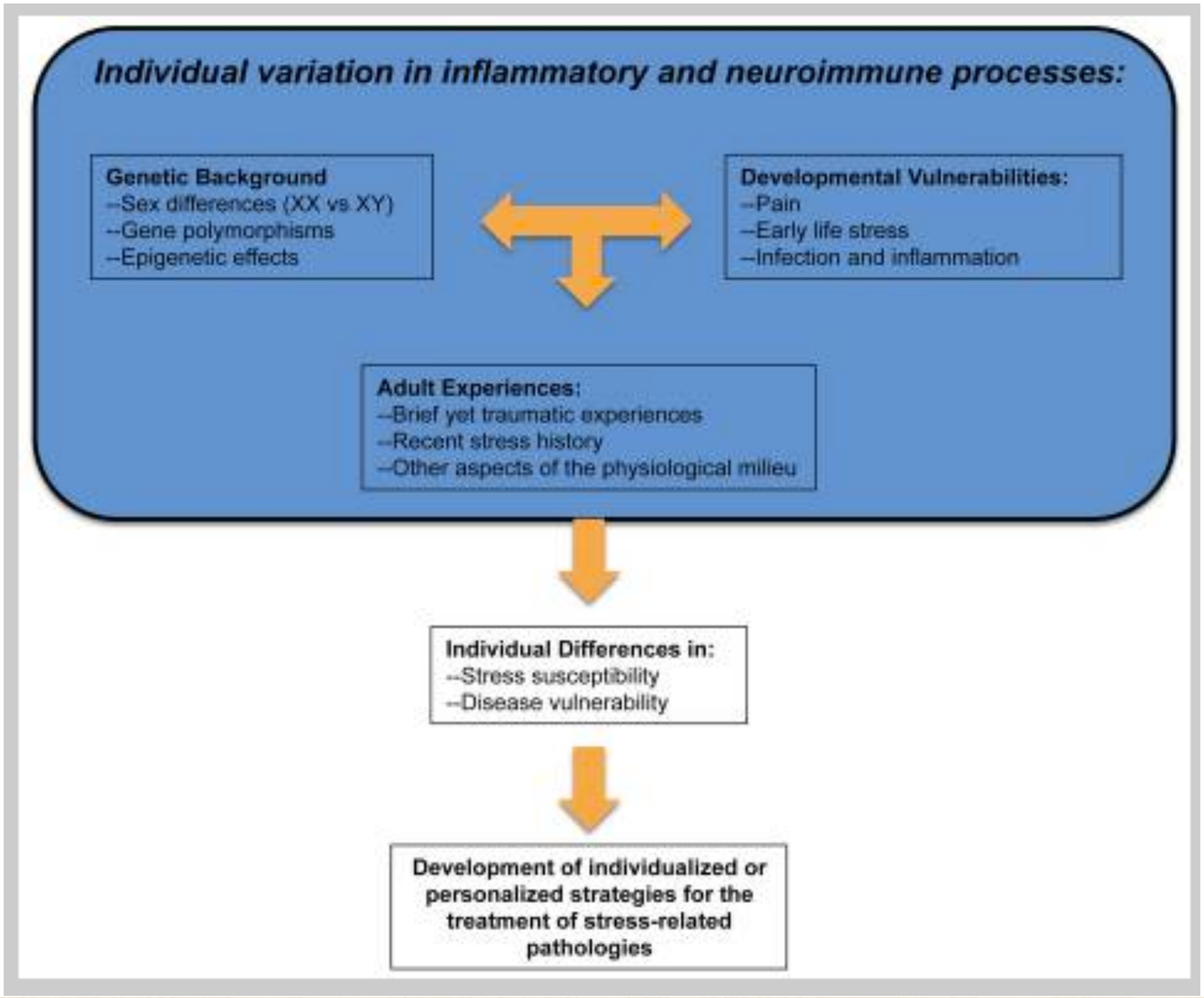


Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

Glucocorticoid and Estradiol regulated genes in human uterine epithelial cells

Venn diagram of significantly regulated genes by Dexamethasone (Dex), Estradiol (E2) and the combination of Dex+E2 from microarray analysis performed in human uterine epithelial cells. Figure adapted from Whirledge et al., (PMID 23843231) with permission.

The Stress Response Depends on a Variety of Factors…



Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

The Stress Response: Can be Dramatically Affected by Early Life Experiences of Stress and Pain

- Early life stress in mouse models:
- Maternal separation of guinea pig pups produces a variety of sickness-like behaviors that are ameliorated by drugs with anti-inflammatory properties.
- There appear to be a multitude of mechanisms by which noxious (or antigenic) stimuli intersect with neuroimmune signaling pathways during early development and have the ability to produce profound re-architecture of the stress axis.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

Early Life Stress and Pain and The Stress Response

- Many possible mechanisms by which noxious (or antigenic) stimuli intersect with neuroimmune signaling pathways during early development and have the ability to produce profound re-architecture of the stress axis, including…

- Lack of pain management for early life stress and pain.

- A potential role for glia (microglia, astrocytes, etc) in the propagation of pain signals, indicating a prominent role for cytokines in the development of pathological pain processes and other sensitization phenomena.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

Early Life Stress and Pain and The Stress Response

- Many mechanisms by which noxious (or antigenic) stimuli intersect with neuroimmune signaling pathways during early development and have the ability to produce profound re-architecture of the stress axis.
  - Use of viral vectors to deliver anti-inflammatory cytokines/chemokines seems to effectively reverse long-term changes in pain sensitivity evoked by inflammation.
  - Opioid analgesics such as morphine interact with Toll-Like Receptor 4 (TLR4), a pathogen-recognition receptor whose activation spurs the expression of cytokines suggesting that either endogenous opioids (released in response to noxious stimuli) or exogenous opiates (to control pain) might exert certain effects through inflammatory signaling pathways downstream of TLR4 activation.

Deak, T., Quinn, M., Cidlowski, J. A., Victoria, N. C., Murphy, A. Z., & Sheridan, J. F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress (Amsterdam, Netherlands), 18(4), 367–380. http://doi.org/10.3109/10253890.2015.1053451

Do Women Buffer Stress with Affiliation?

- As in rodent studies, humans under stress (especially females) can seek affiliative behavior.
- In female prairie voles, stress impairs partner preference formation, but this effect is prevented in adrenalectomized voles.
- Exposure to cortisol during (but, not after) cohabitation with a novel male prevents partner preference formation, and adrenalectomized females form partner preferences after shorter cohabitation periods than are typically necessary.
- Cortisol levels are naturally low immediately following cohousing with a male, and partner preferences are formed before they return to baseline.

Beery, A. K., & Kaufer, D. (2015). Stress, social behavior, and resilience: Insights from rodents. Neurobiology of Stress, 1, 116–127. http://doi.org/10.1016/j.ynstr.2014.10.004

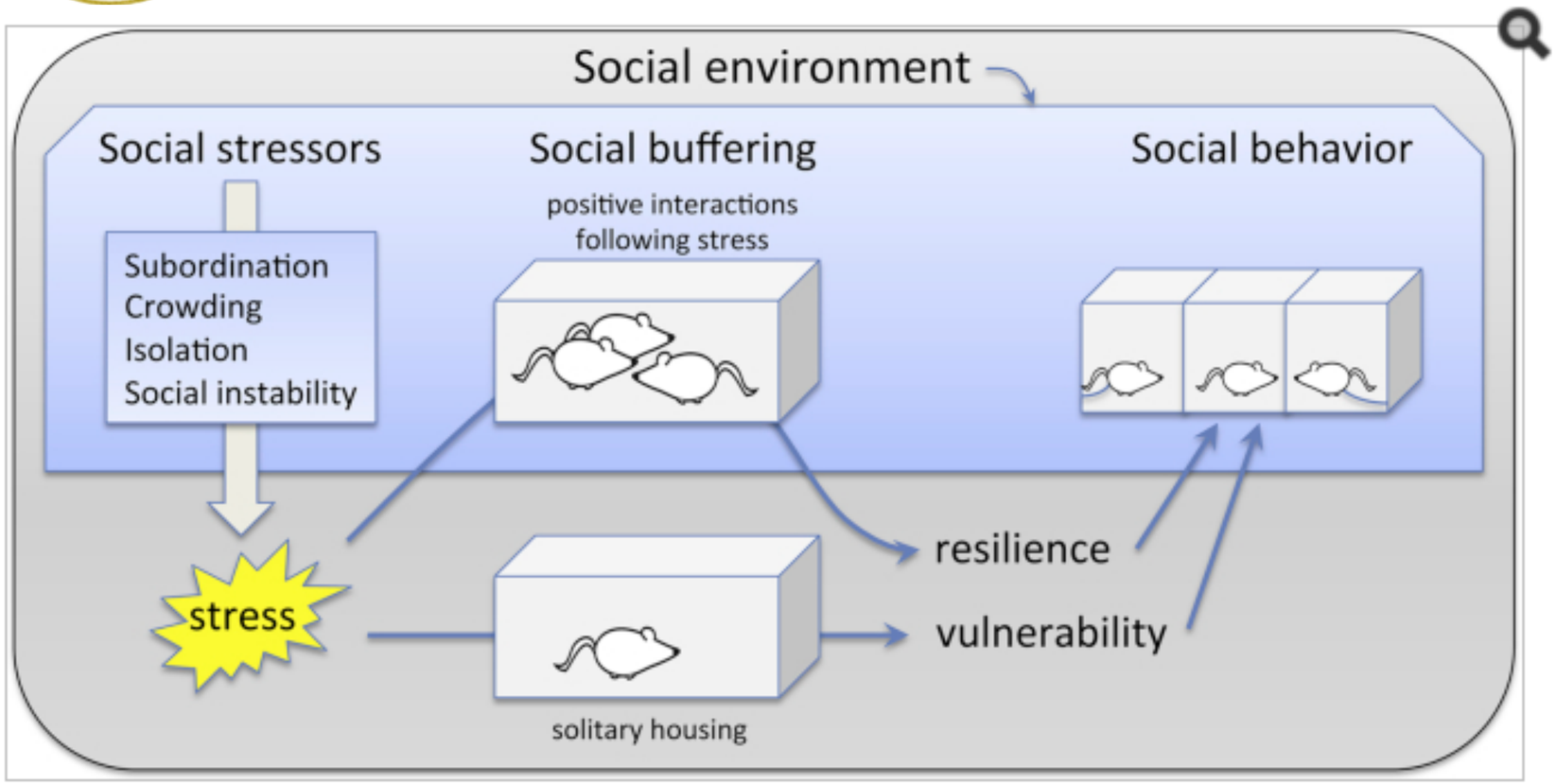
Beery, A. K., DeVries A.C., DeVries M.B., Taymans S., Carter C.S. Modulation of pair bonding in female prairie voles (Microtus ochrogaster) by corticosterone. Proc. Natl. Acad. Sci. U.S.A. 1995;92:7744–7748.
DeVries A.C., DeVries M.B., Taymans S.E., Carter C.S. The effects of stress on social preferences are sexually dimorphic in prairie voles. Proc. Natl. Acad. Sci. U.S.A. 1996;93:11980–11984.

Same Sex Affiliation

- Some data suggest same-sex affiliative behavior in prairie voles may be enhanced following a stressor.
- Meadow voles are conditionally social rodents, with seasonal variation in social huddling.
- Females are aggressive and territorial in summer months.
- Females live in social groups and huddle in winter months.
- Cortisol levels vary seasonally and may modulate same-sex affiliations to buffer stress.

Beery, A. K., & Kaufer, D. (2015). Stress, social behavior, and resilience: Insights from rodents. Neurobiology of Stress, 1, 116–127. http://doi.org/10.1016/j.ynstr.2014.10.004

Social Stress and Social Buffering of Stress



Schematic representation of the levels at which the social environment impacts and reflects the individual. To the left and in Section 2 of this review, we consider aversive social environments as potent stressors. This stress has far-reaching impacts on individual physiology as well as on social behavior (Section 3), but these impacts are potentially moderated by social buffering (Section 4).

Beery, A. K., & Kaufer, D. (2015). Stress, social behavior, and resilience: Insights from rodents. Neurobiology of Stress, 1, 116–127. http://doi.org/10.1016/j.ynstr.2014.10.004

Affiliative Stress Buffering in Human Females

- For women, stress can induce an affiliative response - likely modulated by oxytocin.

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

Psychoneuroendocrinology. 2013 Nov;38(11):2800-4. doi: 10.1016/j.psyneuen.2013.05.006. Epub 2013 Jun 12.
Stress-induced negative mood moderates the relation between oxytocin administration and trust: evidence for the tend-and-befriend response to stress?
Cardoso C1, Ellenbogen MA, Serravalle L, Linnen AM.

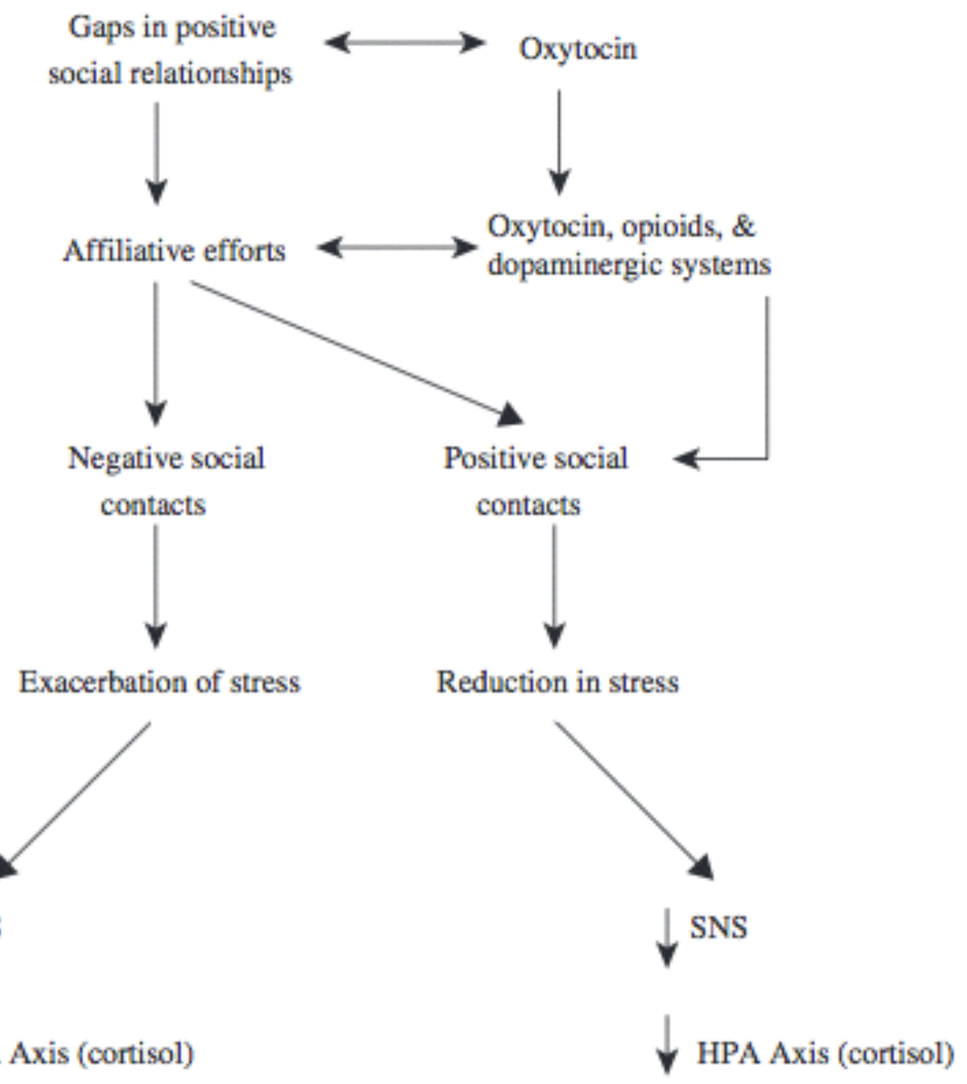


Fig. 1. A model of affiliative responses to stress. Elevations in plasma oxytocin accompany gaps in positive social relationships and are believed to prompt affiliative efforts aimed at restoring positive social contacts; engagement of opioid and dopaminergic systems coupled with oxytocin may lead to a reduction in stress responses, including those of the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenocortical (HPA) axis. However, negative social contacts exacerbate stress, leading to an increase in these same biological stress responses.

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

Biological Signaling Occurs if Your Affiliations Fall Below Adequate Levels

- **Biological signals go off if your social relationship needs are not met!**

- Oxytocin is released in response to (at least some) stress, and it promotes affiliative behaviors.

- Works in conjunction with the opioid and dopaminergic systems.

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

The Importance of A Social Circle for Women

- **Women with high levels of oxytocin are more likely to report reduced contact with…**

- their mothers
- best friends
- pets
- social groups

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

High Oxytocin Signaling Relationship Distress

- **Women with high levels of oxytocin and significant others are more likely to report that their significant others…**

- are not supportive.
- do not understand the way that they feel about things.
- do not care for them,
- and, that their partners did not display affection for them.

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

High Levels of Oxytocin

- **Lower stress responses in animals and some human studies.**
- decrease SNS activity
- decrease blood pressure
- decrease pain sensitivity
- decrease corticosteriod levels

- Protect against the adverse effects of stress by suppressing the HPA axis.

- Thus, stress is lowered when affiliative behaviors increase in response to high oxytocin levels, but stress is worsened if those affiliative efforts are negative or unrequited.
- **There is a PHYSIOLOGIC RISK to women for ASKING FOR SUPPORT and NOT GETTING IT.**

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

Estrogen Enhances The Effect of Oxytocin

- **There is more evidence that oxytocin relates to social behavior in women than men.**

- This makes sense from an evolutionary perspective, since women were traditionally more involved in childcare, and would have to respond to stress with consideration of the children in her care.
- (Can’t fight or flight and leave all of the children behind.)

Taylor, SE. (2006) Tend and Befriend: Biobehavioral Bases of Affiliation Under Stress. *Current Directions in Psychological Science*, 15(6), 273-277.

What Happens When… Women Receive Inadequate Social Support During Pregnancy?

- **Secrete higher levels of cortisol in response to stress.**
- Social support moderates (by about 50%) the association between psychological distress and cortisol in pregnant women potentially shielding the fetus from the harmful effects of the stress response.

Psychosom Med. 2013 Nov-Dec;75(9):856-62. doi: 10.1097/PSY.0000000000000004. Epub 2013 Oct 25.
The buffering effect of social support on hypothalamic-pituitary-adrenal axis function during pregnancy.

Giesbrecht GF[1], Poole JC, Letourneau N, Campbell T, Kaplan BJ; APrON Study Team.

Touch Decreases Stress in Women, Not Men

- **Touch decreases the stress of hospitalization in women (in a 1979 study)**

- But, actually felt to be aversive by males under the stress of hospitalization.

- **Crowding stresses male rodents, but calms female rodents**. (lowers their cortisol levels.)

Psychol Rev. 2000 Jul;107(3):411-29.
Biobehavioral responses to stress in females: tend-and-befriend, not fight-or-flight.

Taylor SE[1], Klein LC, Lewis BP, Gruenewald TL, Gurung RA, Updegraff JA.

Women Choose To Affiliate with Other Women

- **Given the choice women will buffer stress by affiliating with women.**
- But, they prefer to wait out the stressor alone than affiliate with an unfamiliar male.
- **This sex difference in women choosing to be more affiliative than men remains consistent across 12 cultures.**

Psychol Rev. 2000 Jul;107(3):411-29.
Biobehavioral responses to stress in females: tend-and-befriend, not fight-or-flight.

Taylor SE[1], Klein LC, Lewis BP, Gruenewald TL, Gurung RA, Updegraff JA.

Affiliative Stress Buffering in Human Females

- 80 healthy participants (40 females) between 18 and 40 years were included in the study.
- Female participants were not using hormonal contraceptives and participated in the experiment during their luteal phase of the menstrual cycle, as it has been shown that cortisol responses during this phase are most comparable to those of men.
- Stressed women showed reduced emotional egocentricity bias - enabling them to judge the emotions of the other person in a way that was less influenced by their own emotional state.
- This may be a reason why stress tends to increase affiliative and prosocial behavior in women.

L. Tomova[a,b], B. von Dawans[c], M. Heinrichs[c,d], G. Silani[e], C. Lamm Is stress affecting our ability to tune into others? Evidence for gender differences in the effects of stress on self-other distinction, Psychoneuroendocrinology (2014) 43, 95—104

Affiliative Stress Buffering in Human Males

- This study looked at 80 male students (40 dyads)
- Participants took part in a stressful challenge with a partner or a control situation with a partner.
- Those men with high cortisol responses to the stressor showed significantly higher ratings of psychological closeness to their interaction partner than participants with low cortisol responses.
- Men may form closer temporary bonds following stressful situations **that are accompanied by a significant cortisol response**.
- The traditional characterization of the male stress response in terms of "fight-or-flight" may be incomplete, and that social affiliation may in fact represent a common, adaptive response to stress in men.

Psychoneuroendocrinology. 2016 Jan;63:1-9. doi: 10.1016/j.psyneuen.2015.09.004. Epub 2015 Sep 5.
Cortisol modulates men's affiliative responses to acute social stress.
Berger J1, Heinrichs M2, von Dawans B3, Way BM4, Chen FS5.

Affiliative Stress Buffering in Human Males

- In another study of 145 men - the men were individually exposed to either a psychosocial stressor or a control condition, while primed with affiliation by interacting either with members of an in- or an out-group.
- Stressed participants were less trusting and engaged in less costly punishment compared to the non-stressed control group.
- Interacting with out-group members led to less reciprocity and more spiteful punishment.
- There was no interaction between stress and the affiliation conditions in any of the used social-decision-making paradigms.
- Stress-reactive cortisol levels had no effect on trust behavior, **higher baseline cortisol was correlated with greater trust.**

Psychoneuroendocrinology. 2015 Dec;62:138-48. doi: 10.1016/j.psyneuen.2015.08.003. Epub 2015 Aug 10.
The effects of stress and affiliation on social decision-making: Investigating the tend-and-befriend pattern.
Steinbeis N1, Engert V2, Linz R2, Singer T2.

Variation in Physiologic Stress Response in Human Females

- One hundred and eighty-five military members (78% males) were studied before, during, and 24 h after stressful mock captivity. Cardiovascular (heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP]) and dissociative states were measured at all three time points.

- Psychological impact of mock captivity was assessed during recovery.

Stress. 2014 Jan;17(1):70-8. doi: 10.3109/10253890.2013.869208.
Sex differences in cardiovascular and subjective stress reactions: prospective evidence in a realistic military setting.
Taylor MK1, Larson GE, Hiller Lauby MD, Padilla GA, Wilson IE, Schmied EA, Highfill-McRoy RM, Morgan CA 3rd.

Variation in Physiologic Stress Response in Human Females

- Females had lower SBP than males at all three time points, the difference was most pronounced at baseline and during stress.
- Females showed greater residual elevation in SBP during recovery.
- Females had lower DBP at all three time points.
- Females reported greater psychological impact of mock captivity than males.

Stress. 2014 Jan;17(1):70-8. doi: 10.3109/10253890.2013.869208.
Sex differences in cardiovascular and subjective stress reactions: prospective evidence in a realistic military setting.
Taylor MK1, Larson GE, Hiller Lauby MD, Padilla GA, Wilson IE, Schmied EA, Highfill-McRoy RM, Morgan CA 3rd.

CLINICAL GOAL: Increase Resilience of the HPA Axis and Optimize Cortisol Quantity and Rhythm

- **HOW?**
- Start with what she is ready to start with:
  - Exercise?
  - Nutrition?
  - Stress Buffering Strategies? Shift from “Anxiety Girl” coping strategies to “Cashmere Blanket Therapy” receiving.
  - Stressors?

Start with Coaching to Align Your Goals with Hers

- **5 Minutes of mindful listening**

Start with Coaching to Align Your Goals with Hers

- **Reflect**

Start with Coaching to Align Your Goals with Hers

- **Powerful Questions**

Start with Coaching to Align Your Goals with Hers

- **Vision/ Goal Setting**

Start with Coaching to Align Your Goals with Hers

- **Readiness to Change**

Start with Coaching to Align Your Goals with Hers

- **Implementation of Action Steps/ Accountability**

PART 3: You Are What You Absorb

Digestive FUNCTION

- Chewing
- Parasympathetic activation
- Enough stomach acid?
- Enough digestive enzymes?
- Small intestine absorption? (Leaky gut, SIBO, motility, etc.)
- Large intestine function
- Hydration
- Bowel habits

The DIGIN Model

- **D**igestion/ Absorption
- **I**ntestinal Permeability
- **G**ut Microbiota/ Dysbiosis
- **I**nflammation/ Immune
- **N**ervous System

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

What Your Client Eats is Important,
But How Her Body Processes it is also Essential

- **Step 1**: Nutrition Focused Clinical Exam
- What is your client absorbing?
- Physical Signs of Nutrient Deficiencies of Excess
  - Review the handout.

LAB: Observation for Physical Signs of Nutrient Deficiencies
Protein
Omega-3 Fats
Minerals

What Your Client Eats is Important, But How Her Body Processes it is also Essential

- **Step 2**: Assess current diet.
- 3-day food journal.
- **Is she eating any foods that commonly contribute to chronic inflammation?** soy, dairy, gluten/ grains, corn, peanuts, shellfish, tree nuts, sugar/ sweeteners, eggs

https://farrp.unl.edu/informallbig8

J Am Coll Nutr. 2004 Apr;23(2):163-8.
Fast food consumption of U.S. adults: impact on energy and nutrient intakes and overweight status.
Bowman SA1, Vinyard BT.

What Your Client Eats is Important,
But How Her Body Processes it is also Essential

- **Inflammation doesn't always come directly from the diet…**

- Is she inflamed secondary to abdominal adiposity?
- Is she inflamed due to heavy metal or environmental chemical exposures?
- Is she inflamed due to chronic infections?

- Is she inflamed due to psychosocial/ community support factors?

What Your Client Eats is Important,
But How Her Body Processes it is also Essential

- **Step 2**: Assess current diet.
- 3-day food journal.
- **Or, simply a nutrient deficient diet?** 8-10 servings of veggies/ fruits?
- **SAD Diet (or Standard Western Diet)**
- Fast food

https://farrp.unl.edu/informallbig8

J Am Coll Nutr. 2004 Apr;23(2):163-8.
Fast food consumption of U.S. adults: impact on energy and nutrient intakes and overweight status.
Bowman SA1, Vinyard BT.

What Your Client Eats is Important,
But How Her Body Processes it is also Essential

- If she's not eating an anti-inflammatory, nutrient dense food plan, start with…

http://integrativewomenshealthinstitute.com/hormone-balance-cleanse-spring/

What Your Client Eats is Important, But How Her Body Processes it is also Essential

- If she is eating a nutrient dense diet…
- There are a range of healthy diets, the challenge is finding the right nutrition program for your client.
- Vegan —> Vegetarian —> Mediterranean —> Whole Foods —> Autoimmune Paleo —> GAPS —> Paleo —> Ketogenic (and more)

- **Step 3:** Determine if she is able to absorb the nutrients that she is eating with proper digestive functioning.

The Brain and The Gut Brain

- Is your client relaxed and eating with pleasure (or fear, or rushing, or stress?)

- Just the sight of foods can trigger thoughts in the brain that trigger stress responses, or pleasure and preparation for digestion responses (such as the flow of digestive juices, saliva, enzymes, and digestive hormones.)

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

The Mouth

- Is your client chewing?
- **40 times** is the evidence based goal (especially for hard foods like nuts)
- According to a study presented at the 2013 Institute of Food Technologists (IFT) Annual Meeting and Food Expo in Chicago.
- The subjects chewed almonds either 10 times, 25 times or 40 times. Results showed that in participants who chewed the almonds more, the smaller particles entered were absorbed into the system at a faster pace, and in those who chewed the almonds less, the body eliminated the larger particles.
- ***After this lecture at lunch… slow down and chew. Is doing so challenging for you?**

http://www.medicalnewstoday.com/articles/263541.php

Determining the Health of The Digestive System

- **History**
- Empiric Assessment
- Functional Testing

History

- Do you eat under stress or in a relaxed situation?
- Do you have any digestive complaints? (can include: heartburn, difficulty swallowing, bloating, abdominal pain, gas, diarrhea, constipation)
- Do you notice any signs of nutrient malabsorption or deficiency (hair loss, thin or weak nails, peripheral neuropathy, dry skin, bleeding gums, keratosis pilaris, muscle spasm, fatigue, etc.)
- How many times do you chew each bite of food? 10 vs 25 vs 40 lead to differences in nutrient absorption, fullness, and hormonal response to eating (generally more chewing is better.)

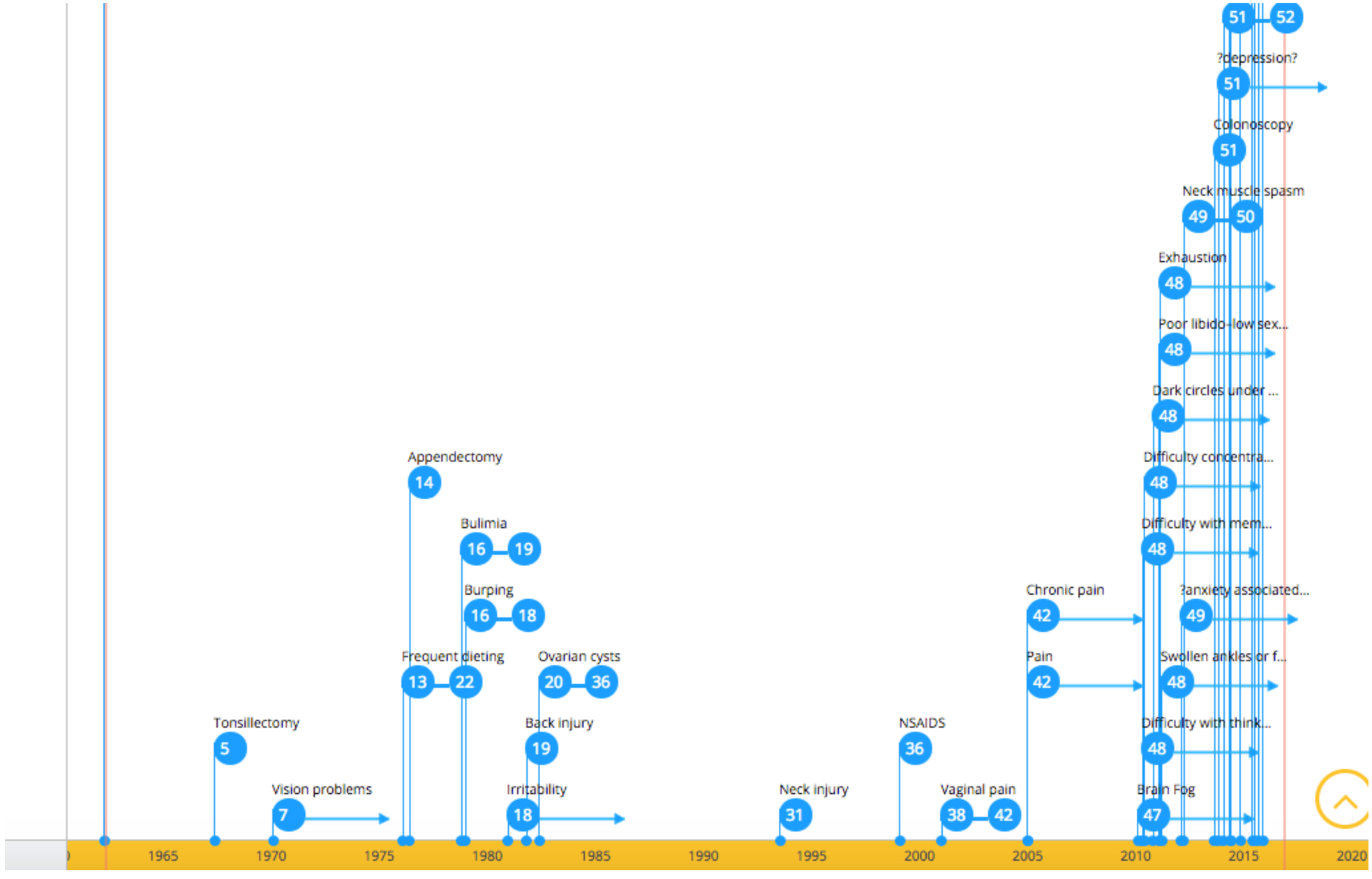
Am J Clin Nutr. 2009 Mar;89(3):794-800. doi: 10.3945/ajcn.2008.26669. Epub 2009 Jan 14.
Mastication of almonds: effects of lipid bioaccessibility, appetite, and hormone response.
Cassady BA1, Hollis JH, Fulford AD, Considine RV, Mattes RD.

History

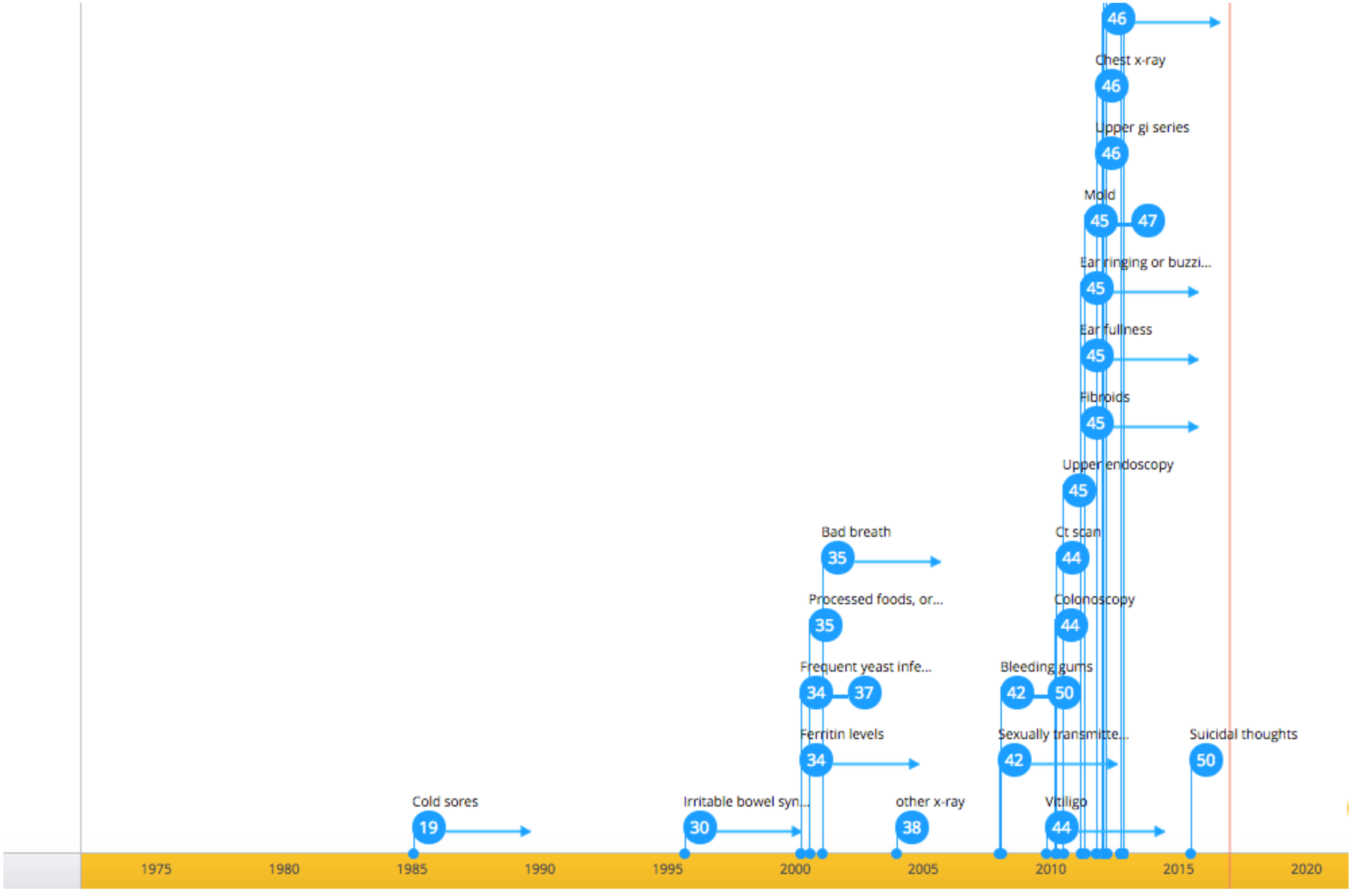
- Do you have any other symptoms of food sensitivities such as skin issues, headaches, sinus infections, weight loss resistance, difficulty gaining weight, allergies, or asthma?
- Have you been on antibiotics at any time in your life? How often? What what condition?
- Were you born via C-section or vaginal delivery?
- Were you breast fed or bottle fed?

- Use the Timeline for documentation. Don't forget to begin with preconception and consider childhood health.

Chronic Pain



Chronic Fatigue/ EBV Reactivation/ Anemia



History

- Has your client been on any medications that may negatively impact her digestive function?

Resources for drug-nutrient interactions and drug side effects:
https://www.epocrates.com/
https://www.researchgate.net/
http://www.mytavin.com/
https://naturalmedicines.therapeuticresearch.com/ ***Natural Medicines Database**
Drug Muggers by Suzy Cohen

Pharmaceuticals that Impact Digestive Health

- **NSAIDs** induce intestinal damage, the effect is worsened with the addition of proton pump inhibitors.

- **Antibiotics** (especially clindamycin and ciprofloxacin) impact the health of the fecal microbiota (but, not the saliva microbiota) long term, even with just one course of antibiotics.)

- Even short term use of some antibiotics can have a long term impact on the ability of the gut microbiota to produce butyrate, a health promoting short chain fatty acid.

Digestion. 2015;91(3):218-32. doi: 10.1159/000374106. Epub 2015 Mar 18.
NSAID-induced small intestinal damage--roles of various pathogenic factors.
Takeuchi K1, Satoh H.

MBio. 2015 Nov 10;6(6). pii: e01693-15. doi: 10.1128/mBio.01693-15.
Same Exposure but Two Radically Different Responses to Antibiotics: Resilience of the Salivary Microbiome versus Long-Term Microbial Shifts in Feces.
Zaura E1, Brandt BW2, Teixeira de Mattos MJ3, Buijs MJ2, Caspers MP4, Rashid MU5, Weintraub A5, Nord CE5, Savell A6, Hu Y6, Coates AR6, Hubank M7, Spratt DA8, Wilson M8, Keijser BJ4, Crielaard W2.

Pharmaceuticals that Impact Digestive Health

- **Proton Pump Inhibitors:**
  - In the small bowel, PPIs cause polymicrobial small bowel bacterial overgrowth and have been associated with the diagnosis of celiac disease.
  - In the colon, PPIs associate with incident but not recurrent Clostridium difficile infection, putatively through alterations in commensal colonic anaerobes.
  - Reduce B12 and protein absorption.

Freedberg, D. E., Lebwohl, B., & Abrams, J. A. (2014). The impact of proton pump inhibitors on the human gastrointestinal microbiome. Clinics in Laboratory Medicine, 34(4), 771–785. http://doi.org/10.1016/j.cll.2014.08.008

Birth Control Pills and Depletion

- Some micronutrients are not well absorbed by women on oral contraceptives.
- **Folic acid -** essential to prevent neural tube defects in fetuses.
- **Vitamins B2, B6, and B12 -** essential to reduce inflammation/ homocysteine which is a primary cardiac risk factor.
- **Vitamins C and E -** antioxidants minimize inflammation and may influence the environment for healthy sperm.
- **Magnesium, selenium, and zinc -** minerals to displace heavy metal toxicity, keep the uterus relaxed, and protect the maternal thyroid perinatally.

M. Palmery, A. Saraceno, A. Vaiarelli, G. Carlomagno Oral contraceptives and changes in nutritional requirements. Eur Rev Med Pharmacol Sci, Year: 2013, Vol. 17 - N. 13, Pages: 1804-1813

Antidepressants and Depletion

- Cymbalta (Duloxetine) and Pristiq (Desvenlafaxine) were the most common antidepressants prescribed in 2014.
- **Both deplete folate.**

http://mentalhealthdaily.com/2014/08/30/most-popular-antidepressants-in-2014-cymbalta-pristiq-viibryd/

http://www.naturemade.com/~/media/Images/NatureMade/PDF/Health%20Care%20Professionals/HCP%20Updates%20042315/Common%20Drug%20Classes%20and%20Nutrient%20Interactions%20Chart%20FNL.ashx

Antidepressant Use is Very Common

- 23% of women aged 40–59 take antidepressants, more than in any other age-sex group.

- Eleven percent of Americans aged 12 years and over take antidepressant medication.

- Females are more likely to take antidepressants than are males, and non-Hispanic white persons are more likely to take antidepressants than are non-Hispanic black and Mexican-American persons.

http://www.cdc.gov/nchs/products/databriefs/db76.htm

Antidepressant Use is Very Common

- More than 60% of Americans taking antidepressant medication have taken it for 2 years or longer, with 14% having taken the medication for 10 years or more.
- Less than 1/3 of Americans taking one antidepressant medication and less than 1/2 of those taking multiple antidepressants have seen a mental health professional in the past year.

http://www.cdc.gov/nchs/products/databriefs/db76.htm

Empiric Testing of Digestive Health

- Does your client have adequate stomach acid?

Optimal Functioning of The Stomach

- It is essential that the stomach is acidic enough for optimal nutrient absorption. (Intrinsic factor + B12, and the ability of pepsin to begin protein breakdown, pepsinogen —> pepsin.)
- Signs and symptoms of **hypochlorhydria**:
  - bloating or belching immediately following a meal
  - feels like food sits in the stomach
  - sense of fullness after eating
  - also, any signs of protein or deficiency - weak/ cracked/ peeling nails, iron deficiency, chronic intestinal infections,
  - undigested food in stool
  - history of proton pump inhibitor medications for GERD (*Designed for short term use, 16 weeks.)

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

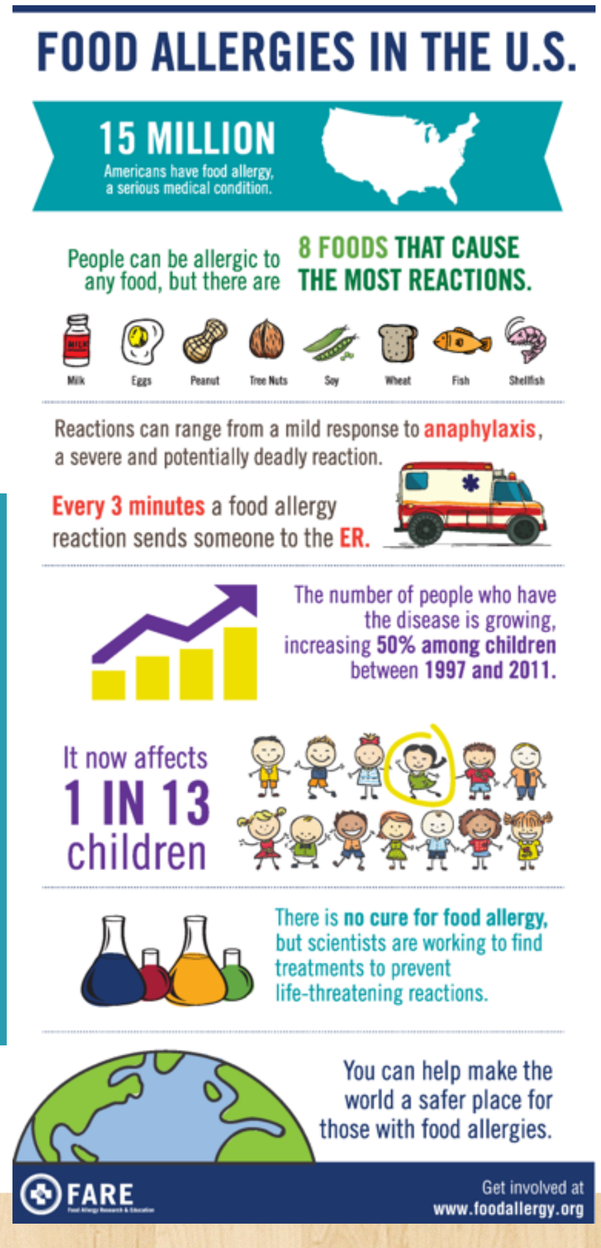
Hypochlorhydria

- Causes:
  - Aging
  - Stress
  - Fasting
  - Viral or bacterial infection
  - Any debilitating chronic conditions (it takes approx. 600-800 cal per day to concentrate enough hydrogen ions to make strong stomach acid.)
  - PPI’s, H2 blockers, and antacid abuse for GERD

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

Hypochlorhydria

- **Increases IgE reactions!**



FASEB J. 2005 Apr;19(6):656-8. Epub 2005 Jan 25.
Anti-ulcer drugs promote IgE formation toward dietary antigens in adult patients.
Untersmayr E1, Bakos N, Schöll I, Kundi M, Roth-Walter F, Szalai K, Riemer AB, Ankersmit HJ, Scheiner O, Boltz-Nitulescu G, Jensen-Jarolim E.

How to Support Healthy Stomach Acid

- Betaine HCl challenge: With a protein containing meal take one, 350 mg tablet of Betaine HCl + pepsin. If that feels fine or decreases symptoms continue doing so with 1-2 protein containing meals per day, and increase the dose, SLOWLY (add another pill approx 3 days later), up to a max dose of 3500 mg.
- Stop/ back way off IF any burning, back/ neck stiffness, worse digestive issues, etc.
- DON'T try this with PPI's, or antacids of any kind.
- DON'T try this with ULCERS or ULCERATIVE COLITIS

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

How to Support Healthy Stomach Acid

- Less aggressive options *(*Pt. needs to have enough ATP to generate her own stomach acid. This strategy will not work as well if your patient is fatigued.)*
  - Umeboshi plums (or made into tea)
  - Swedish bitters
  - Apple cider vinegar (begin with 1 Tbsp in 8 Tbsp of water)
  - Gentian root (in bitters)
  - Stress management

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

Determining Healthy Digestive Enzyme Levels

- Empiric testing by a trial of digestive enzyme supplementation
- Testing for pancreatic elastase (GI Effects stool test): >200 mcg/g (optimal is at least 400 mcg/g)
- If less than 200 mcg/g may need long term supplementation.

- Low products of protein breakdown (GI Effects stool test): Valerate, Isobutyrate, Isovalerate. These can also be elevated with too much protein intake. Consider dietary intake.
- Excess fecal fat may be due to decreased bile acids and lipase. Again, consider fat intake.

Lipski, E. (2012) Digestive Wellness 4th Edition, McGraw Hill USA.

Digestive Enzyme Supplementation

- Depends on the needs:
- Can be combination of amylase, lipase, protease
- Also available are specialty preparations - lactase, enzymes specifically to breakdown gluten, etc.
- Some high quality options I have used clinically or that have been recommended by trusted colleagues:
  - nutraMetrix
  - Transformation Enzyme products: Protease, Purezyme, and Repairzyme.
  - Houston, Loomis, Kirkman
  - Designs for Health
  - Orthomolecular

Nutritional Digestive Enzyme Stimulation

- Spices can increase secretion of bile and digestive enzymes.
- For example, curcumin stimulated lipase activity by 80%, and a single dose of mint led to a 43% increase in lipase activity.
- The dietary intake of whole spices - ginger, ajowan, fennel, coriander, garlic, and onion - significantly enhanced trypsin activity. Ginger by 133%.
- An increase in intestinal lipase activity was observed in animals given single oral doses of mint, garlic, onion, ajowan, ginger, fennel, piperine, fenugreek and curcumin (between 20% and 461% depending on the spice.)

Indian J Med Res. 2004 May;119(5):167-79.
Digestive stimulant action of spices: a myth or reality?
Platel K1, Srinivasan K.

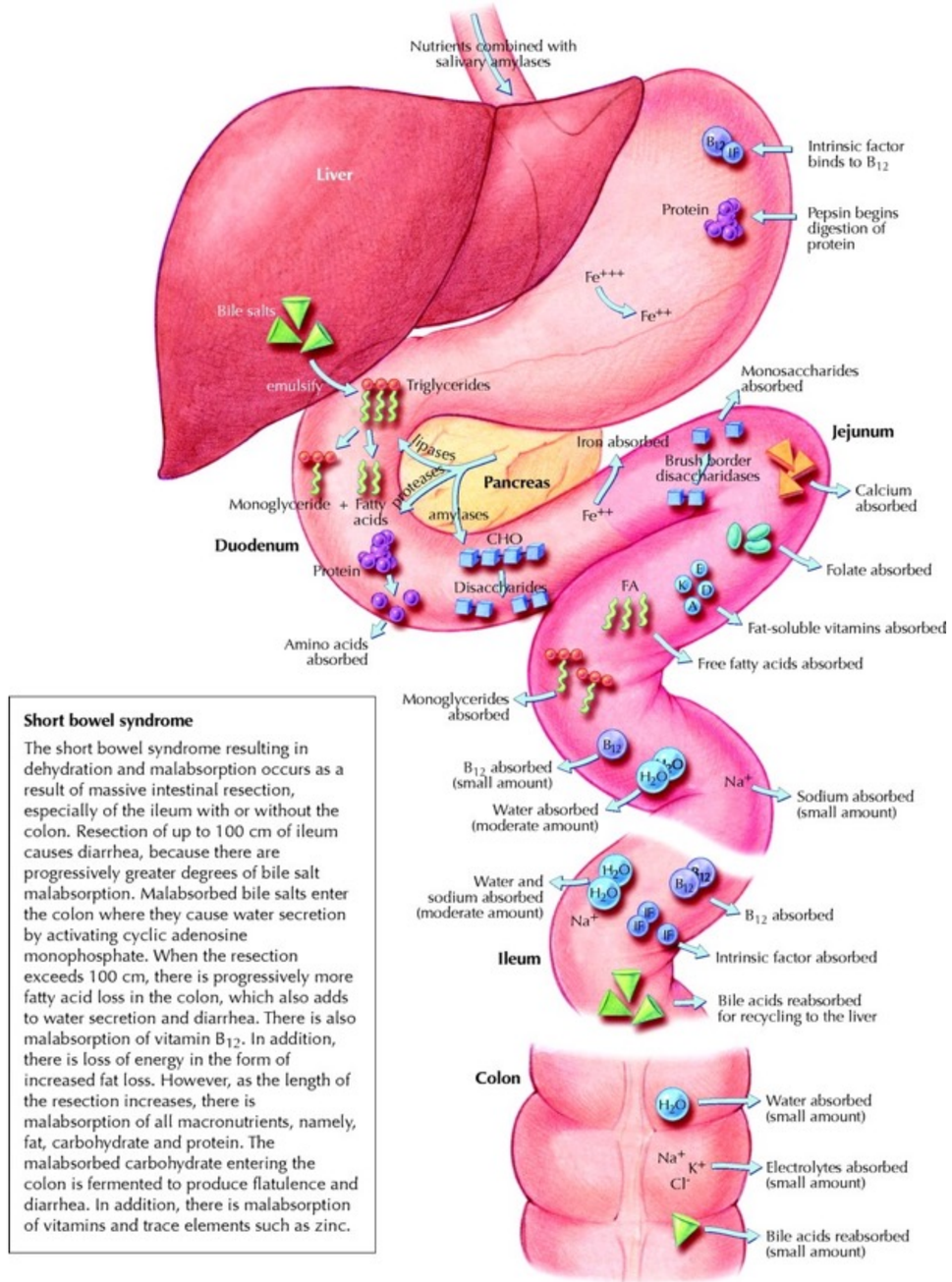
Intestinal Function

- Now that we have considered risks to digestive health based on her history (including digestive symptoms, history of pharmaceutical use, known allergies/ sensitivities, current nutrition program - 3 day food journal, etc.)

- And… we have assessed the function of the mouth and stomach by discussing chewing and eating behaviors and empirically testing stomach acidity, which play an important role in B12 absorption and protein digestion.

- Now… it's time to look at the health of the intestines.
- **Where are all of the nutrients absorbed?**

Fig. 1: The relative locations of digestion and absorption of nutrients in the healthy gastrointestinal tract.

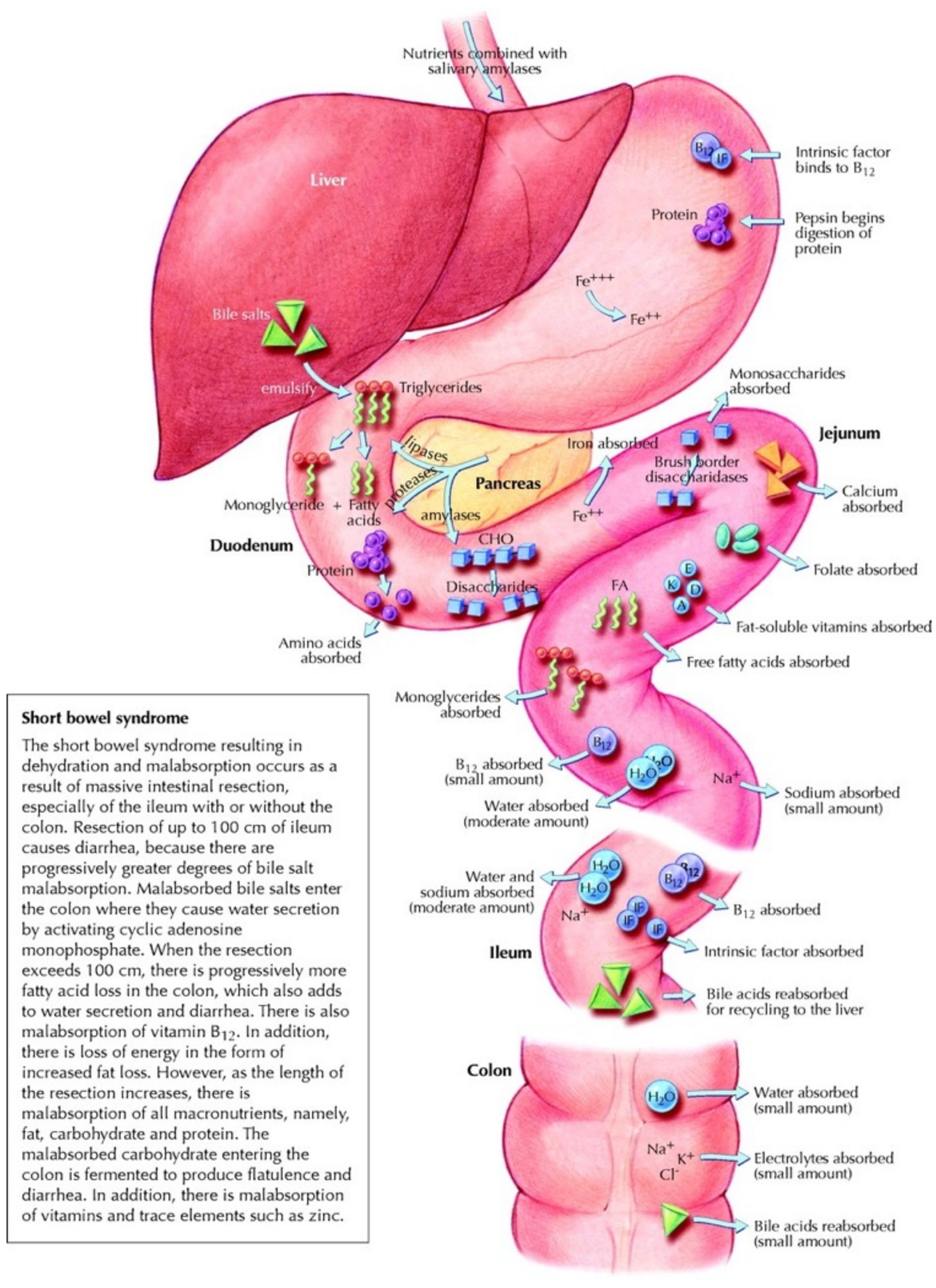


Short bowel syndrome

The short bowel syndrome resulting in dehydration and malabsorption occurs as a result of massive intestinal resection, especially of the ileum with or without the colon. Resection of up to 100 cm of ileum causes diarrhea, because there are progressively greater degrees of bile salt malabsorption. Malabsorbed bile salts enter the colon where they cause water secretion by activating cyclic adenosine monophosphate. When the resection exceeds 100 cm, there is progressively more fatty acid loss in the colon, which also adds to water secretion and diarrhea. There is also malabsorption of vitamin B_{12}. In addition, there is loss of energy in the form of increased fat loss. However, as the length of the resection increases, there is malabsorption of all macronutrients, namely, fat, carbohydrate and protein. The malabsorbed carbohydrate entering the colon is fermented to produce flatulence and diarrhea. In addition, there is malabsorption of vitamins and trace elements such as zinc.

Khursheed N. Jeejeebhoy CMAJ 2002;166:1297-1302

CMAJ·JAMC



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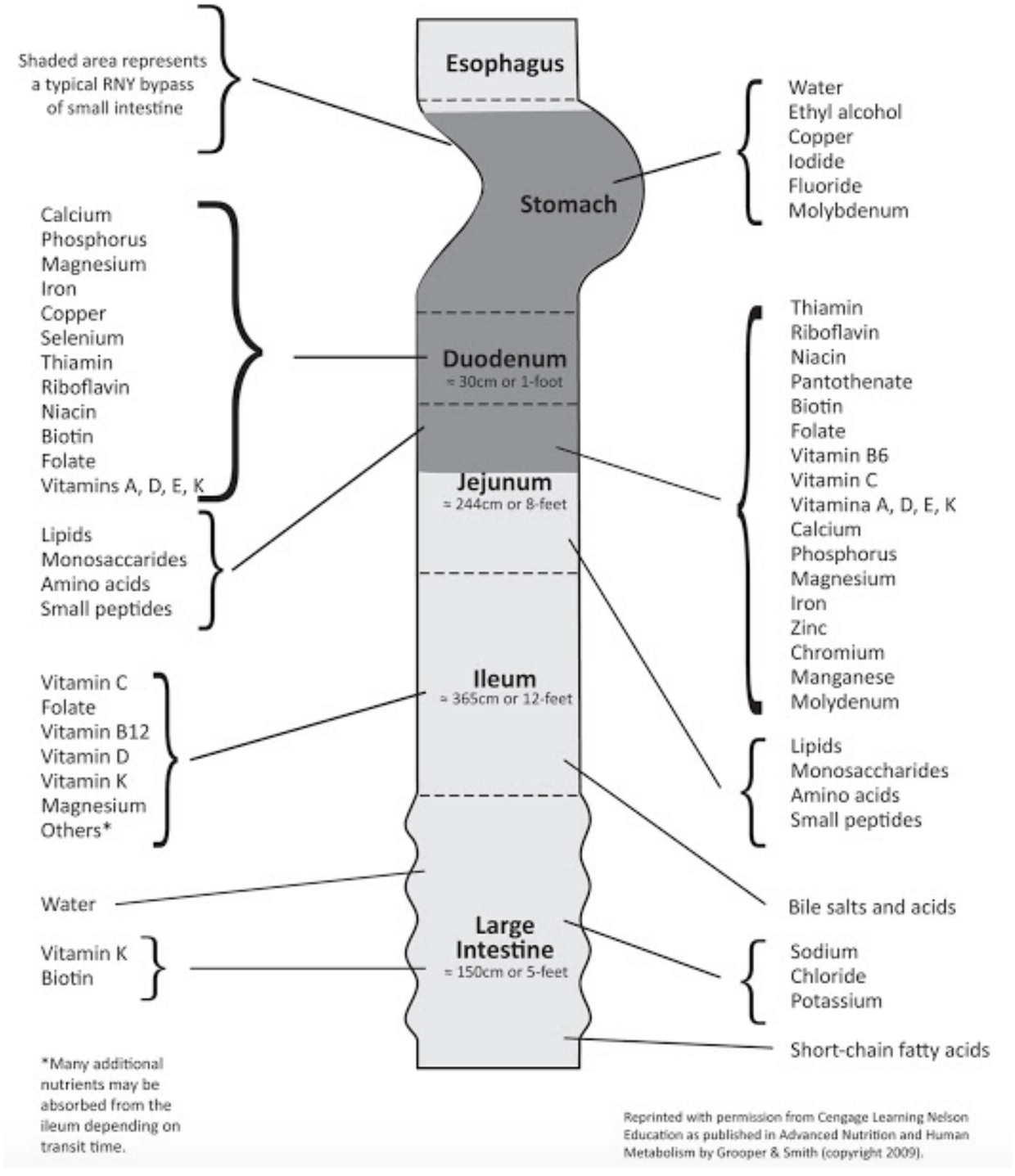
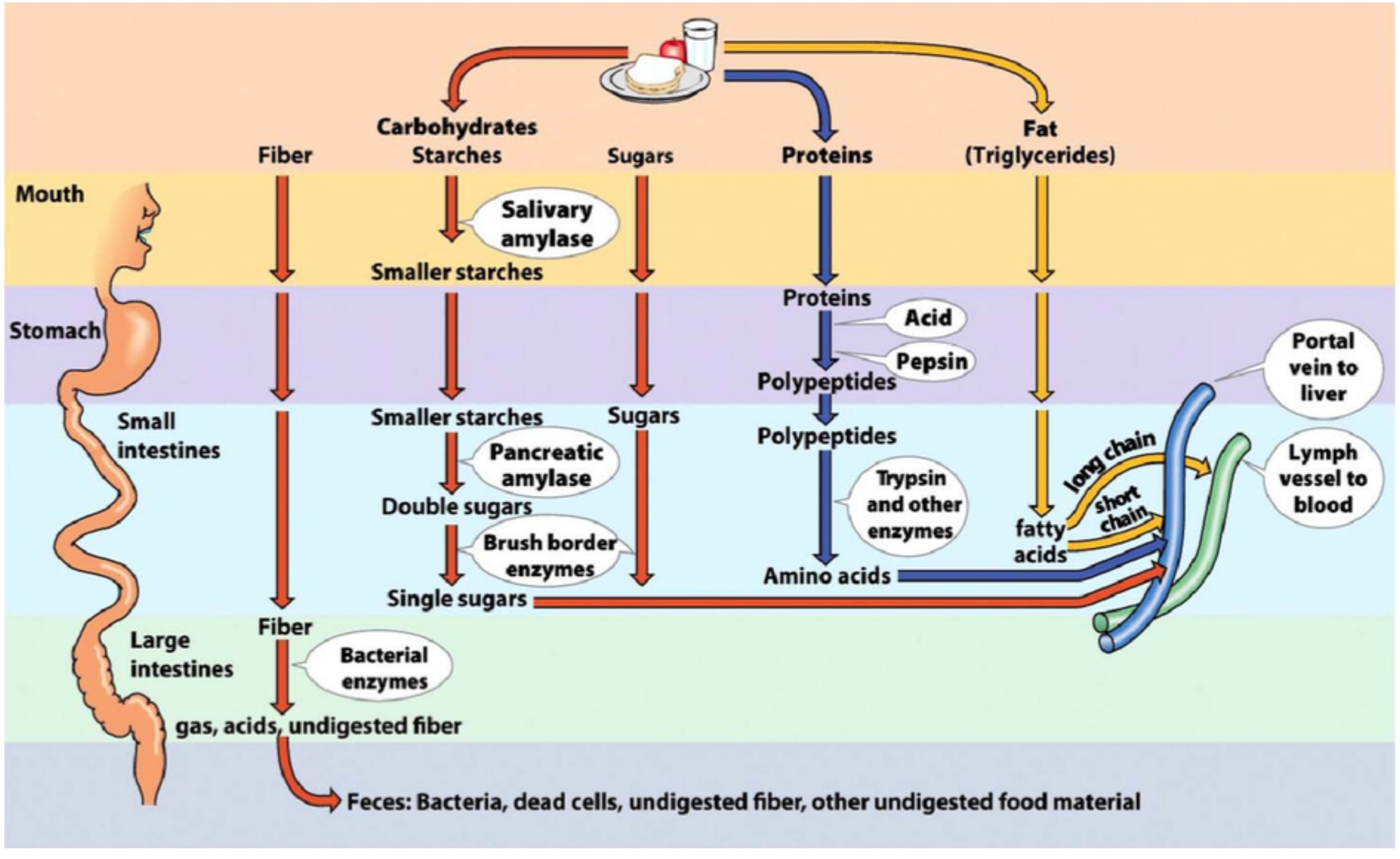
- Mouth: salivary amylase
- Stomach: Intrinsic factor + B12, and protein + pepsin, need HCl (very low pH)
- Duodenum (higher pH): bile salts mix with triglycerides, and pancreatic enzymes released, iron absorbed
- Jejunum: many nutrients absorbed - Calcium, folate, free fatty acids, fat soluble vitamins, B12 (at the end), some water and sodium absorbed.
- Ileum: water, sodium, B12, intrinsic factor, Bile acids recycled.

liskahttp://www.cmaj.ca/content/166/10/1297/F1.expansion.html



- **ALL of these nutrients are needed to maintain health of the detoxification organs, hormonal balance, general cellular functioning, metabolism, energy, etc.**

http://pamtremble.blogspot.com/2008/05/where-are-nutrients-absorbed.html


Carbohydrates
Fiber
Starches
Sugars
Proteins
Fat
(Triglycerides)
Mouth
Salivary amylase
Smaller starches
Stomach
Proteins
Acid
Pepsin
Polypeptides
Portal vein to liver
Small intestines
Smaller starches
Sugars
Pancreatic amylase
Polypeptides
Trypsin and other enzymes
long chain
short chain
Lymph vessel to blood
Double sugars
Brush border enzymes
fatty acids
Amino acids
Single sugars
Fiber
Large intestines
Bacterial enzymes
gas, acids, undigested fiber
Feces: Bacteria, dead cells, undigested fiber, other undigested food material

Nutrient Supplementation and Healthy Aging

- 3966 older French adults: During 1994-2002, the participants received a daily combination of vitamin C (120 mg), β-carotene (6 mg), vitamin E (30 mg), selenium (100 μg), and zinc (20 mg) or placebo.
- Healthy aging was then assessed in 2007-2009 by using multiple criteria, including the absence of major chronic disease and good physical and cognitive functioning.
- The participants were initially free of major chronic disease, with a mean age of 65.3 years in 2007-2009.

Am J Epidemiol. 2015 Oct 15;182(8):694-704. doi: 10.1093/aje/kwv105. Epub 2015 Sep 15.
Healthy Aging 5 Years After a Period of Daily Supplementation With Antioxidant Nutrients: A Post Hoc Analysis of the French Randomized Trial SU.VI.MAX.
Assmann KE, Andreeva VA, Jeandel C, Hercberg S, Galan P, Kesse-Guyot E.

Nutrient Supplementation and Healthy Aging in Women

- Supplementation was associated with a greater healthy aging probability among men (relative risk = 1.16, 95% confidence interval: 1.04, 1.29) but not among women (relative risk = 0.98, 95% confidence interval: 0.86, 1.11)

- Exploratory subgroup analyses indicated effect modification by initial serum concentrations of zinc and vitamin C.

Am J Epidemiol. 2015 Oct 15;182(8):694-704. doi: 10.1093/aje/kwv105. Epub 2015 Sep 15.
Healthy Aging 5 Years After a Period of Daily Supplementation With Antioxidant Nutrients: A Post Hoc Analysis of the French Randomized Trial SU.VI.MAX.
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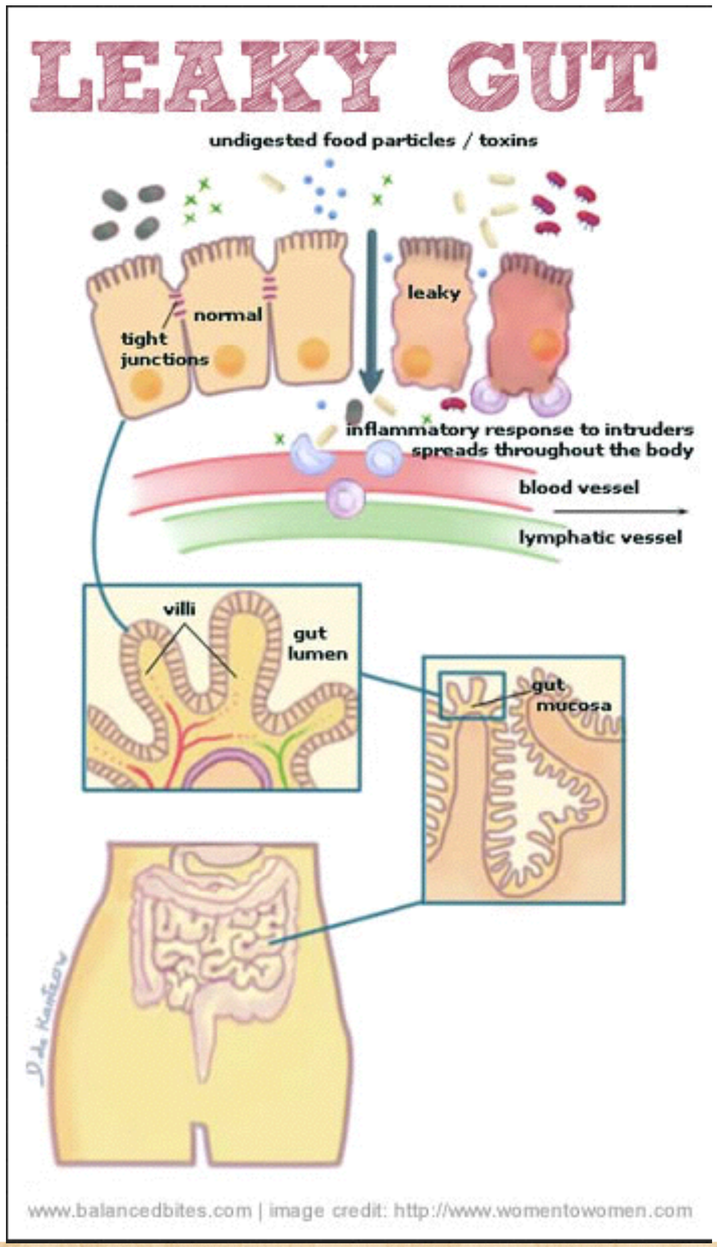
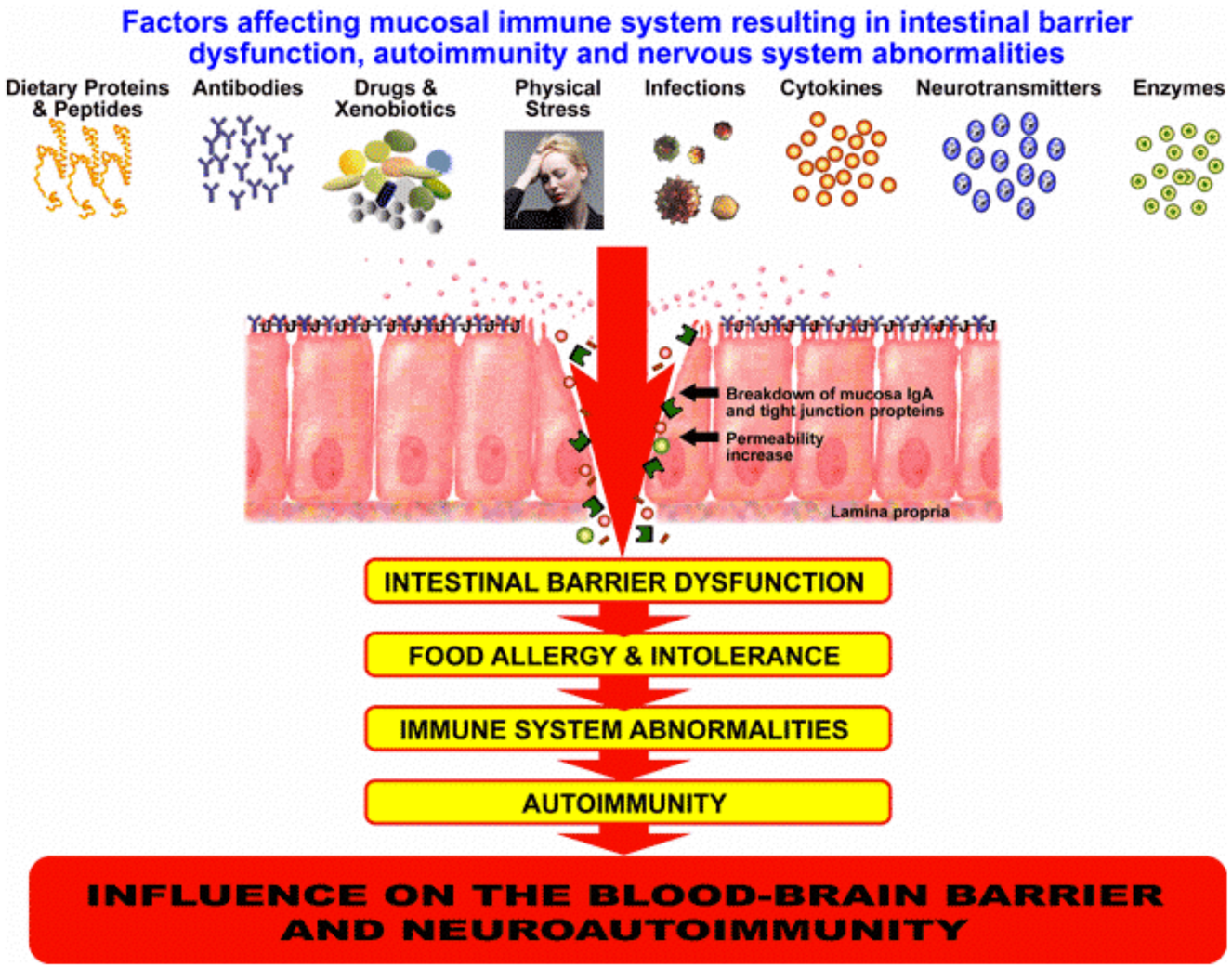


What is leaky gut?

How to Determine if your client has leaky gut?

Gut Permeability



History to Determine Increased Intestinal Permeability

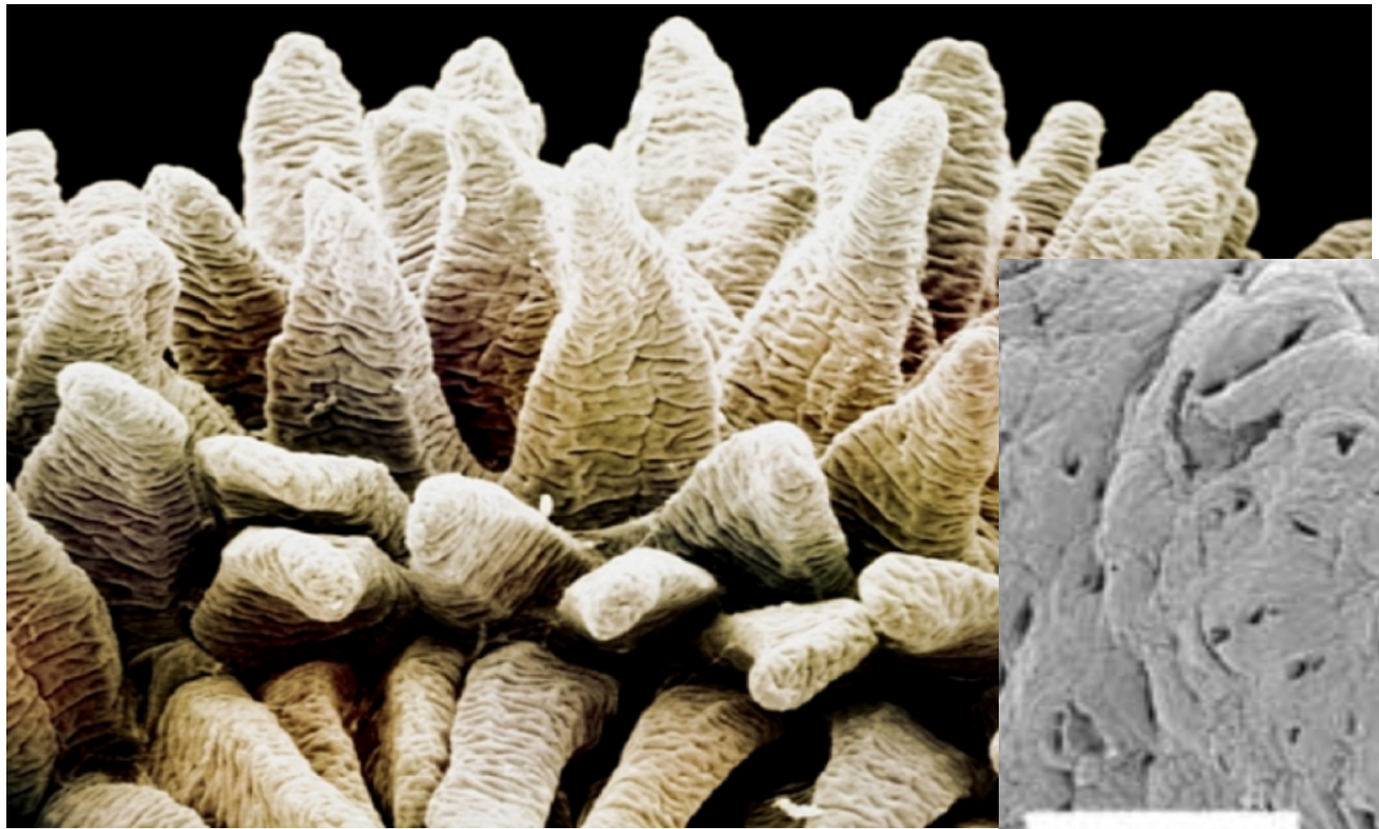
- Potential Signs: food sensitivities, allergies, nutrient deficiencies, chronic inflammation, joint pain, skin issues, GI pain/ complaints, headaches, autoimmune conditions.

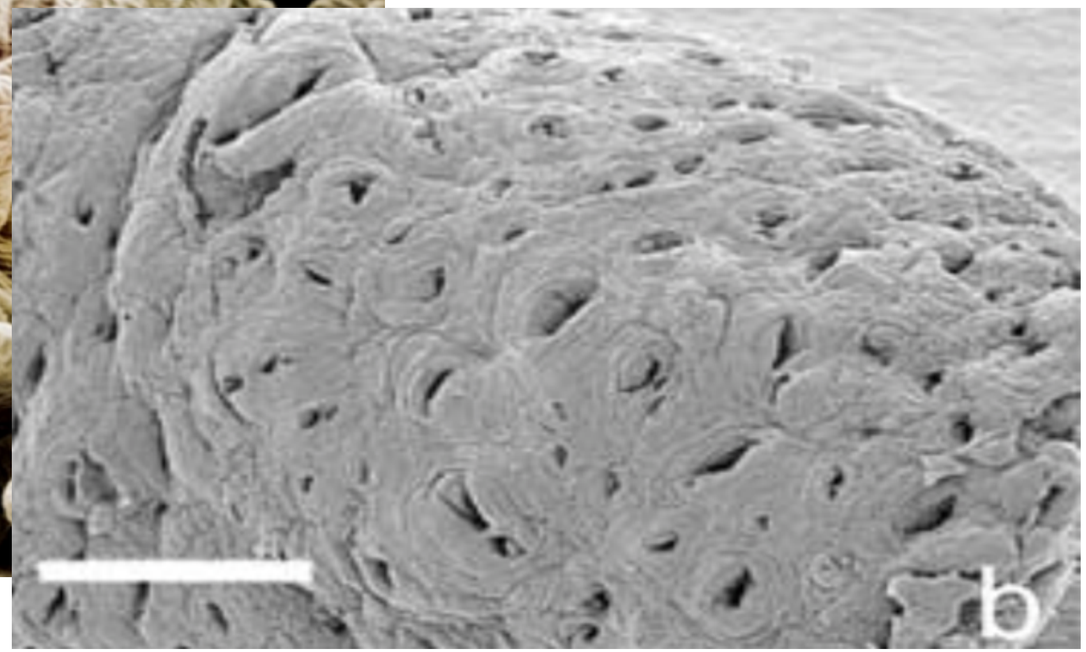
- Potential Causes: pharmaceuticals, lack of chewing, hypochlorhydria, weak digestive enzymes (common after age 35 and with chronic stress/ pain/ illness), physical stress, emotional stress, inflammatory cytokines, infections, toxins, intense exercise + dehydration, etc.

It's not just about elimination of foods,
but also about healing the small intestine epithelium.
Think elimination AND addition of nourishment!

THE iwh INSTITUTE

Damaged Brush Boarder





Am J Gastroenterol. 2004 May;99(5):894-904.
Presence of bacteria and innate immunity of intestinal epithelium in childhood celiac disease.
Forsberg G1, Fahlgren A, Hörstedt P, Hammarström S, Hernell O, Hammarström ML.

Causes of Leaky Gut

- Factors that can affect the tight junctions and health of the enterocytes:
  - Infections, elevated SIgA levels (can be seen on stool tests)
  - Enzymes, low stomach acid
  - Neuropeptides, Neurotransmitters
  - Dietary peptides (i.e. gluten) and lectins
  - Dietary additives: glucose, salt, emulsifiers, organic solvents, gluten, microbial transglutaminase, and nanoparticles
  - Parasites
  - Proinflammatory cytokines
  - Free radicals
  - Drugs, environmental toxins
  - Low O2, ischemia (low iron, lack of motility, poor circulation)

Autoimmun Rev. 2015 Jun;14(6):479-89. doi: 10.1016/j.autrev.2015.01.009. Epub 2015 Feb 9.
Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease.
Lerner A1, Matthias T2.

Causes of Leaky Gut: Zonulin and Gliadin

- Zonulin is a protein that increases gut permeability
- Gliadin induces increased intestinal permeability by releasing preformed zonulin.
- Gluten containing grains contain gliadin.

- May be more of an issue of **wheat/ FODMAPS** (especially with IBS) vs. gluten alone. (http://www.ncbi.nlm.nih.gov/pubmed/23648697) (more a bit later on FODMAPS…)

Ann N Y Acad Sci. 2009 May; 1165: 195–205.
doi: 10.1111/j.1749-6632.2009.04037.x
PMCID: PMC2886850
NIHMSID: NIHMS199724
Tight Junctions, Intestinal Permeability, and Autoimmunity Celiac Disease and Type 1 Diabetes Paradigms Jeroen Visser,[a] Jan Rozing,[a] Anna Sapone,[b] Karen Lammers,[b] and Alessio Fasano[b]

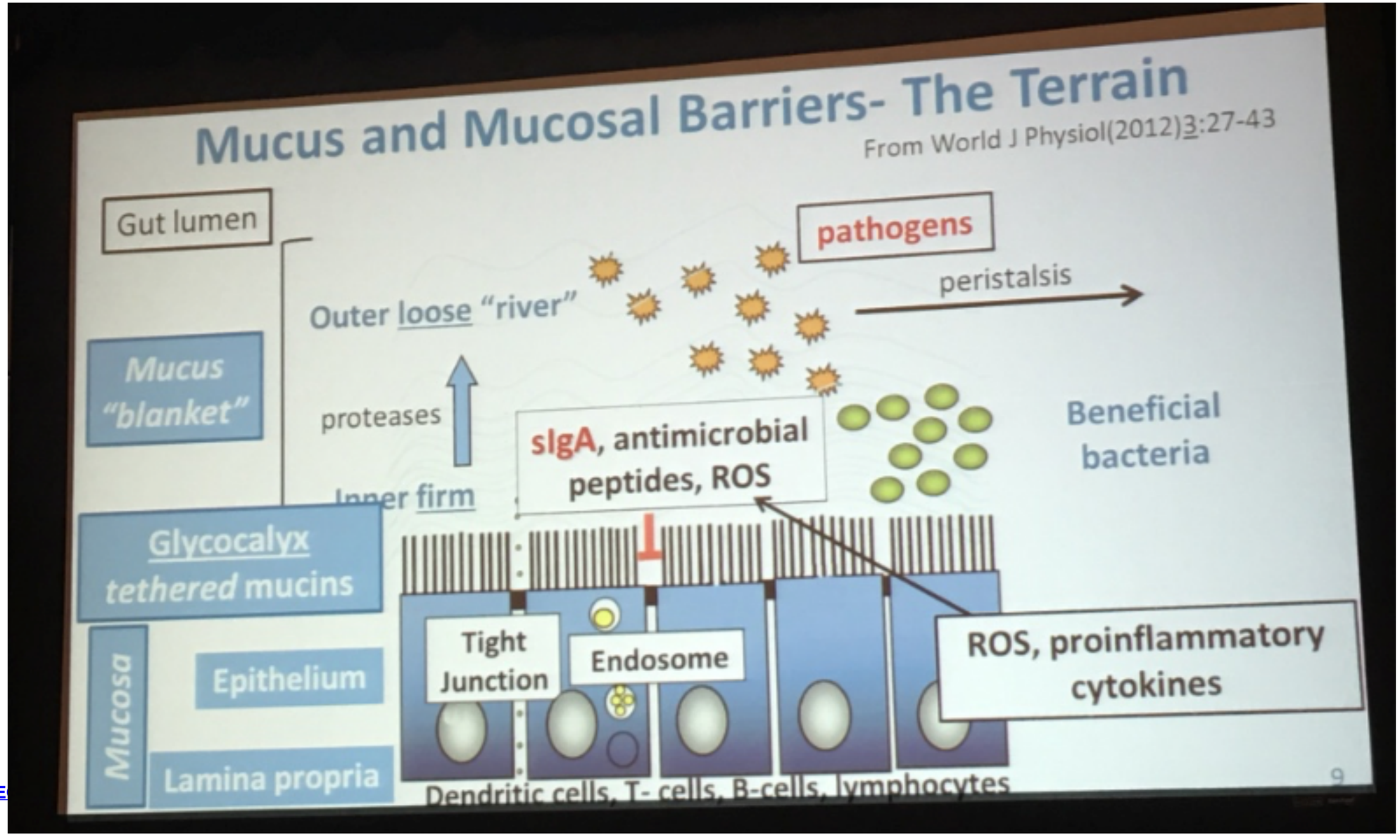
Testing to Determine Increased Intestinal Permeability

- What is the intestinal barrier? It includes the physical barrier, support from the gut microbiota (more in a moment…), and the functional barrier of the immune system.

- The most commonly used functional test to determine the integrity of the intestinal barrier in the small intestine where most nutrients are absorbed: Mannitol-Lactulose test

Jones, DS (2010) Textbook of Functional Medicine, Institute for Functional Medicine, Gig Harbor, MA.

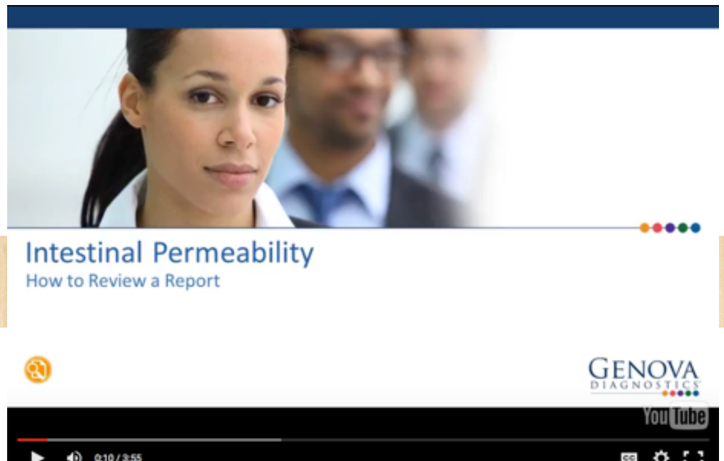
Barrier Layers



INTE

Testing to Determine Increased Intestinal Permeability

- **Mannitol-lactulose test:** Mannitol is a small, non-metabolized sugar that is readily absorbed and excreted in urine. Lactulose is a large, non-metabolized sugar that is generally not absorbed and excreted in stool.
- High lactulose/ mannitol ratio = increased intestinal permeability.
- Low mannitol recovery = impaired nutrient absorption.
- See the Interpretation Guide and Video from Genova for those who are licensed to order testing.



Leaky Gut and Autoimmunity

- "...the autoimmune process can be **arrested** if the interplay between genes and environmental triggers is prevented by re-establishing intestinal barrier function."

- Look beyond digestive symptoms when considering leaky gut. Consider pain, headaches, skin issues, autoimmune conditions, endocrine conditions, etc.
- **If nutrients are not being well absorbed and pathogens are able to pass through protective barriers, all physiologic functions can be affected.**

http://www.direct-ms.org/pdf/LeakyGutMS/Fasano%20intestinal%20barrier%20autoimmunity.pdf

Intestinal Permeability

- Tight junction dysfunction seems to be a primary defect in autoimmune disease (AD.)
- Intestinal permeability is increased in many AD: Ulcerative colitis, Crohn's disease, celiac disease, inflammatory joint disease, ankylosing spondylitis, juvenile onset arthritis, psoriatic arthritis, type 1 diabetes mellitus and primary biliary cirrhosis. **Our research on vulvodynia showing this as well.*

- In addition to genetic predisposition and exposure to triggering non-self antigens, the loss of protective function of mucosal barriers that interact with the environment is necessary for autoimmunity to develop.

Autoimmun Rev. 2015 Jun;14(6):479-89. doi: 10.1016/j.autrev.2015.01.009. Epub 2015 Feb 9.
Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease.
Lerner A1, Matthias T2.

Addressing Digestive Function

- **Step 4: Use The 5 R's to address Increased Intestinal Permeability and Gut Dysbiosis**

- What does this patient need to have **removed**? (food sensitivities, medications, stress, toxic exposures, kill the "pathogens", etc.)

- What does this patient need to have **replaced**? (Nutrient deficiencies, gut healing nutrients (L-glutamine, zinc, L. plantarum), feeling of underlying safety and support in her life —> reduced stress & hormonal balance, healthy relationships, financial stability, community support, spiritual practice, quality sleep)

Addressing Digestive Function

- **Step 4: Use The 5 R's to address Increased Intestinal Permeability and Gut Dysbiosis**
  - What does this patient need in terms of support and/or re-establishment of a healthy balance of microflora; that is, what does he/she require to **reinoculate** the gut with pre- or probiotics? (Over time this will involve dietary changes to actually change the microbiota composition in the long term. In the short term, pre- and pro- biotic supplements can be helpful.)

Addressing Digestive Function

- **Step 4: Use The 5 R's to address Increased Intestinal Permeability and Gut Dysbiosis**

- What support does this patient need to **repair** the GI (and other) barriers? (zinc, glutamine, etc. to repair the gut lining)

- What does this patient need to do to **rebalance** her lifestyle (and/or hormones)? The Holistic Women's Health Assessment, health coaching… (and/or hormone testing)

The Elimination Diet (Remove)

- Comprehensive Elimination Diet

http://integrativewomenshealthinstitute.com/hormone-balance-cleanse-spring/

- **ADD**: bone broths/ mineral broths, medical foods (non dairy, soy, or gluten-containing), fermented and cultured foods, apple cider vinegar, collagen/ pea/ hemp/ beef protein supplements
- L-glutamine, zinc, demulcent herbs

Elimination Diet (Remove)

- Elimination Diets can be personalized:
  - Based on IgG testing
  - Based on the literature for a specific condition (Endometriosis/ IC, pelvic pain)
  - The 6 Food Elimination Diet: “An empiric 6-food elimination diet effectively induced remission of active adult EoE, which was maintained for up to 3 years with individually tailored, limited exclusion diets.”
  - IWHI Patient Level Programs
  - Whole Life Nutrition

J Allergy Clin Immunol. 2013 Mar;131(3):797-804. doi: 10.1016/j.jaci.2012.12.664. Epub 2013 Jan 31.
Empiric 6-food elimination diet induced and maintained prolonged remission in patients with adult eosinophilic esophagitis: a prospective study on the food cause of the disease.
Lucendo AJ1, Arias Á, González-Cervera J, Yagüe-Compadre JL, Guagnozzi D, Angueira T, Jiménez-Contreras S, González-Castillo S, Rodríguez-Domíngez B, De Rezende LC, Tenias JM.

Normalizing The Intestinal Barrier Function
(Replace/ Repair)

- **Zinc**
- Supplemental zinc has been shown to improve gut permeability in pigs under stress. (The stress induced the gut permeability.)
- Tightens leaky gut in Crohn's Disease research.

Gut. 2007 Feb;56(2):168-75. Epub 2006 Jun 15.
Zinc carnosine, a health food supplement that stabilises small bowel integrity and stimulates gut repair processes. Mahmood A, FitzGerald AJ, Marchbank T, Ntatsaki E, Murray D, Ghosh S, Playford RJ.

Animal. 2014 Jan;8(1):43-50. doi: 10.1017/S1751731113001961. Epub 2013 Nov 7.
Effects of supplemental zinc amino acid complex on gut integrity in heat-stressed growing pigs. Sanz Fernandez MV[1], Pearce SC[1], Gabler NK[1], Patience JF[1], Wilson ME[2], Socha MT[2], Torrison JL[2], Rhoads RP[3], Baumgard LH[1].

Inflamm Bowel Dis. 2001 May;7(2):94-8.
Zinc supplementation tightens "leaky gut" in Crohn's disease.
Sturniolo GC1, Di Leo V, Ferronato A, D'Odorico A, D'Incà R.

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **Zinc**

- Epithelial barrier dysfunction in the distal small intestine plays an important role in alcohol-induced gut leakiness, and zinc deficiency attributable to oxidative stress may interfere with the intestinal barrier function by a direct action on tight junction proteins or by sensitizing to the effects of alcohol.

Am J Physiol Gastrointest Liver Physiol. 2010 May;298(5):G625-33. doi: 10.1152/ajpgi.00350.2009. Epub 2010 Feb 18.
The role of zinc deficiency in alcohol-induced intestinal barrier dysfunction.

Zhong W, McClain CJ, Cave M, Kang YJ, Zhou Z.

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **Zinc: How Much?**
- Look for deficiency, measure if possible. NutrEval, Spectracell
- Per Crohn's Disease research: oral zinc sulfate, 110mg x 3 times daily for 8 weeks (monitor levels for 12 months)
- More common dosage depends on need (usually in the range of approx 25mg - 75mg) and may need to be balanced with copper (if >20mg zinc daily)
- RDA for adult women: 8 mg, 11 mg (pregnant), 12mg (lactating)

https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/

Inflamm Bowel Dis. 2001 May;7(2):94-8.
Zinc supplementation tightens "leaky gut" in Crohn's disease.

Sturniolo GC, Di Leo V, Ferronato A, D'Odorico A, D'Incà R.

A Note on Copper

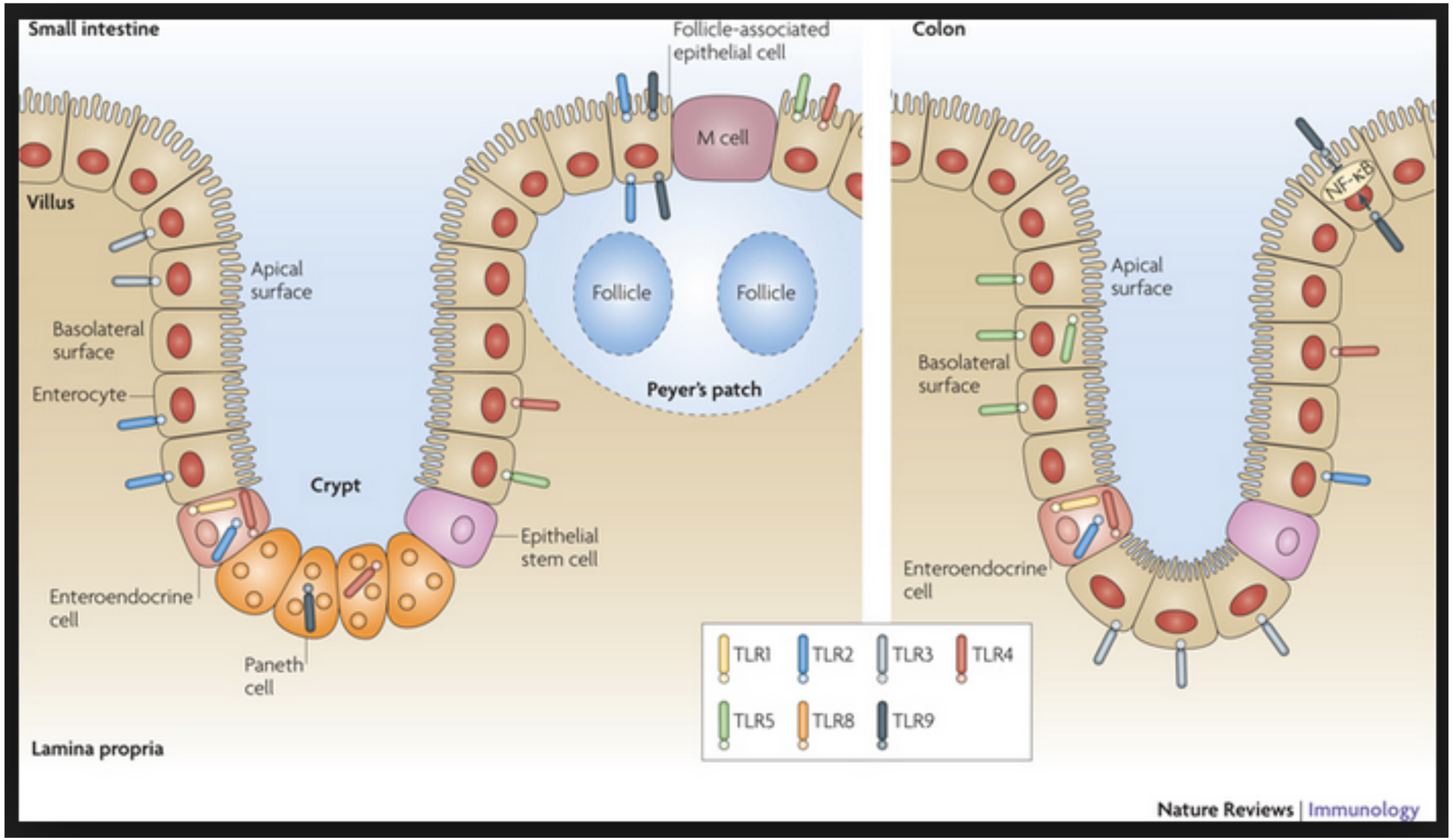
- Elevated levels of copper increase oxidative stress.
- Thus, it's ideal to test prior to any copper recommendation.
- However, be aware that high doses of zinc (above the RDA) can, in some clients, deplete copper.
- A low zinc/copper ratio is seen in hypertension and hypertension + type 2 diabetes.

Ann Biol Clin (Paris). 2016 Apr 1;74(2):233-243.
The link between trace elements and metabolic syndrome/oxidative stress in essential hypertension with or without type 2 diabetes.
Gouaref I1, Bellahsene Z2, Zekri S3, Alamir B4, Koceir EA1.

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **L-glutamine - preferred food of the intestinal enterocytes**
- Enhances intestinal and whole-body growth, and promotes enterocyte proliferation and survival
- Regulates intestinal barrier function in injury, infection, weaning stress, and other catabolic conditions.
- Stimulates growth of the small intestinal mucosa in young animals and also enhances ion transport by the gut in neonates and adults.
- May be an essential amino acid for neonates, and useful under stressful conditions for adults.

Amino Acids. 2015 Oct;47(10):2143-54. doi: 10.1007/s00726-014-1773-4. Epub 2014 Jun 26.
Glutamine and intestinal barrier function.
Wang B1, Wu G1,2, Zhou Z3, Dai Z1, Sun Y1, Ji Y1, Li W1, Wang W1, Liu C1, Han F1, Wu Z4.



INTEGRATIVEWOMENSHEALTHINSTITUTE.COM

Normalizing The Intestinal Barrier Function: Nutrient Supplements

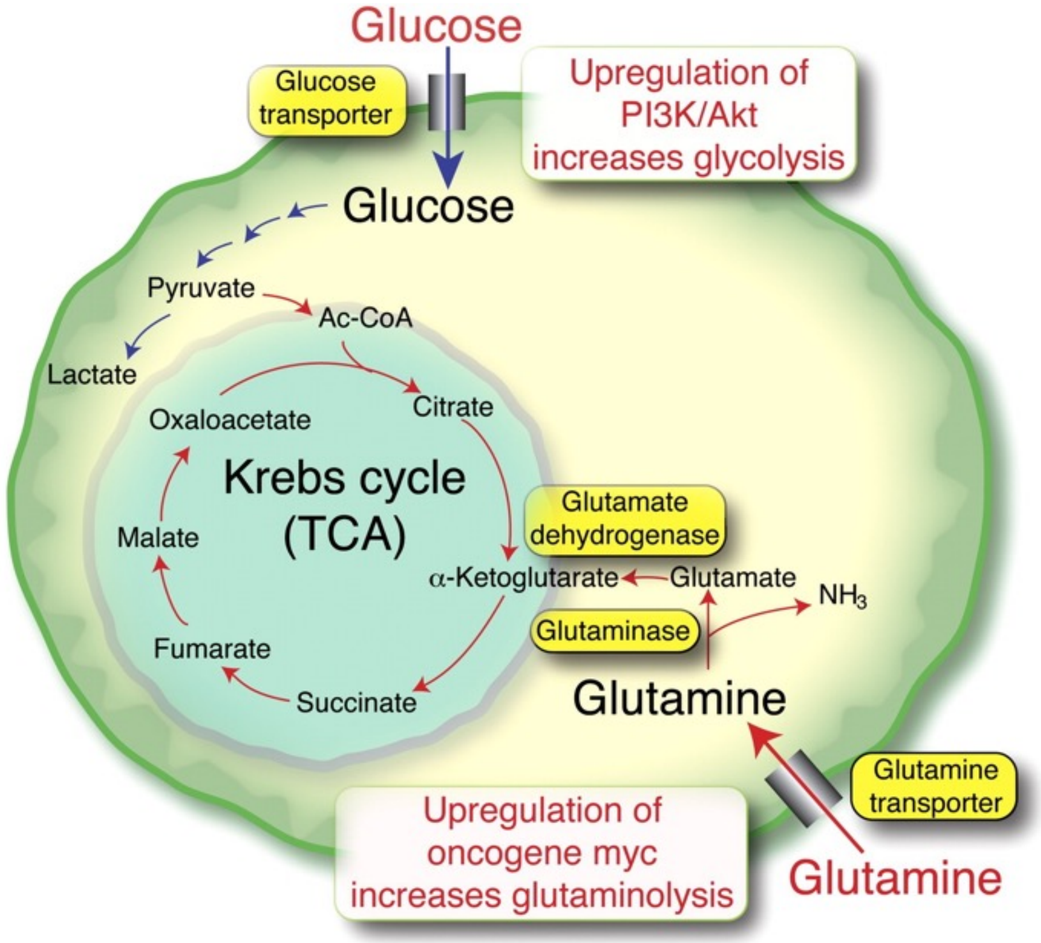
- **L-glutamine**
- Supplementation is helpful for patients with diarrhea-predominant irritable bowel syndrome (IBS-D) to restore the tight junction protein claudin-1.
- Supplementation prevents an exercise-induced rise in intestinal permeability and suppresses NF-κB activation in peripheral blood mononuclear cells

JPEN J Parenter Enteral Nutr. 2015 May 13. pii: 0148607115587330. [Epub ahead of print]
Glutamine Restores Tight Junction Protein Claudin-1 Expression in Colonic Mucosa of Patients With Diarrhea-Predominant Irritable Bowel Syndrome.
Bertrand J1, Ghouzali I1, Guérin C1, Bôle-Feysot C1, Gouteux M1, Déchelotte P2, Ducrotté P3, Coëffier M4.

Cell Stress Chaperones. 2015 Jan;20(1):85-93. doi: 10.1007/s12192-014-0528-1. Epub 2014 Jul 26.
The effects of acute oral glutamine supplementation on exercise-induced gastrointestinal permeability and heat shock protein expression in peripheral blood mononuclear cells.
Zuhl M1, Dokladny K, Mermier C, Schneider S, Salgado R, Moseley P.

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **L-glutamine RISKS**
- May promote the growth of cancer cells
- AND, can be useful to support the healing of cancer side effects.
- Look for supplements that are pure glutamine (some are cut with other things), Perque - Endure Guard (L-glutamine + alpha ketoglutarate is able to recycle it's own L-glutamine, thus lower doses are needed.)
- 1-30grams (with HIV, AIDS, or some cancers higher doses, BUT…)



Simplified schematic drawing of intracellular metabolism of glucose and glutamine is presented to show possible metabolic changes in tumor cells using glycolysis or glutaminolysis. Wenchao Qu et al. J Nucl Med 2011;53:98-105

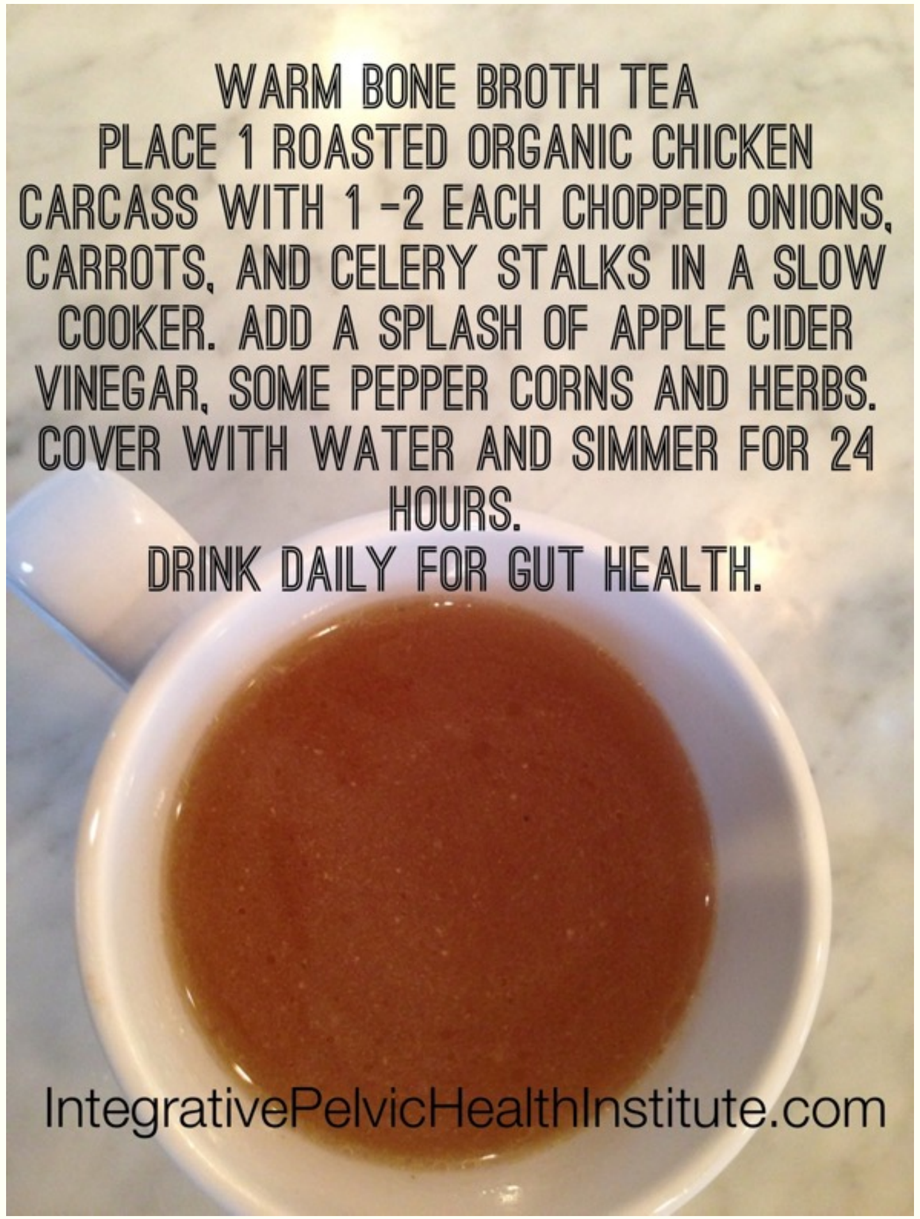
Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **L-glutamine RISKS**
- Since we don't often know who is harboring "hidden" cancer cells, this is an opinion from my colleague, Dr. Nalini Chilkov (integrative cancer expert), "IMHO A "nutritional" dose of glutamine as found in health foods and super foods (bone broths) is not going to promote cancer. However adding a therapeutic dose of glutamine (usually 5-20 grams a day) may promote the growth of tumor cells that are able to use glutamine for fuel. We do not have a way to assess which tumor cell lines have made this adaption. Bone broth is very beneficial to cancer patients."

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- **L-glutamine RISKS**
- There is also data that L-glutamine helps with mucositis in patients with cancer receiving chemotherapy or radiation treatment.
- The results of a recent systemic review: “Oral glutamine was shown to be effective in 11 of the 15 studies included in the systematic review. It significantly reduced the incidence of grade 2, 3, or 4 mucositis and/or reduced weight loss as well as the duration, time of onset, and/or maximum grade of mucositis. The most common dosing regimen was 30 g/d in 3 divided doses, with other regimens ranging from 7.5-24 g/d. Rates of nausea, vomiting, dry mouth, and anorexia were similar in the glutamine and control groups.”

Nutr Clin Pract. 2015 Oct 27. pii: 0884533615611857. [Epub ahead of print]
Oral Glutamine in Preventing Treatment-Related Mucositis in Adult Patients With Cancer: A Systematic Review.
Sayles C1, Hickerson SC1, Bhat RR1, Hall J2, Garey KW1, Trivedi MV3.


WARM BONE BROTH TEA
PLACE 1 ROASTED ORGANIC CHICKEN CARCASS WITH 1 -2 EACH CHOPPED ONIONS, CARROTS, AND CELERY STALKS IN A SLOW COOKER. ADD A SPLASH OF APPLE CIDER VINEGAR, SOME PEPPER CORNS AND HERBS. COVER WITH WATER AND SIMMER FOR 24 HOURS.
DRINK DAILY FOR GUT HEALTH.
IntegrativePelvicHealthInstitute.com

Normalizing The Intestinal Barrier Function: Nutrient Supplements

- Colostrum
- Quercetin (Perque Pain Guard and Repair Guard)
- Gamma-oryzanol
- Fish peptides (Sea Cure)
- Vitamin A
- Marshmallow root, Deglycyrrhized Licorice, Aloe Vera, Triphala and other demulcent herbs have some evidence-based benefit.
- Turmeric
- Vitamin C
- Folate
- Digestive Enzymes

Brinckmann J, et al (2003) Safety and Efficacy of a Traditional Herbal Medicine (Throat Coat ®) in Symptomatic Temporary Relief of Pain in Patients with Acute Pharyngitis: A Multicenter, Prospective, Randomized, Double Blinded, Placebo-Controlled Study, THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE, 9(2):285–298

based on clinical recommendations from Liz Lipski, author of Digestive Wellness

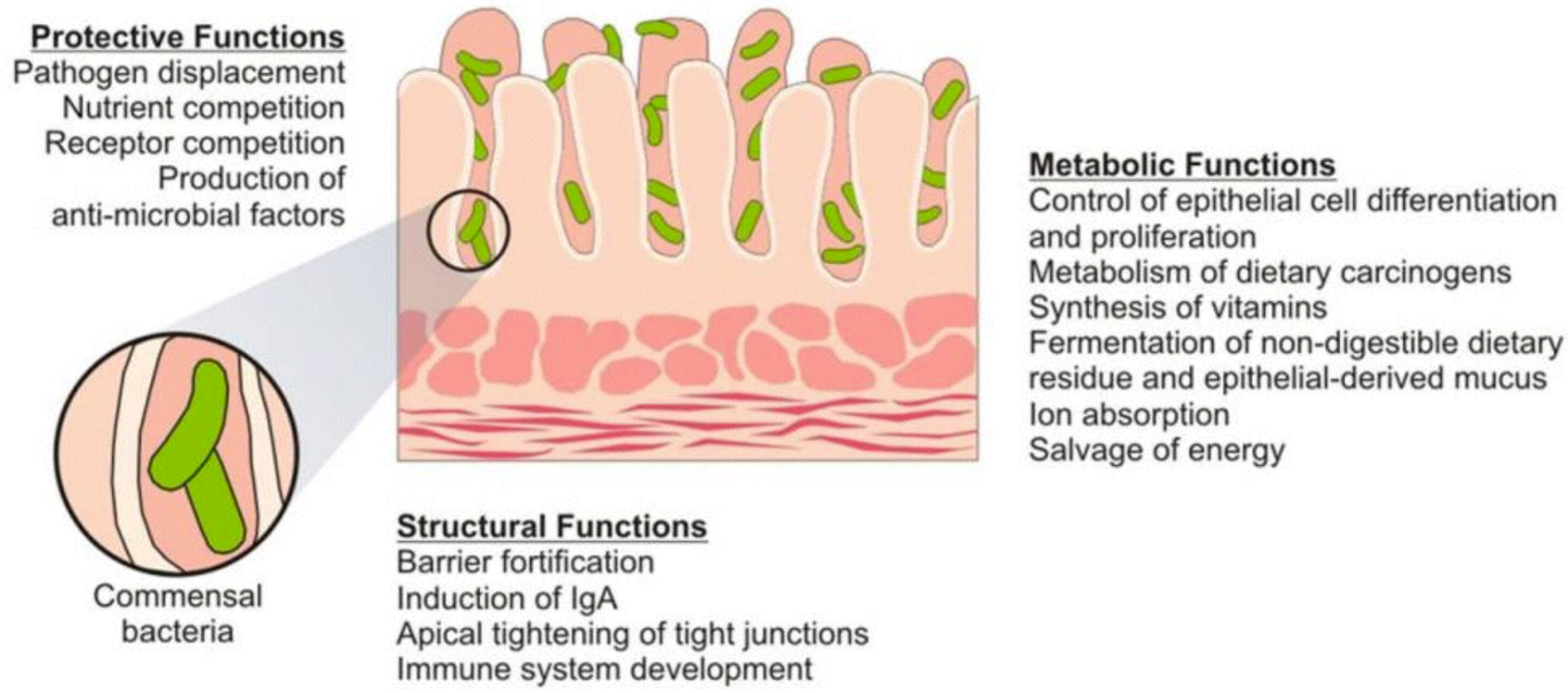
Normalizing The Intestinal Barrier Function: Nutrient Supplements

- Can find combinations of gut healing supplements = L-glutamine + demulcent herbs + amino acids + antioxidants, etc.
- Designs for Health GI Revive
- Thorne EnteroMend
- Apex Energetics
- Pharmax Permeability Complex I (avoid this if low FODMAPs because contains prebiotics - FOS)
- Integrative Therapeutics Permeability Factors

The Role of The Gut Microbiome in Intestinal Function (Reinoculate)

- What is the Gut Microbiome?
- 10^{13}-10^{14} microorganisms in the GI tract.
- 10x the amount of human cells.
- 150x the amount of human genes.
- **Thousands of species and strains.**
- Wide variety of organisms.
- Probiotics are not all the same!

Front Physiol. 2011; 2: 94. Published online 2011 December 7. Prepublished online 2011 October 13. doi: 10.3389/fphys.2011.00094



Front Physiol. 2011; 2: 94. Published online 2011 December 7. Prepublished online 2011 October 13. doi: 10.3389/fphys.2011.00094

Functions of the Probiotic Bacteria in the Human Gut

- Healthy microbiome is essential for the repair of the gut epithelium when injured.
- Microbiota is key to gut associated lymphoid tissue (GALT) and other GI immune system development.
- Digestion.
- Prevention of infection.

Sanjoy Ghosh, Daniella DeCoffe, Kirsty Brown, Ethendhar Rajendiran, Mehrbod Estaki, Chuanbin Dai, Ashley Yip, Deanna L. Gibson. Fish Oil Attenuates Omega-6 Polyunsaturated Fatty Acid-Induced Dysbiosis and Infectious Colitis but Impairs LPS Dephosphorylation Activity Causing Sepsis. *PLOS One*. Published: February 06, 2013. DOI: 10.1371/journal.pone.0055468

Establishment of The Gut Microbiota

- **The gut of the fetus is effectively sterile until birth.** This idea is now being challenged and bacterial colonization of membranes may contribute to premature rupture. (Fortner, et al. 2014)

Kimberly B. Fortner, Chad A. Grotegut, Carla E. Ransom, Rex C. Bentley, Liping Feng, Lan Lan, R. Phillips Heine, Patrick C. Seed, Amy P. Murtha Bacteria Localization and Chorion Thinning among Preterm Premature Rupture of Membranes. *PLOS One*. Published: January 08, 2014. DOI: 10.1371/journal.pone.0083338

Moloney, RD, Desbonnet, L, Clarke, G, Dinan, TG, Cryan, JF. The microbiome: stress, health and disease. *Mamm Genome*, 19 May 2013.

Establishment of The Gut Microbiota

- Gut colonization continues at birth and varies by delivery method.
- With vaginal delivery - microbiota of moms' vagina (*Lactobacillus, Pevotella,* or *Sneathia*)
- With C-Section delivery - microbiota of mom's skin (*Staphylococcus, Corynebacterium,* and *Propionibacterium*)
- *Firmicutes* and *Bacteriodetes* (dominate the adult microbiome) - delayed acquision in C-Section babies.

Moloney, RD, Desbonnet, L, Clarke, G, Dinan, TG, Cryan, JF. The microbiome: stress, health and disease. *Mamm Genome*, 19 May 2013.

Establishment of the Gut Microbiota

- Preterm babies lack two of the main bacerial genera in healthy term infants: *Bifidobacterium* and *Lactobacillus*, instead that have lots of *Proteobacteria*.
- Exclusive breastfeeding leads to more Bifidobacterium.
- In elderly, microbiome is related to residence location and diet.

Moloney, RD, Desbonnet, L, Clarke, G, Dinan, TG, Cryan, JF. The microbiome: stress, health and disease. *Mamm Genome*, 19 May 2013.

What is a Normal Gut Microbiome?

- The billion dollar question.
- Choosing strains of probiotics is important because probiotics vary widely in terms of species, genera, and even phyla.
- Resource: Probiotics Advisor

Bacteria in the SMALL vs LARGE Intestines (SIBO)

- **Not only are the species of bacteria important, but their location in the digestive tract is important to function.**
- Large quantities of some bacteria (such as clostridia) can be healthy in the colon, but abnormal in the small intestine.

Small Intestine Bacterial Overgrowth

- SIBO is linked to abdominal pain in children with functional GI disorders
- And, patients with SIBO have prolonged small bowel transit time.
- **1/3 of women with IBS also report chronic pelvic pain symptoms.**
- **SIBO has been shown to be a cause of joint pain and associated with bladder pain.**

J Pediatr Gastroenterol Nutr. 2015 Apr;60(4):498-502. doi: 10.1097/MPG.0000000000000634.
Glucose hydrogen breath test for small intestinal bacterial overgrowth in children with abdominal pain-related functional gastrointestinal disorders.
Korterink JJ1, Benninga MA, van Wering HM, Deckers-Kocken JM.

J Clin Gastroenterol. 2015 Aug;49(7):571-6. doi: 10.1097/MCG.0000000000000257.
Small Intestinal Transit Time Is Delayed in Small Intestinal Bacterial Overgrowth.
Roland BC1, Ciarleglio MM, Clarke JO, Semler JR, Tomakin E, Mullin GE, Pasricha PJ.

Zhao, H., Zhao, L., Shi, W., Luo, H., Duan, L., You, Y., … Zuo, X. (2016). Is it bowel-associated dermatosis-arthritis syndrome induced by small intestinal bacteria overgrowth? SpringerPlus, 5(1), 1551. http://doi.org/10.1186/s40064-016-3236-8

SIBO Basics

- **Diagnosed by breath test - hydrogen and methane**
- Treatment with antibiotics or herbs targeted to the overgrowth organisms.
- Upon completion of medical/ herbal therapy (or during - conflict among experts regarding when to use) - Use Low FODMAP diet to “starve” the bacteria, and address root cause.
- Root cause could be hypochlorhydria, problems with ileocecal valve, intestinal motility, poor diet, stress, medications, infections, immune challenges, etc.
- In some cases a simpler elimination diet is sufficient - dairy, egg, wheat, soy free.

J Pediatr Gastroenterol Nutr. 2015 Oct;61(4):516. doi: 10.1097/01.mpg.0000472220.63550.71.
OP-16 DIETARY INTERVENTION USING THE LOW FODMAP DIET VERSUS THE "MILK, EGG, WHEAT AND SOYA FREE" DIET FOR TREATMENT OF FUNCTIONAL GUT DISORDERS A SINGLE CENTRE EXPERIENCE.
Keetarut K1, Kiparissi F, McCartney S, Murray C.

SIBO/ SIFO Basics

- Clinically, I like to use the organic acids test to screen for dysbiosis, or fungal overgrowth
- In some of those cases, SIBO breath testing is indicated.
- Clients with immediate bloating after eating, and high abdominal pain are more likely to have SIBO.

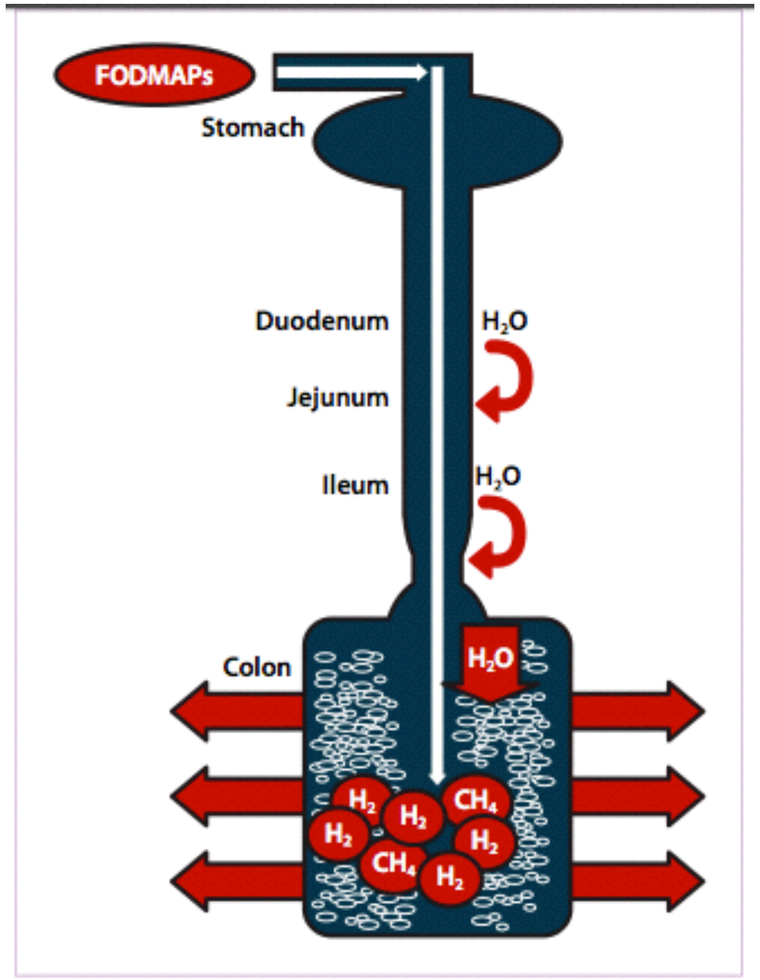


Figure 2. Ingested fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) are poorly absorbed in the small intestine. Their small molecular size results in an osmotic effect, drawing water (H_2O) through to the large intestine. FODMAPs are then fermented by colonic microflora, producing hydrogen (H_2) and/or methane gas (CH_4). The increase in fluid and gas leads to diarrhea, bloating, flatulence, abdominal pain, and distension.

Reproduced from Barrett JS, Gearry RB, Muir JG, et al.[10]

FODMAP	Foods high in FODMAPs	Suitable alternatives low in FODMAPs
Excess fructose	Fruits: apple, clingstone peach, mango, nashi pear, pear, sugar snap pea, tinned fruit in natural juice, watermelon Honey sweeteners: fructose, high-fructose corn syrup Large total fructose dose: concentrated fruit sources, large servings of fruit, dried fruit, fruit juice	Fruits: banana, blueberry, cantaloupe, carambola, durian, grape, grapefruit, honeydew melon, kiwi, lemon, lime, orange, passion fruit, pawpaw, raspberry, strawberry, tangelo Honey substitutes: golden syrup, maple syrup Sweeteners: any sweeteners except polyols
Lactose	Milk: regular and low-fat cow, goat, and sheep milk; ice cream Yogurts: regular and low-fat yogurts Cheeses: soft and fresh cheeses	Milk: lactose-free milk, rice milk Ice cream substitutes: gelato, sorbet Yogurts: lactose-free yogurts Cheeses: hard cheeses
Oligosaccharides (fructans and/or galactans)	Vegetables: artichoke, asparagus, beetroot, broccoli, Brussels sprout, cabbage, fennel, garlic, leek, okra, onion, pea, shallot Cereals: rye and wheat cereals when eaten in large amounts (eg, biscuit, bread, couscous, cracker, pasta) Legumes: baked bean, chickpea, lentil, red kidney bean Fruits: custard apple, persimmon, rambutan, watermelon, white peach	Vegetables: bamboo shoot, bok choy, capsicum, carrot, celery, chives, choko, choy sum, corn, eggplant, green bean, lettuce, parsnip, pumpkin, silverbeet, spring onion (green part only) Onion/garlic substitutes: garlic-infused oil Cereals: gluten-free and spelt bread/cereal products Fruit: tomato
Polyols	Fruits: apple, apricot, avocado, cherry, longon, lychee, nashi pear, nectarine, peach, pear, plum, prune, watermelon Vegetables: cauliflower, mushroom, snow pea Sweeteners: isomalt, maltitol, mannitol, sorbitol, xylitol, and other sweeteners ending in "-ol"	Fruits: banana, blueberry, cantaloupe, carambola, durian, grape, grapefruit, honeydew melon, kiwi, lemon, lime, orange, passion fruit, pawpaw, raspberry Sweeteners: glucose, sugar (sucrose), other artificial sweeteners not ending in "-ol"

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3966170/pdf/GH-08-739.pdf

Low FODMAPs Diets and IBS

- In an Australian study: 30 patients with IBS and 8 healthy controls.
- Randomly assigned to 21 days of a low FODMAPs diet or a typical Australian diet.
- 21 day washout period, the assigned to the other diet.
- For controls: symptoms were minimal and unaltered with either diet.
- **For those with IBS: low FODMAPs significantly lower overall GI symptom scores, bloating, pain and passage of wind were also reduced. Also, better stool consistency, and alterations in stool frequency for those with IBS-D.**

Gastroenterology. 2014 Jan;146(1):67-75.e5. doi: 10.1053/j.gastro.2013.09.046. Epub 2013 Sep 25.
A diet low in FODMAPs reduces symptoms of irritable bowel syndrome.

Halmos EP[1], Power VA[2], Shepherd SJ[2], Gibson PR[3], Muir JG[3].

Factors that Disturb a Healthy Microbiome

- **Antibiotics** - taken by humans or ingested via antibiotic fed meat or dairy. (correlation with obesity likely due to metabolic endotoxemia—an increase in plasma lipopolysaccharide (LPS) levels—as one of the triggering factors that can lead to the development of metabolic inflammation and insulin resistance - **also key factors in chronic pain**.)
- **Western Diet** - n-6 PUFA's can enhance inflammatory factors in mice with colitis.
- **Yeast overgrowth**
- **Infectious (pathogenic) bacterial overgrowth**
- **Drugs** (mentioned earlier in this presentation)
- **Stress**

Petschow, B., Doré, J., Hibberd, P., Dinan, T., Reid, G., Blaser, M., … Sanders, M. E. (2013). Probiotics, prebiotics, and the host microbiome: the science of translation. Annals of the New York Academy of Sciences, 1306(1), 1–17. http://doi.org/10.1111/nyas.12303

Sanjoy Ghosh, Daniella DeCoffe, Kirsty Brown, Ethendhar Rajendiran, Mehrbod Estaki, Chuanbin Dai, Ashley Yip, Deanna L. Gibson. Fish Oil Attenuates Omega-6 Polyunsaturated Fatty Acid-Induced Dysbiosis and Infectious Colitis but Impairs LPS Dephosphorylation Activity Causing Sepsis. *PLOS One*. Published: February 06, 2013. DOI: 10.1371/journal.pone.0055468

Vicious Cycle b/t Gut Microbiota Health and Inflammation

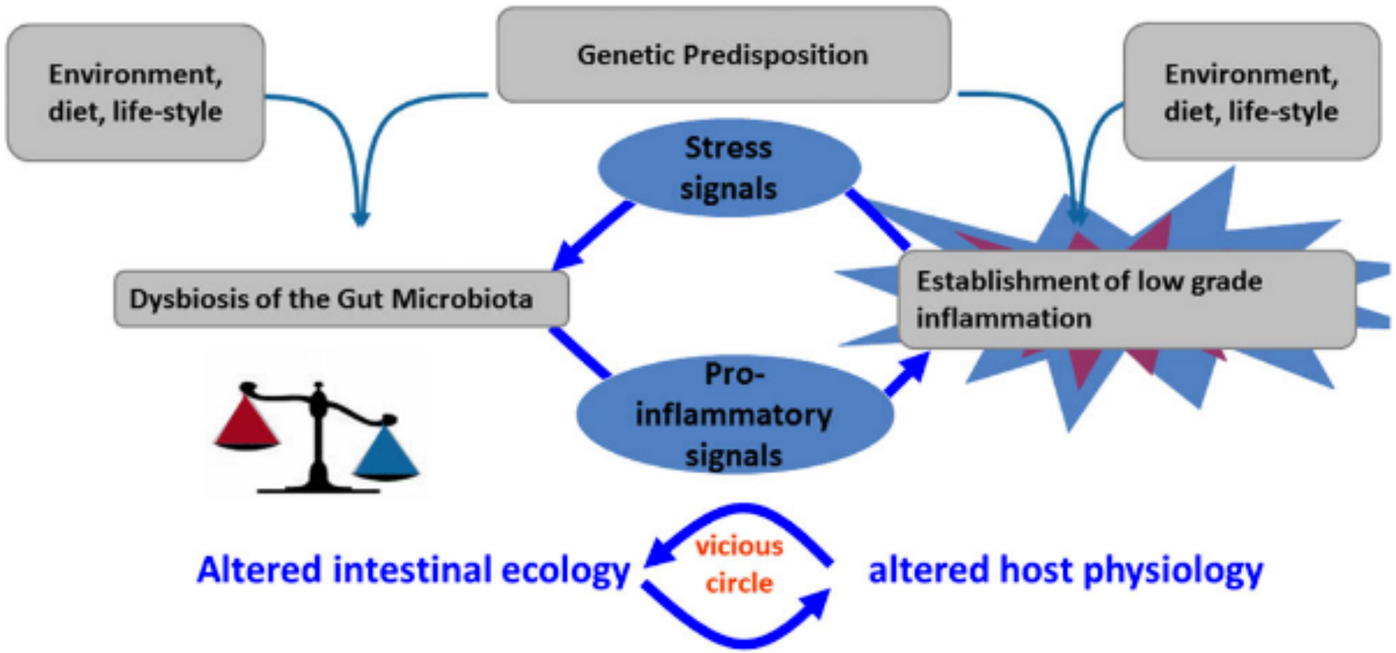


Figure 6. Alterations of the gut microbiota and low-grade inflammation may contribute to a cycle of events that induces a chronic state in immune-mediated diseases. Interventions that target the combined modulation of gut microbiota and inflammation may be the most effective way to manage such conditions.

Petschow, B., Doré, J., Hibberd, P., Dinan, T., Reid, G., Blaser, M., … Sanders, M. E. (2013). Probiotics, prebiotics, and the host microbiome: the science of translation. Annals of the New York Academy of Sciences, 1306(1), 1–17. http://doi.org/10.1111/nyas.12303

Factors that Restore A Health Gut Microbiota

- **Hydration**: Probiotic supplements have been shown to improve the hydration status in healthy elderly. (Remember that bladder patients tend to limit water causing increased bladder pain.)
- **Specific Probiotic Strains** (mixed opinion on higher vs. lower doses)
- **Anti-microbial/ anti-yeast medical and/or herbal protocols.**
- **Prebiotic fibers.**
- **High nutrient density low inflammatory "elimination" diet** as discussed above.
- **Probiotic foods and supplements.**

Nutrients. 2013 Apr 17;5(4):1276-86. doi: 10.3390/nu5041276.
Effects of three-month intake of synbiotic on inflammation and body composition in the elderly: a pilot study. Neto JV, de Melo CM, Ribeiro SM.

Clinical Summary - Nutrition and Lifestyle for Optimal Digestive Function

- Functionally - think through the digestive system any time you have a patient with… joint pain, other pain, brain injury, cardiovascular disease, osteopenia/ osteoporosis, autoimmune disease, post surgical inflammation, post-injury inflammation, etc.

- When the patient can't absorb nutrients —> can't heal well (think athletic injury, surgery, postpartum, post-any injury or acute illness)

- When the patient's digestive barrier function/ gut microbiome health is compromised —> can't heal well.

- **Start with the gut!**

Clinical Summary - Nutrition and Lifestyle for Optimal Digestive Function

- Chew
- Is Stress Addressed? (May put it on the back burner and address as resilience improves.)
- Nutrient Dense Diet/ Consider deficiencies
- Adequate hydration (1/2 body weight in lbs, in ounces daily)
- Stomach Acid/ Digestive Enzymes
- Healthy small intestinal barrier: address stress, medications, overtraining, getting adequate zinc, glutamine, etc. avoiding inflammatory foods, thoughts, people, fitness programs
- SIBO/ SIFO?
- Gut Microbiome - diversity, strong balance of probiotic species, may also need antimicrobial herbs
- Fiber: 8-10 servings of veggies daily
- Visceral mobilization of the ileocecal valve
- Good toileting habits and consistency

PART 4: Brain Health

Three RED FLAGS for Midlife Brain Health/ Libido…

- **Dysglycemia -** without sugar brain can't function well, risk for cardiovascular disease and cancer.
- **Anemia (Ferritin 70-90) -** without oxygen brain can't function well, risk for fatigue.
- **Inflammation -** root cause of heart disease, stroke, dementia, and cancer.

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:** Reactive hypoglycemia
- Women presenting with anxiety, brain fog or jitters when skipping meals or not eating for awhile (*How many of your patients skip lunch, squeeze in one more errand or forget to eat breakfast, maybe just coffee?)
- More common in thin women.
- Seen in women on high carbohydrate-low fat diet
- Corresponds with alcohol intake.
- Those with HPA axis dysregulation also struggle with reactive hypoglycemia.

Diabetes Metab. 2000 Nov;26(5):337-51.
Postprandial reactive hypoglycemia.
Brun JF1, Fedou C, Mercier J.

J Rheumatol. 1993 Mar;20(3):469-74.
Altered reactivity of the hypothalamic-pituitary-adrenal axis in the primary fibromyalgia syndrome.
Griep EN1, Boersma JW, de Kloet ER.

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:** Diabetes
- Perimenopausal women and postmenopausal women (over age 50 - no matter the age at menopause have an increased risk for diabetes.
- Women after natural menopause had an age-adjusted OR of 1.40 (95% CI 1.03–1.89) for diabetes, and women after menopause by surgical or other causes had an age-adjusted OR of 1.59 (1.07–2.37).

Heianza, Y., Arase, Y., Kodama, S., Hsieh, S. D., Tsuji, H., Saito, K., … Sone, H. (2013). Effect of Postmenopausal Status and Age at Menopause on Type 2 Diabetes and Prediabetes in Japanese Individuals: Toranomon Hospital Health Management Center Study 17 (TOPICS 17). Diabetes Care, 36(12), 4007–4014. http://doi.org/10.2337/dc13-1048

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:** PCOS and long term risk of diabetes
- The likelihood of developing type 2 diabetes for mid-life women with PCOS significantly increases with elevated BMI, elevated fasting glucose, and elevated glucose area under the curve.
- The risk decreases with increasing levels of sex hormone–binding globulin (SHBG).
- In general, having PCOS increases risk of having diabetes at mid-life by approx 2-fold.
- If women have persistent PCOS symptoms into mid-life, the risk of having diabetes increases 7-fold.

Gambineri, A., Patton, L., Altieri, P., Pagotto, U., Pizzi, C., Manzoli, L., & Pasquali, R. (2012). Polycystic Ovary Syndrome Is a Risk Factor for Type 2 Diabetes: Results From a Long-Term Prospective Study. Diabetes, 61(9), 2369–2374. http://doi.org/10.2337/db11-1360

Wang, E. T., Calderon-Margalit, R., Cedars, M. I., Daviglus, M. L., Merkin, S. S., Schreiner, P. J., … Bibbins-Domingo, K. (2011). Polycystic Ovary Syndrome and Risk for Long-Term Diabetes and Dyslipidemia. Obstetrics and Gynecology, 117(1), 6–13. http://doi.org/10.1097/AOG.0b013e31820209bb

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:** gestational diabetes and long term risk of diabetes
- 17 years after the initial diagnosis of GDM, 40% of women were diabetic compared with 10% in a matched control group of women who had normal glucose tolerance in pregnancy.
- The incidence of diabetes was higher among women who were older, more obese, of greater parity, with more severe degrees of glucose intolerance during pregnancy, and in those who had GDM in two or more pregnancies.

Baillieres Clin Obstet Gynaecol. 1991 Jun;5(2):461-83.
Long-term implications of gestational diabetes for the mother.
Henry OA, Beischer NA.

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:** How does dysglycemia contribute to cognitive impairments in perimenopausal women.
- **The brain needs fuel to survive and activate - including to remember, attend, and focus.**
- Neurons can’t store glycogen.
- Glucose is a key fuel source for neurons, thus glycemic control is critical.
- There are a few exceptions…

Mergenthaler, P., Lindauer, U., Dienel, G. A., & Meisel, A. (2013). Sugar for the brain: the role of glucose in physiological and pathological brain function. Trends in Neurosciences, 36(10), 587–597. http://doi.org/10.1016/j.tins.2013.07.001

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:**
- **There are a few exceptions…**
  - During periods of intense activity of the nervous system, when the energy demand exceeds supply, astrocyte glycogen is immediately converted to lactate, some of which is transported to the neurons.
  - Glycogen from astrocytes functions as a kind of protection against hypoglycemia, ensuring preservation of neuronal function. (*short term)

Falkowska, A., Gutowska, I., Goschorska, M., Nowacki, P., Chlubek, D., & Baranowska-Bosiacka, I. (2015). Energy Metabolism of the Brain, Including the Cooperation between Astrocytes and Neurons, Especially in the Context of Glycogen Metabolism. International Journal of Molecular Sciences, 16(11), 25959–25981. http://doi.org/10.3390/ijms161125939

Mechanisms of Cognitive Impairments in Perimenopause

- **Dysglycemia:**
- **There are a few exceptions…**
  - Ketones can also feed neurons by supporting the mitochondria to produce ATP, and by reducing oxidative stress that would otherwise negatively impact the neuronal mitochondria.

Kim, D. Y., Vallejo, J., & Rho, J. M. (2010). Ketones prevent synaptic dysfunction induced by mitochondrial respiratory complex inhibitors. Journal of Neurochemistry, 114(1), 130–141. http://doi.org/10.1111/j.1471-4159.2010.06728.x

Mechanisms of Cognitive Impairments in Perimenopause

- **Anemia: When women in perimenopause are more likely to be anemic…**
- There are two phases of menopause…
  - Early transition, defined as a persistent difference in consecutive menstrual cycle length of seven or more days, begins on average 6-8 years before the final menstrual period.
  - Late transition, defined by an episode of 60 or more days of amenorrhea, begins on average two years before the FMP.

Harlow, S. D., & Paramsothy, P. (2011). Menstruation and the Menopause Transition. Obstetrics and Gynecology Clinics of North America, 38(3), 595–607. http://doi.org/10.1016/j.ogc.2011.05.010

Mechanisms of Cognitive Impairments in Perimenopause

- **Anemia: When women in perimenopause are more likely to be anemic…**
- The Massachusetts Women's Health Study (MWHS): among women over age 50 years, short menstrual cycles and short bleeding/spotting episodes occurred more frequently during **early perimenopause**.
- More cycles may = more bleeding overall —> more anemia.

Harlow, S. D., & Paramsothy, P. (2011). Menstruation and the Menopause Transition. Obstetrics and Gynecology Clinics of North America, 38(3), 595–607. http://doi.org/10.1016/j.ogc.2011.05.010

Mechanisms of Cognitive Impairments in Perimenopause

- **Anemia: When women in perimenopause are more likely to be anemic**
- The classic study of menstrual blood loss volume documented:
  - Average 50-year-old women bled about 6 ml more than average women aged 20-45.
  - The 90th percentile of menstrual blood loss being 133 ml in women aged 50, versus 86-88 ml for women aged 30-45.
  - Perimenopausal menstrual blood loss in excess of 200 mL was associated in ovulatory cycles with high E2 levels. (*consider estrogen dominance & xenoestrogens in this population.)
  - Heavy bleeding may also be associated with obesity and fibroids in this population.

Harlow, S. D., & Paramsothy, P. (2011). Menstruation and the Menopause Transition. Obstetrics and Gynecology Clinics of North America, 38(3), 595–607. http://doi.org/10.1016/j.ogc.2011.05.010

Mechanisms of Cognitive Impairments in Perimenopause

- **Inflammation:** “Two factors theorized to contribute to the initiation and/or progression of Alzheimer’s Disease pathogenesis are age-related increases in inflammation and obesity. These factors may be particularly problematic in women.”
- The combination of increased age and central adiposity increase inflammation-related risks of Alzheimer’s Disease in perimenopausal women.

Christensen, A., & Pike, C. J. (2015). Menopause, obesity and inflammation: interactive risk factors for Alzheimer’s disease. Frontiers in Aging Neuroscience, 7, 130. http://doi.org/10.3389/fnagi.2015.00130

Do perimenopausal brain fog, memory issues, and reduced cognitive endurance, increase a woman's risk for Alzheimer's, dementia, or other disabling brain health issues that we normally associate with the elderly?

YES! Risk for Alzheimer's and Other Dementias can be Increased

- Because of the impact of dysglycemia and inflammation on neuronal health that often begins or worsens in perimenopause…
- A reduction in brain glucose metabolism (associated with altered insulin signaling) has been shown to be a preclinical symptom of AD.
- Increased adiposity (especially abdominal adiposity) elevates neuroinflammation, which has been implicated as a pathologic mechanism in AD.

Christensen, A., & Pike, C. J. (2015). Menopause, obesity and inflammation: interactive risk factors for Alzheimer's disease. Frontiers in Aging Neuroscience, 7, 130. http://doi.org/10.3389/fnagi.2015.00130

YES! Risk for Alzheimer's and Other Dementias can be Increased

- Perimenopausal women with Mild Cognitive Impairment (MCI), episodic memory loss without dementia, are more likely to progress to dementia (including Alzheimer'd disease.)
- Over half of those with MCI will develop dementia within 5 years, especially AD - BUT, that also means that lots of people with MCI will not develop dementia. (*good news!)
- **MCI can be regarded as preclinical dementia, and the prevention of it is very important clinically.**

Kim, S. A., & Jung, H. (2015). Prevention of Cognitive Impairment in the Midlife Women. Journal of Menopausal Medicine, 21(1), 19–23. http://doi.org/10.6118/jmm.2015.21.1.19

What nutrition, movement, sleep, supplement, lifestyle medicine, and social support strategies can get to the root causes of these challenges and resolve the brain health symptoms?

Therapeutic Goals for Perimenopausal Brain Health

- Reduce estrogen dominance/ xenoestrogen exposure, and hormonally smooth the menopause transition.
- Normalize HPA axis response to stress
- Stabilize blood sugar.
- Minimize the effects of excess perimenopausal menstrual blood loss.
- Reduce inflammation and oxidative stress, while optimizing neuronal mitochondrial function and body weight/ body fat.

Nutrition for Perimenopausal Brain Health

- In patients with diabetes: Paleo diet based on lean meat, fish, fruits, vegetables, root vegetables, eggs and nuts beneficial
- In obese postmenopausal women: paleo diet also beneficial
- Eating a paleo diet (studied for 3 months - 2 years) —>
  - Lower mean values of HbA1c.
  - Lower diastolic blood pressure.
  - Improvements in weight, fat mass, BMI, and waist circumference.
  - Improvements in triglyceride levels.
  - Higher HDL cholesterol.

Jönsson, T., Granfeldt, Y., Ahrén, B., Branell, U.-C., Pålsson, G., Hansson, A., … Lindeberg, S. (2009). Beneficial effects of a Paleolithic diet on cardiovascular risk factors in type 2 diabetes: a randomized cross-over pilot study. Cardiovascular Diabetology, 8, 35. http://doi.org/10.1186/1475-2840-8-35

Mellberg, C., Sandberg, S., Ryberg, M., Eriksson, M., Brage, S., Larsson, C., … Lindahl, B. (2014). Long-term effects of a Palaeolithic-type diet in obese postmenopausal women: a two-year randomized trial. European Journal of Clinical Nutrition, 68(3), 350–357. http://doi.org/10.1038/ejcn.2013.290

Nutrition for Perimenopausal Brain Health

- Thus eating a paleo diet based on lean meat, fish, fruits, vegetables, root vegetables, eggs and nuts…
  - Improved blood sugar balance/ insulin resistance.
  - Improved inflammatory abdominal adiposity.

Are anti-inflammatory, blood sugar, and hormonal benefits (that impact cognition) even better with a more strict carb restriction?

Nutrition for Perimenopausal Brain Health

- Taking it even further and eating a a low-carbohydrate, ketogenic diet (LCKD) - limiting carbohydrate intake to 20 grams or less per day for 24 weeks…
  - This study looked at overweight and obese women with PCOS (poor compliance ~50%).
  - Reduced body weight (-12%)
  - Reduced percent free testosterone (-22%)
  - Reduced LH/FSH ratio (-36%)
  - Reduced fasting insulin (-54%).

Mavropoulos, J. C., Yancy, W. S., Hepburn, J., & Westman, E. C. (2005). The effects of a low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: A pilot study. Nutrition & Metabolism, 2, 35. http://doi.org/10.1186/1743-7075-2-35

Nutrition for Perimenopausal Brain Health

- Too low carb in some women can be counterproductive.
- If low cortisol (poor HPA axis function), gluconeogenesis can be reduced.
- Increase carbs as needed
- Consider adding L-carnitine to support transport of free fatty acids into the mitochondria.
- 1-3 grams of acetyl-L-carnitine or L-carnitine tartrate + 2-3 grams of EPA & DHA fish oil

Clin Sci (Lond). 2001 Dec;101(6):739-47.
Cortisol increases gluconeogenesis in humans: its role in the metabolic syndrome.
Khani S1, Tayek JA.

Sharma, S., & Black, S. M. (2009). CARNITINE HOMEOSTASIS, MITOCHONDRIAL FUNCTION, AND CARDIOVASCULAR DISEASE. Drug Discovery Today. Disease Mechanisms, 6(1-4), e31–e39. http://doi.org/10.1016/j.ddmec.2009.02.001

Nutrition for Optimal Brain Health in Perimenopausal Women
SUMMARY

- As low carb as tolerated, high in nutrient dense and anti-inflammatory proteins, fats, vegetables, fruits, nuts and seeds.
- http://integrativewomenshealthinstitute.com/hormone-balance-cleanse-spring/

Movement and Exercise for Perimenopausal Brain Health

- **Body image issues persist into mid-life:** thus, women are not eating regularly to reduce risk of reactive hypoglycemia, and they may be inconsistently (or consistently) overexercising and/ or dieting.
- In a sample of over 1,800 women ages 50 years and older:
  - Nearly 64% of the sample reported experiencing thoughts about their weight on a daily basis and almost 62% endorsed that weight/shape negatively affected their lives at least occasionally.
  - 71% reported dissatisfaction with weight.
  - Nearly 84% of women over 50 report dissatisfaction with their stomach.

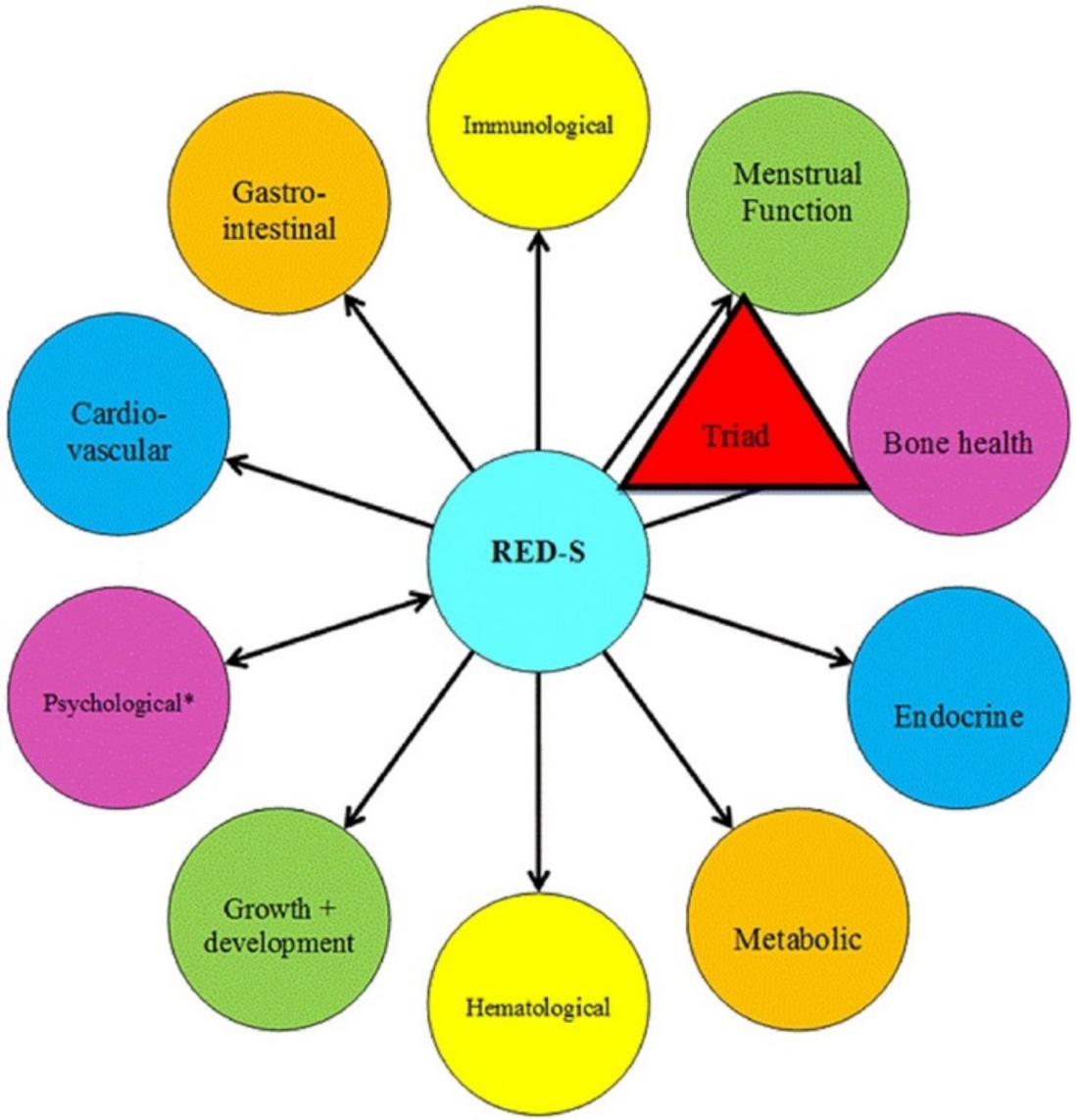
In a sample of 405 Caucasian and African American middle-aged women, 47% reported being dissatisfied with their appearance.

Kilpela, L. S., Becker, C. B., Wesley, N., & Stewart, T. (2015). Body Image in Adult Women: Moving Beyond the Younger Years. Advances in Eating Disorders (Abingdon, England), 3(2), 144–164. http://doi.org/10.1080/21662630.2015.1012728

Movement and Exercise for Perimenopausal Brain Health

- **Overexercising is a risk in this population.**
- **RED-S (Formerly “The Female Athlete Triad”)…**

Health Consequences of Relative Energy Deficiency in Sport (RED-S) showing an expanded concept of the Female Athlete Triad to acknowledge a wider range of outcomes and the application to male athletes (*Psychological consequences can either precede RED-S or be the



Effects on cortisol/ HPA axis

Effects on estrogen and other sex hormone balance and menstruation.

Effects on metabolism/ insulin signaling.

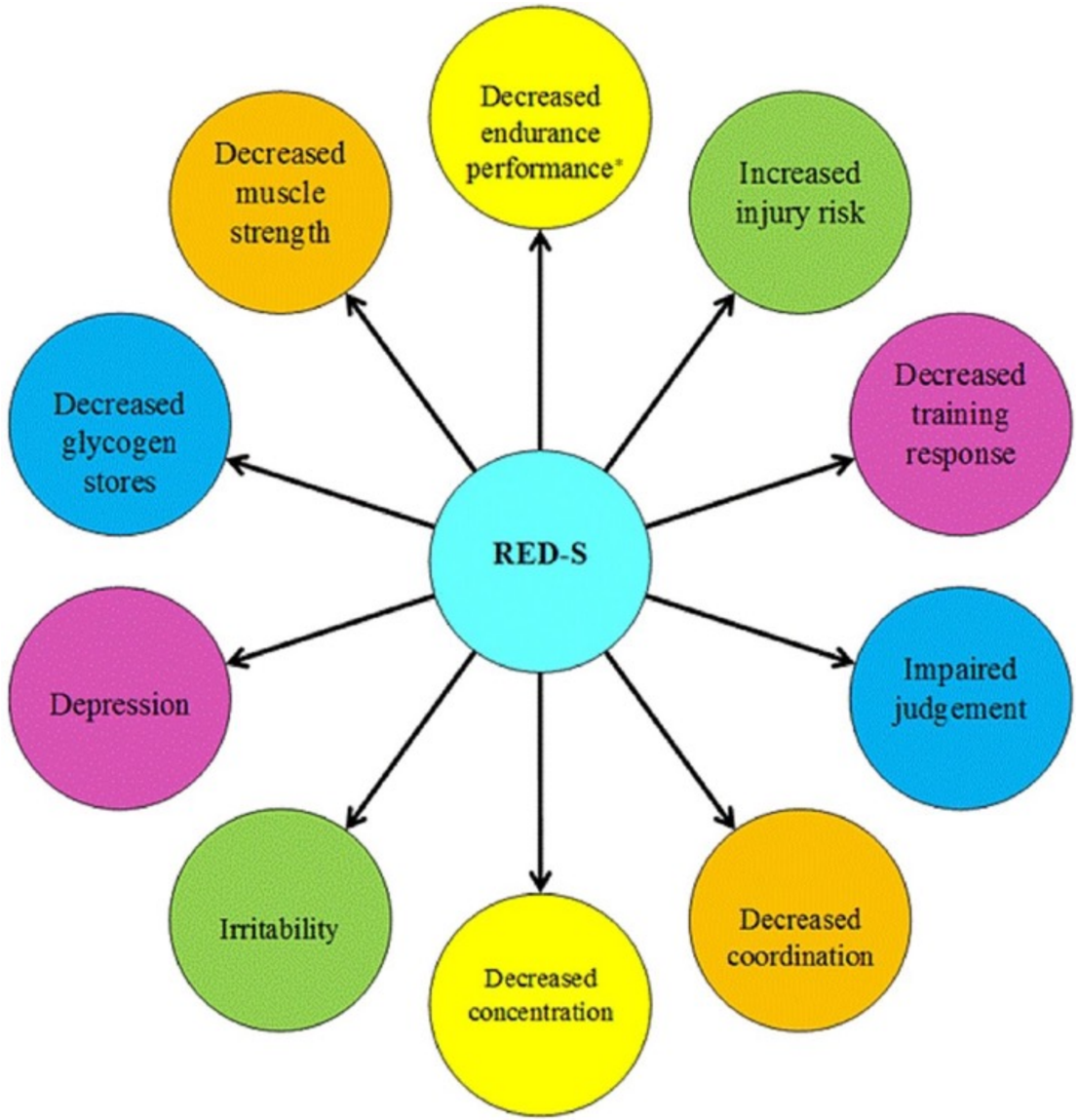
Effects on inflammation/ immune suppression.

— Via all of these mechanisms —> impact on cognitive function.

Margo Mountjoy et al. Br J Sports Med 2014;48:491-497

BJSM

Potential Performance Effects of Relative Energy Deficiency in Sport (*Aerobic and anaerobic performance).



Margo Mountjoy et al. Br J Sports Med 2014;48:491-497

Movement and Exercise for Perimenopausal Brain Health

- **Overexercising is a risk in this population.**
- **But, so is under exercise -**
  - In rats… the dopamine system in the brain is the reward system that intrinsically motivates running.
  - Those rats with a greater ratio of excitatory/inhibitory DA mRNA expression, ran more.
  - But, both groups - those with more dopamine system excitation (who loved to run!) and those with less, reduced running (the high exercisers actually reduced more) after surgical or medical menopause.

Physiol Behav. 2016 Oct 1;164(Pt A):383-9. doi: 10.1016/j.physbeh.2016.06.006. Epub 2016 Jun 11.
Effects of intrinsic aerobic capacity and ovariectomy on voluntary wheel running and nucleus accumbens dopamine receptor gene expression.
Park YM1, Kanaley JA1, Padilla J2, Zidon T1, Welly RJ1, Will MJ3, Britton SL4, Koch LG4, Ruegsegger GN5, Booth FW5, Thyfault JP6, Vieira-Potter VJ7.

The Interaction Between Estrogen and Exercise for Perimenopausal Brain Health

- In female rats prior to menopause, physical activity increases hippocampal BDNF mRNA and protein levels.
- However, the exercise effect on BDNF up-regulation is reduced in the absence of estrogen, in a time-dependent manner.
- Voluntary activity is stimulated by the presence of estrogen. In exercising animals, estrogen deprivation reduced voluntary activity levels, while estrogen replacement restored activity to normal levels.

Eur J Neurosci. 2001 Dec;14(12):1992-2002.
Estrogen and exercise interact to regulate brain-derived neurotrophic factor mRNA and protein expression in the hippocampus.
Berchtold NC1, Kesslak JP, Pike CJ, Adlard PA, Cotman CW.

The Interaction Between Estrogen and Exercise for Perimenopausal Brain Health

- Thus, prior to menopause, women need to establish and exercise routine, and have support to continue through menopause.
- Also, strategies to optimize hormonal balance (normalize HPA axis function, and maintain estrogen production of the adrenals through menopause) through perimenopause —> menopause.

Exercise and Movement Program for Optimal Perimenopausal Brain Health

- Bouts of intense exercise, such as HIIT, best increase BDNF, but the effect is less in females.

- Mindfulness meditation (even just 4 days) significantly improved visuo-spatial processing, working memory, and executive functioning.

Szuhany, K. L., Bugatti, M., & Otto, M. W. (2015). A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. Journal of Psychiatric Research, 60, 56–64. http://doi.org/10.1016/j.jpsychires.2014.10.003

Conscious Cogn. 2010 Jun;19(2):597-605. doi: 10.1016/j.concog.2010.03.014. Epub 2010 Apr 3.
Mindfulness meditation improves cognition: evidence of brief mental training.
Zeidan F1, Johnson SK, Diamond BJ, David Z, Goolkasian P.

Exercise and Movement Program for Optimal Perimenopausal Brain Health

- According to the results of a meta-analysis, yoga leads to small, but significant reductions in the number of psychological and vasomotor symptoms experienced by peri- and post-menopausal women —> better sleep, less depression, and fewer hot flashes —> better cognitive function.

Sliwinski, J. R., Johnson, A. K., & Elkins, G. R. (2014). Memory Decline in Peri- and Post-menopausal Women: The Potential of Mind–Body Medicine to Improve Cognitive Performance. Integrative Medicine Insights, 9, 17–23. http://doi.org/10.4137/IMI.S15682

Exercise and Movement Program for Optimal Perimenopausal Brain Health

- 108 perimenopausal women were randomly assigned to an eight week integrated yoga intervention (n = 54) or an exercise control group (n = 54).
- Memory performance was assessed before and after treatment with the Punit Govil Intelligence Memory Scale (PGIMS) - The PGIMS is composed of 10 different subscales, which measure various cognitive abilities, such as long-term and short-term memory, attention, and concentration.

Sliwinski, J. R., Johnson, A. K., & Elkins, G. R. (2014). Memory Decline in Peri- and Post-menopausal Women: The Potential of Mind–Body Medicine to Improve Cognitive Performance. Integrative Medicine Insights, 9, 17–23. http://doi.org/10.4137/IMI.S15682

Exercise and Movement Program for Optimal Perimenopausal Brain Health

- Results: Participants assigned to the control condition experienced significant improvements on 6 of the 10 PGIMS subscales.
- AND… **participants assigned to the yoga condition scored significantly better following treatment on 8 of the 10 subscales.**
- **On 7 of the 10 subscales, the yoga group performed significantly better within the subscale compared to controls.**

Sliwinski, J. R., Johnson, A. K., & Elkins, G. R. (2014). Memory Decline in Peri- and Post-menopausal Women: The Potential of Mind–Body Medicine to Improve Cognitive Performance. Integrative Medicine Insights, 9, 17–23. http://doi.org/10.4137/IMI.S15682

Exercise and Movement Program for Optimal Perimenopausal Brain Health SUMMARY

- **HIIT** - as tolerated to maintain good HPA axis function. (May not tolerate HIIT well if INSIG2 snp, will respond better to low weight/ high rep exercise. Studied so far in men.)
- **Mindfulness meditation**
- **Yoga**

Sleep Strategies for Perimenopausal Brain Health

- Perimenopause symptoms cause significant sleep challenge.
  - Women had an average of 3.5 (95% confidence interval: 2.8-4.2, range = 1-9) objective hot flashes per night.
  - A total of 69.4% of hot flashes were associated with an awakening.
  - Hot flash-associated time awake per night was, on average, 16.6 minutes (95% confidence interval: 10.8-22.4 minutes).

De Zambotti, M., Colrain, I. M., Javitz, H. S., & Baker, F. C. (2014). Magnitude of the impact of hot flashes on sleep in perimenopausal women. Fertility and Sterility, 102(6), 1708–1715.e1. http://doi.org/10.1016/j.fertnstert.2014.08.016

Sleep Strategies for Perimenopausal Brain Health

- Sleep is essential for brain autophagy.
- Chronic sleep fragmentation disrupts (mildly) the 24 h rhythm of autophagy related protein expression.
- Thus, for perimenopausal women struggling with sleep fragmentation related to hot flashes and other sleep issues, sleep hygiene strategies are essential.

Chronobiol Int. 2016;33(5):553-60. doi: 10.3109/07420528.2015.1137581. Epub 2016 Apr 14.
Circadian rhythm of autophagy proteins in hippocampus is blunted by sleep fragmentation.
He Y1,2, Cornelissen-Guillaume GG3, He J4, Kastin AJ4, Harrison LM4, Pan W1.

SLEEP

- **Problems Falling Asleep:** dysglycemia?, high cortisol at night (inhibiting melatonin?), GABA - especially if pt. reports “I can’t turn off my mind at night.” and/or dizziness, tics, tremors, vertigo.
- **Problems Staying Asleep:** dysglycemia, DUTCH adrenal stress, GABA, acetylcholine can be an issue if memory and learning are also significant problems. (May also need support from alpha-S1-casein-Tryptic Hydrolysate - Lactium 10aa peptide + long acting melatonin support)
- **Sleep is NOT Restorative:** “I can sleep for 10 hours and still not feel rested.” - start with dysglycemia/ DUTCH adrenal stress? High cortisol can disrupt the dream association with memory/ learning. Dopamine dysregulation may also be involved, esp if restless legs.

Payne, J. D., & Nadel, L. (2004). Sleep, dreams, and memory consolidation: The role of the stress hormone cortisol. Learning & Memory, 11(6), 671–678. http://doi.org/10.1101/lm.77104

Pagel, J. F., & Parnes, B. L. (2001). Medications for the Treatment of Sleep Disorders: An Overview. Primary Care Companion to The Journal of Clinical Psychiatry, 3(3), 118–125.

Classic Neurotransmitter Sx Related to SLEEP

- **Serotonin:** lack of joy, depressed (and feels guilty about it - “but, my life is pretty good.”), overwhelmed, can’t FALL asleep.
- **Dopamine:** low motivation, depressed (but, not guilty about it), unreasonably irritated, issues with speed/ amplitude of motor control.
- **GABA:** nervous and jittery - feel inner trembling, even if they don’t look like they are trembling, can’t turn brain off, worrier (and guilty about it), waking through the night, can’t attend.
- **Acetylcholine:** poor learning and memory - problems with recall testing, “senior moments.”
- **Catecholamines** (cross the BBB - check adrenals!!), poor focus and concentration, easily distracted, rely on caffeine or exercise to get brain going in the morning.

From neuro lecture, Dr. Noseworthy, MUIH, 2016

Sleep Strategies for Perimenopausal Brain Health SUMMARY

- Dark, cool, uncluttered room to sleep in - no blue light screens.
- “Laptop curfew” - eliminate blue light exposure 2 hours before bed.
- Sunlight exposure - 1 hour per day without sunglasses to improve circadian rhythm.
- Ear plugs as needed.
- Consistent sleep schedule - bedtime routine (may include bath, magnesium/ melatonin/ zinc supplement, light reading, calming tea such as camomile)
- Stress reduction strategies (stay tuned…)
- Reduce or eliminate caffeine and alcohol
- Consistent, regular exercise within the limits of patient’s HPA axis resilience and including HIIT/ yoga as tolerated.
- NT formulas: start low and go slow (herbs/ AAs/ nutrient formulas)
- Address dysglycemia/ inflammation.

SUMMARY

- Ask your clients if they struggle with brain fog, difficulty with word finding, verbal acuity declines.
- Ask your clients if they're struggling with low libido.
- WHY??
  - Stress/ lack of restoration/ lack of pleasure/ overworked/ overextended/ belief that she can't say, "No."
  - High sugar/ inflammatory diet?
  - Poor sleep/ quality of sleep?
  - Her fitness program is not matched to her HPA axis resilience/ genetics.
  - She's anemic? Gut issues? Can't absorb nutrients? Low grade chronic infection?

How To Right Size The Fitness Program

- HPA Resilience? Cortisol? DHEA?
- Digestive Function?
- Fueling for performance?
- Sleeping/ Recovering For Performance?
- What stage of the menstrual cycle? (More about that in our Female Athlete Wellness Program)
- Risk Factors - Brain, Cardiovascular, Bone (coming up)
- Pleasure
- Time
- Support

Exercise: Fitness Program

- 48 year old, Jennifer
- Regular cycling, but cycles are shortening to 25-26 days
- mid-follicular phase
- AM fatigue - needs coffee to get up
- PM “wired” second wind at 9pm
- Yogurt and fruit breakfast, salad for lunch, paleo dinner, wine at night
- Gets 6-7 broken hours of sleep - awakes for hot flashes, going to the bathroom, new puppy
- Recent labs: low HDL, normal LDL, fasting glucose 100, FHx of HTN
- Brain foggy at work with complex tasks or presentations - better with sugar boost, then sleepy after brain exertion
- Slowly gained 15 lbs over last 3 years - mostly abdominal fat

Exercise: Fitness Program

- 50 year old, Amanda
- Skipped 2 periods in the last 5 months, flow is heavier
- Mid-luteal phase
- Anxious, fatigued around 3pm, mild recent hair loss
- Stressed about her college aged daughter
- Breakfast smoothie - almond milk, fruit, vegan protein powder, lunch - out to eat with work colleagues, dinner - pasta and vegetables
- Craves sugar, feels bad after 1 glass of wine with friends, losing social connections
- Recent labs: high normal TSH, low normal ferritin, high triglycerides
- Mild short term memory loss - word finding, losing keys
- Intense workouts - irregular. Hard to stick to the plan. Long hours on computer work - but, she's starting to find her work/ life dull
- Loss of sex drive, vaginal dryness

SUMMARY

- Create programs to help your clients find their inner pleasure/ purpose/ joy —> align with their fitness, nutrition, sleep, career, and relationships.
- You will be doing a GREAT SERVICE to the women in your community… literally preventing cancer, heart disease, and dementia.

PART 5: Bone Health

Bone Heath Risk: How Common?

- The proportion of Australian women categorized as having osteoporosis at the PA spine, femoral neck, or midforearm:
  - 0.9% among those aged 40-44 yr
  - 87.0% for those older than 79 yr.

- **A large proportion of elderly Australian women has osteoporosis according to the WHO guidelines.**

J Clin Densitom. 2000 Fall;3(3):261-8.
Prevalence of osteoporosis in Australian women: Geelong Osteoporosis Study.
Henry MJ1, Pasco JA, Nicholson GC, Seeman E, Kotowicz MA.

Bone Heath Risk: How Common?

- Osteoporosis, defined as low bone mass leading to increased fracture risk, is a major health problem that affects approximately 10 million Americans.
- The aging U.S. population is predicted to contribute to as much as a 50% increase in prevalence by 2025.

Kling, J. M., Clarke, B. L., & Sandhu, N. P. (2014). Osteoporosis Prevention, Screening, and Treatment: A Review. Journal of Women's Health, 23(7), 563–572. http://doi.org/10.1089/jwh.2013.4611

Bone Heath Risk: How Common?

- GLOW is an international, observational, cohort study involving 723 physician practices in 17 sites in ten countries in Europe, North America, and Australia.
- Participants included 60,393 women ≥55 years attended by their physician during the previous 24 months. The sample was enriched so that two thirds were ≥65 years.
- Only 33% (4,185/12,612) of those with ≥2 risk factors perceived themselves as being at higher risk. ***Among women reporting a diagnosis of osteopenia or osteoporosis, only 25% and 43%, respectively, thought their risk was increased.***

Siris, E. S., Gehlbach, S., Adachi, J. D., Boonen, S., Chapurlat, R. D., Compston, J. E., … Greenspan, S. L. (2011). Failure to perceive increased risk of fracture in women 55 years and older: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporosis International, 22(1), 27–35. http://doi.org/10.1007/s00198-010-1211-8

Bone Heath Risk Factors

- Low weight for height, Low BMI
- Early menopause
- Parental hip fracture
- Two or more falls in the past 12 months
- Current use of cortisone or prednisone
- Diagnosis of rheumatoid arthritis
- Personal history of fracture (clavicle, arm, wrist, spine, rib, hip, pelvis, upper leg, lower leg, and ankle) since age 45
- Current cigarette smoking
- Consumption of three or more units of alcohol daily.

Siris, E. S., Gehlbach, S., Adachi, J. D., Boonen, S., Chapurlat, R. D., Compston, J. E., … Greenspan, S. L. (2011). Failure to perceive increased risk of fracture in women 55 years and older: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporosis International, 22(1), 27–35. http://doi.org/10.1007/s00198-010-1211-8

Many Women are At Risk for Bone Health Problems, BUT…

- They underestimate their risk.
- ***Even women reporting a diagnosis of osteopenia or osteoporosis, only 25% and 43%, respectively, thought their risk was increased.***

Siris, E. S., Gehlbach, S., Adachi, J. D., Boonen, S., Chapurlat, R. D., Compston, J. E., … Greenspan, S. L. (2011). Failure to perceive increased risk of fracture in women 55 years and older: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporosis International, 22(1), 27–35. http://doi.org/10.1007/s00198-010-1211-8

Strategies to Optimize Bone Health: Testing

- Guidelines recommend screening women 65 years and older and men 70 years and older.
- Screening is recommended for all high-risk postmenopausal women and male patients older than 50.
- For older postmenopausal women with normal BMD or mild osteopenia at baseline, clinicians may wait up to 15 years before repeat screening.
- Older postmenopausal women with moderate osteopenia at baseline can be screened every 5 years, and those with advanced osteopenia likely should be screened yearly.

Kling, J. M., Clarke, B. L., & Sandhu, N. P. (2014). Osteoporosis Prevention, Screening, and Treatment: A Review. Journal of Women's Health, 23(7), 563–572. http://doi.org/10.1089/jwh.2013.4611

Strategies to Optimize Bone Health: Testing

- Osteoporosis treatment reduces fracture risk and is recommended after hip or vertebral fracture for patients with a T-score that is –2.5 or more negative at the femoral neck or spine without secondary causes.

- Treatment also is recommended for patients with a FRAX 10-year risk of at least 3% for hip fracture or at least 20% for major osteoporotic fracture with osteopenia.
- *(FRAX is a computerized fracture-risk algorithm developed by the WHO that uses global models of population-based cohorts combined with clinical risk factors, it is most useful in patients with low hip BMD)*

- Bisphosphonates are considered first-line treatment.

Kling, J. M., Clarke, B. L., & Sandhu, N. P. (2014). Osteoporosis Prevention, Screening, and Treatment: A Review. Journal of Women's Health, 23(7), 563–572. http://doi.org/10.1089/jwh.2013.4611

Strategies to Optimize Bone Health: Testing

- Other first line measurements:
- Serum total calcium
  - Albumin (to calculate albumin adjusted calcium) and phosphate to detect conditions associated with hypercalcemia such as primary hyperparathyroidism or hypocalcemia and consequent secondary hyperparathyroidism causing bone loss.

  - Serum creatinine and estimated glomerular filtration rate (GFR) are useful to detect renal failure which can affect bone health.

Lee, J., & Vasikaran, S. (2012). Current Recommendations for Laboratory Testing and Use of Bone Turnover Markers in Management of Osteoporosis. Annals of Laboratory Medicine, 32(2), 105–112. http://doi.org/10.3343/alm.2012.32.2.105

Strategies to Optimize Bone Health: Testing

- Serum alkaline phosphatase (ALP) measurement is useful to detect conditions including Paget's disease, metastatic bone disease and osteomalacia, etc.
- Total ALP is adequate for demonstrating gross increases in bone formation such as those found in most patients with active Paget's disease, osteomalacia, fracture healing or metastatic bone disease, but is not sensitive enough to detect changes in bone remodeling seen in most cases of uncomplicated osteoporosis.
- Although gamma-glutamyl transpeptidase (GGT) is suggested by some to distinguish an increase in liver ALP from bone ALP, this is neither sensitive nor specific for this purpose. If changes in bone formation need to be determined with sensitivity, or distinguished from an increase in total ALP due to liver disease, a specific bone formation marker such as PINP could be measured.

Lee, J., & Vasikaran, S. (2012). Current Recommendations for Laboratory Testing and Use of Bone Turnover Markers in Management of Osteoporosis. Annals of Laboratory Medicine, 32(2), 105–112. http://doi.org/10.3343/alm.2012.32.2.105

Strategies to Optimize Bone Health: Testing

- Vitamin D nutrition should be determined by measuring serum 25-hydroxy vitamin D [25(OH)D].

- There is controversy about the optimum level of 25(OH)D for bone health:
- 50 nmol/L is considered acceptable
- 75 nmol/L as desirable for optimum bone health

- ***If the higher cut-off is used, then the vast majority of menopausal women (76.8%) would be considered to have sub-optimal vitamin D nutrition.***

Lee, J., & Vasikaran, S. (2012). Current Recommendations for Laboratory Testing and Use of Bone Turnover Markers in Management of Osteoporosis. Annals of Laboratory Medicine,

Strategies to Optimize Bone Health: Testing

- Bone Turnover Markers (BTM's)
- Measurement of bone turnover markers (BTMs) is currently not included in algorithms for fracture risk calculations due to the lack of data. However, BTMs may be useful for monitoring osteoporosis treatment.

- Serum carboxy terminal telopeptide of collagen type I (s-CTX)
- Serum procollagen type I N-terminal propeptide (s-PINP)

Lee, J., & Vasikaran, S. (2012). Current Recommendations for Laboratory Testing and Use of Bone Turnover Markers in Management of Osteoporosis. Annals of Laboratory Medicine, 32(2), 105–112. http://doi.org/10.3343/alm.2012.32.2.105

Strategies to Optimize Bone Health: Testing

- Heavy Metals: Displace trace minerals
- Urine testing - can be provoked, but the evidence is generally against using chelation agents due to risks and limitations of benefit.
- Hair, Toenail, Blood analysis

Singh, R., Gautam, N., Mishra, A., & Gupta, R. (2011). Heavy metals and living systems: An overview. Indian Journal of Pharmacology, 43(3), 246–253. http://doi.org/10.4103/0253-7613.81505

Ruha, A.-M. (2013). Recommendations for Provoked Challenge Urine Testing. Journal of Medical Toxicology, 9(4), 318–325. http://doi.org/10.1007/s13181-013-0350-7

Strategies to Optimize Bone Health: Testing

- Nutrient deficiency testing:
- Spectracell
- Nutreval
- Urinary Organic Acids

Calcium, Magnesium, Vitamin D, K2, potassium

Strategies to Optimize Bone Health: Nutrition

- The key is to take in the nutrients that will strengthen bone but NOT calcify arteries.
- Only 30% of the US population consumes the RDA of calcium, which is 1000–1200 mg daily
- People absorb only about 30% of calcium from foods depending on the specific source.
- The body will demineralize its own skeletal system to maintain serum calcium levels in situations where dietary calcium is insufficient and/or absorption is decreased, and/or excretion is increased.

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition

- DAIRY???
- A recent meta-analysis of over 270 000 people showed a strong trend for dairy intake protecting against hip fracture
- BUT…
- Consumption of cow's milk has been associated with cataracts, ovarian and prostate cancers, Parkinson's disease, and in autoimmune diseases, such as type 1 diabetes and multiple sclerosis.
- The evidence for dairy-induced human disease appears to be most consistent for prostate cancer and for type 1 diabetes.

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition

- DAIRY???
- A study of over 106,000 adults followed for 20 years showed that drinking three or more glasses of milk per day was associated with increased risks for bone fracture and higher mortality rates compared with drinking not more than one glass of milk per day.

- In contrast, for the women in that study, each daily serving of cheese and/or other ***fermented*** milk product such as yogurt was associated with a 10–15% decrease in the rates of mortality and hip fractures ($p<0.001$).

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition

- Vegetables???

- Most vegetarians, especially vegans, appear to absorb less calcium because of the oxalic and phytic acid contained in many plant, grain and legume products.

- Several studies have reported that risks of bone fracture are higher in vegans—likely due, at least in part, to their lower dietary calcium intake, and/or poor calcium absorption.

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

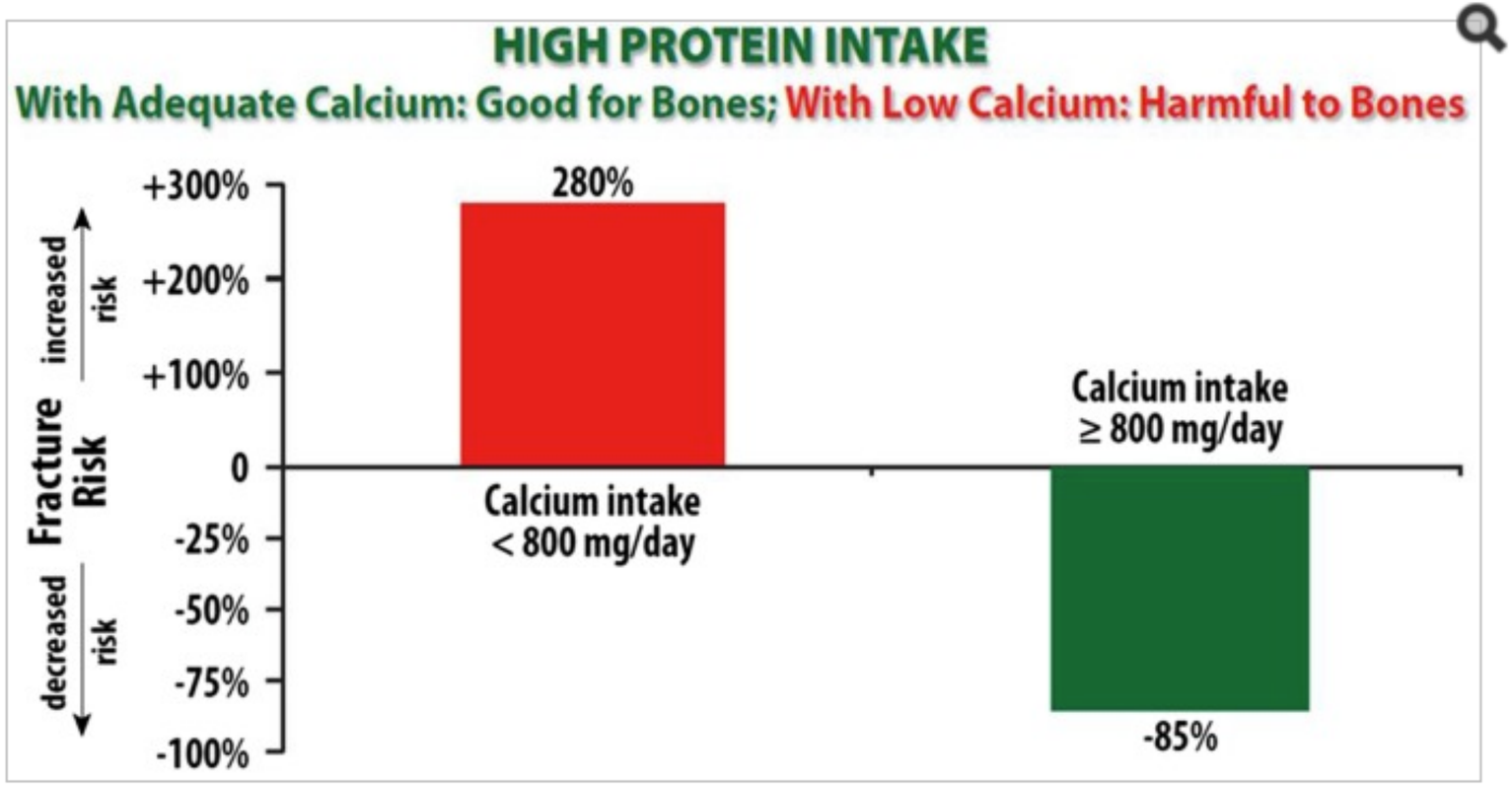
Strategies to Optimize Bone Health: Nutrition

Calcium-rich foods

Food	Serving size	Calcium (mg)
Yogurt	6 oz	300
Sardines	3.5 oz with bones	250
Salmon	3.5 oz with bones	240
Spinach	1 cup cooked	240
Chia seeds	1 oz	200
Kale	1 cup chopped	100
Orange	1 medium size	80
Almonds	Raw, ¼ cup (1 oz)	80
Broccoli	1 cup cooked	60
Brussels sprouts	1 cup cooked	60
Brazil nuts	1 oz	50

From the USDA: http://www.usda.gov/wps/portal/!ut/p/_s.7_0_1OB?navtype=SU&navid=FOOD_NUTRITION.

Strategies to Optimize Bone Health: Nutrition



A diet that contains moderate amounts of fresh, lean, animal protein, when combined with adequate calcium intake, promotes bone strength and reduces fracture risk. In contrast, high protein diet with inadequate calcium intake increases risk of fracture.[28]

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition

- Protein???
- Protein intake raises levels of insulin-like growth factor 1, which is anabolic, and contributes to bone building.
- Diets moderate in protein (≈1.0–1.5 g/kg/day) are associated with normal calcium metabolism, and do not adversely alter bone metabolism; however, at lower protein intakes (<0.8 g/kg/day), intestinal calcium absorption is reduced and levels of parathyroid hormone rise, causing the mobilization of calcium from bone.

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition

- Diets higher in **animal protein** are associated with greater bone mass and fewer fractures, particularly if the calcium intake is also sufficient (approximately 1000 mg of calcium/day)

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Nutrition SUMMARY

- Ample dietary calcium
- Alkalising nutrients —> such as fruits and vegetables, and possibly also alkaline mineral waters
- Moderate intake of animal protein.
- Supplement with calcium, magnesium, Vitamin D3, K2 (decreases arterial calcium and increases bone strength/ reduces fractures —> hip fx decreased by 77%!!)
- High potassium with lower sodium

— Aim for: a moderate sodium diet (2800–3300 mg/day) in conjunction with a high potassium intake (>3000 mg/day)

O'Keefe, J. H., Bergman, N., Carrera-Bastos, P., Fontes-Villalba, M., DiNicolantonio, J. J., & Cordain, L. (2016). Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. Open Heart, 3(1), e000325. http://doi.org/10.1136/openhrt-2015-000325

Strategies to Optimize Bone Health: Exercise

- With nearly a year of strength or power exercise, premenopausal women **both showed maintenance of bone mineral density.**

- Power exercises: jumping rope, skipping, hopping
- Strength exercises: 8-10 whole-body strengthening exercises at 70% one-repetition maximum (1RM)

J Sports Med Phys Fitness. 2013 Aug;53(4):428-36.
The effects of power and strength training on bone mineral density in premenopausal women.
Gray M1, Di Brezzo R, Fort IL.

Strategies to Optimize Bone Health: Exercise

- In postmenopausal women (and men) WITH osteoporosis:
- Weight bearing vs. non-weight bearing exercise…
- T-tests proved that mean values of BMD of the lumbar spine, right neck of femur and right distal radial head were ***significantly increased in both groups with greater improvement in the weight-bearing group.***
- The QoL was significantly improved in both groups.

Shanb, A. A., & Youssef, E. F. (2014). The impact of adding weight-bearing exercise versus nonweight bearing programs to the medical treatment of elderly patients with osteoporosis. Journal of Family & Community Medicine, 21(3), 176–181. http://doi.org/10.4103/2230-8229.142972

Strategies to Optimize Bone Health: Exercise

- In postmenopausal women WITH osteoporosis (NOT on medications):
- Vibrational frequency varied from 12 to 90 Hz.
- The time used in the protocols varied from 2 up to 22 months.
- Among the twelve articles analyzed, seven of them have shown an improvement of the BMD of some bone of postmenopausal women exposed to whole body vibration exercises not associated to medications; as well as modifications in biomarkers.

Dionello, C. F., Sá-Caputo, D., Pereira, H. V. F. S., Sousa-Gonçalves, C. R., Maiworm, A. I., Morel, D. S., … Bernardo-Filho, M. (2016). Effects of whole body vibration exercises on bone mineral density of women with postmenopausal osteoporosis without medications: novel findings and literature review. Journal of Musculoskeletal & Neuronal Interactions, 16(3), 193–203.

Strategies to Optimize Bone Health: Exercise

- Start with lower vibration frequencies and increase through the therapy time.
- Ideally therapy lasting 6-12 months

- Most effective in women weighing less than 65kg (143 lbs)

- Whole body vibration increases the level of growth hormone and testosterone in serum, preventing sarcopenia and osteoporosis
- Improves balance, neuromuscular and proprioceptive function.
- BMD can actually be INCREASED.

Weber-Rajek, M., Mieszkowski, J., Niespodziński, B., & Ciechanowska, K. (2015). Whole-body vibration exercise in postmenopausal osteoporosis. Przegląd Menopauzalny = Menopause Review, 14(1), 41–47. http://doi.org/10.5114/pm.2015.48679

Exercise: Fitness Program

- 48 year old, Jennifer
- Regular cycling, but cycles are shortening to 25-26 days
- mid-follicular phase
- AM fatigue - needs coffee to get up
- PM “wired” second wind at 9pm
- Yogurt and fruit breakfast, salad for lunch, paleo dinner, wine at night
- Gets 6-7 broken hours of sleep - awakes for hot flashes, going to the bathroom, new puppy
- Recent labs: low HDL, normal LDL, fasting glucose 100, FHx of HTN
- Brain foggy at work with complex tasks or presentations - better with sugar boost, then sleepy after brain exertion
- Slowly gained 15 lbs over last 3 years - mostly abdominal fat

What if she has a family history of osteoporosis? Thin?

Exercise: Fitness Program

- 50 year old, Amanda
- Skipped 2 periods in the last 5 months, flow is heavier
- Mid-luteal phase
- Anxious, fatigued around 3pm, mild recent hair loss
- Stressed about her college aged daughter
- Breakfast smoothie - almond milk, fruit, vegan protein powder, lunch - out to eat with work colleagues, dinner - pasta and vegetables
- Craves sugar, feels bad after 1 glass of wine with friends, losing social connections
- Recent labs: high normal TSH, low normal ferritin, high triglycerides
- Mild short term memory loss - word finding, losing keys
- Intense workouts - irregular. Hard to stick to the plan. Long hours on computer work - but, she's starting to find her work/ life dull
- Loss of sex drive, vaginal dryness

What if she had a fracture last year from a mild fall playing with child?

Strategies to Optimize Bone Health: Exercise SUMMARY

- Consider genetics
- Consider hormone (especially HPA axis) resilience vs. estrogen dominance
- Strength and power training
- Whole Body Vibration

Weber-Rajek, M., Mieszkowski, J., Niespodziński, B., & Ciechanowska, K. (2015). Whole-body vibration exercise in postmenopausal osteoporosis. Przegląd Menopauzalny = Menopause Review, 14(1), 41–47. http://doi.org/10.5114/pm.2015.48679

PART 6: Case and Questions

Case

- 55 year old woman, Nathalie - still cycling, irregular
- Yoga and fitness instructor, 4 classes per week.
- Raised 3 sons - the youngest is not transitioning well to college. Having issues with him. He was home, and is back at school now.
- Sleeps well.
- Painful sex.
- Doesn’t feel much pleasure, purpose in her life.
- Nutrition - depriving, often on a “deep detox” Can’t keep the weight off if I eat intuitively. I love food, and cook gourmet meals for my husband and son, but don’t eat any of it.

Summary of Abnormal Findings

	Findings	Intervention Options	Common Metabolic Association
Fatty Acid Metabolism			
Adipate	↑	Carnitine, B2	Fatty acid oxidation
Ethylmalonate	↑	Carnitine, B2	Fatty acid oxidation
Carbohydrate Metabolism			
b-Hydroxybutyrate	↑	Cr, V, Lipoic Acid, Mg, Mn	Ketosis
Energy Production Markers			
Citrate	↑	Arginine	Renal ammonia loading
a-Ketoglutarate	↓	CoQ10, Lipoic Acid, B1, B2, B3, B5	Citric acid cycle
Succinate	↓	CoQ10	ATP production
Malate	↑	CoQ10	ATP production
B-Complex Vitamin Markers			
b-Hydroxyisovalerate	↑	Biotin, B2	Impaired Isoleucine metabolism
Methylation Cofactor Markers	No Abnormality Found		
Neurotransmitter Metabolism Markers			
Homovanillate	↑	Evaluate stress issues	Dopamine turnover stimulation

Oxidative Damage and Antioxidant Markers	No Abnormality Found		
Detoxification Indicators			
Sulfate	↓	Antioxidants and removal of toxicant or oxidant stress source	Acute detox or oxidant stress

Commentary

Bacterial - General			
Hippurate	↓	Glycine	Hepatic Phase II conjugation
Indican	↓	Probiotics	Intestinal Bacterial Overgrowth
Tricarballylate	↓	Probiotics	Intestinal Bacterial Overgrowth
L. acidophilus / general bacteria	No Abnormality Found		
Clostridial Species	No Abnormality Found		
Yeast/Fungal			
D-Arabinitol	↑	Antifungals	Yeast overgrowth

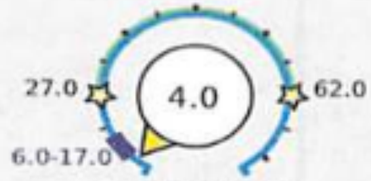
Hormone Testing Summary

All units are given in ng/mg creatinine

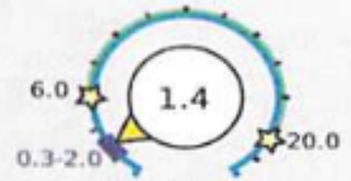
How to read the graphical representation of results

Sex Hormones

See Pages 2 and 3 for a thorough breakdown of sex hormone metabolites



Total Estrogen
(Sum of 8 Estrogen Metabolites)



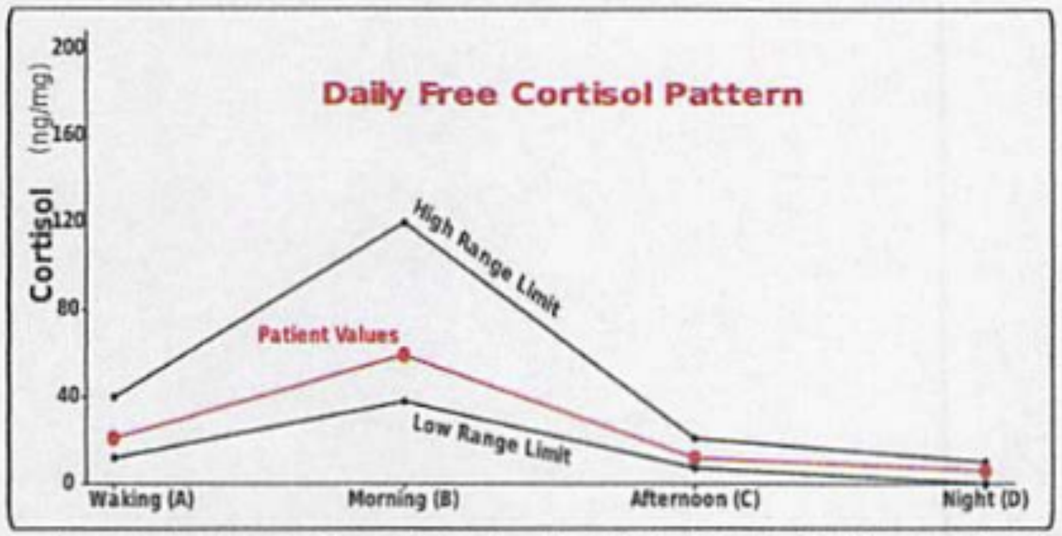
Progesterone
(Serum Equivalent, ng/mL)

Testosterone

Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.

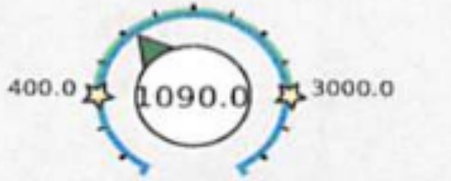
Adrenal Hormones

See pages 4 and 5 for a more complete breakdown of adrenal hormones



Total DHEA Production

Age	Range
20-30	1000-3000
30-40	800-2000
40-60	530-1550
>60	400-1350



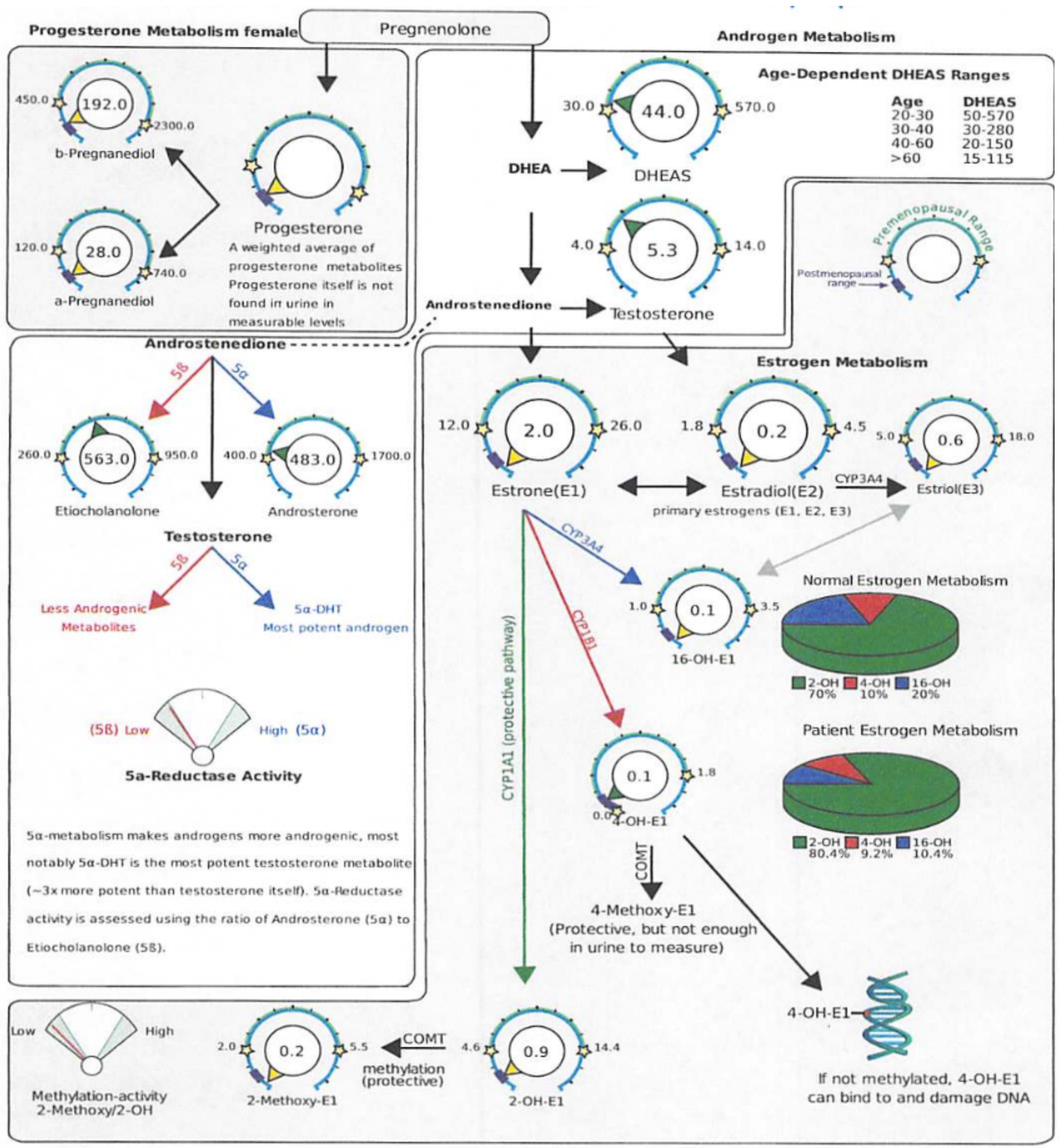
Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)

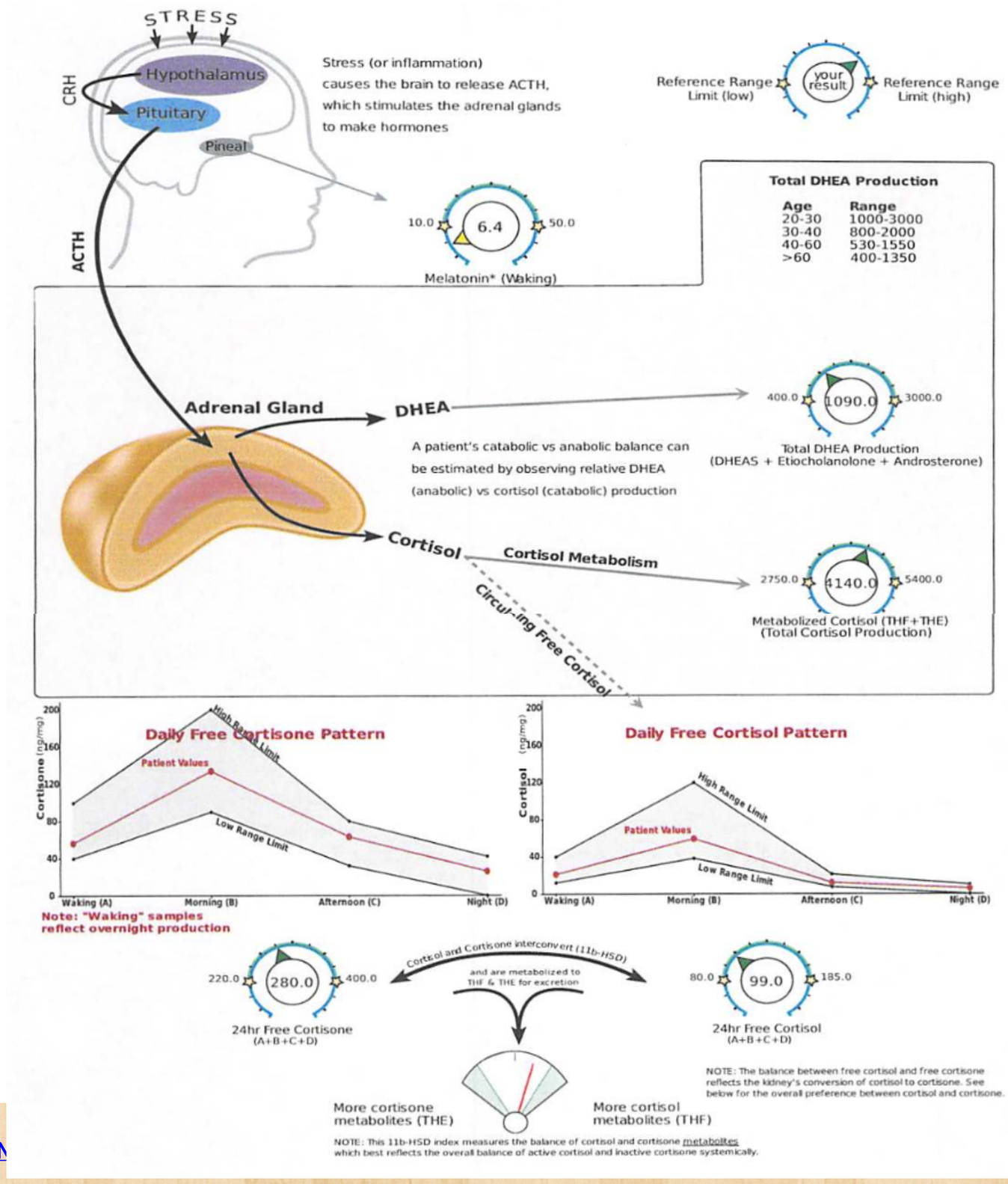
24hr Free Cortisol
(A+B+C+D)

cortisol metabolism

Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.


Progesterone Metabolism female
Pregnenolone
Androgen Metabolism
450.0
192.0
2300.0
b-Pregnanediol
120.0
28.0
740.0
a-Pregnanediol
Progesterone
A weighted average of progesterone metabolites Progesterone itself is not found in urine in measurable levels
30.0
44.0
570.0
DHEA
DHEAS
Age-Dependent DHEAS Ranges
Age DHEAS
20-30 50-570
30-40 30-280
40-60 20-150
>60 15-115
4.0
5.3
14.0
Androstenedione
Testosterone
Premenopausal Range
Postmenopausal range
Androstenedione
5ß
5α
260.0
563.0
950.0
Etiocholanolone
400.0
483.0
1700.0
Androsterone
Testosterone
5ß
5α
Less Androgenic Metabolites
5α-DHT
Most potent androgen
(5ß) Low
High (5α)
5a-Reductase Activity
5α-metabolism makes androgens more androgenic, most notably 5α-DHT is the most potent testosterone metabolite (~3x more potent than testosterone itself). 5α-Reductase activity is assessed using the ratio of Androsterone (5α) to Etiocholanolone (5ß).
Estrogen Metabolism
12.0
2.0
26.0
Estrone(E1)
1.8
0.2
4.5
Estradiol(E2)
CYP3A4
5.0
0.6
18.0
Estriol(E3)
primary estrogens (E1, E2, E3)
CYP3A4
CYP1A1 (protective pathway)
CYP1B1
1.0
0.1
3.5
16-OH-E1
Normal Estrogen Metabolism
2-OH 70%
4-OH 10%
16-OH 20%
Patient Estrogen Metabolism
0.1
1.8
0.0
4-OH-E1
2-OH 80.4%
4-OH 9.2%
16-OH 10.4%
COMT
4-Methoxy-E1
(Protective, but not enough in urine to measure)
4-OH-E1
If not methylated, 4-OH-E1 can bind to and damage DNA
Low
High
Methylation-activity 2-Methoxy/2-OH
2.0
0.2
5.5
2-Methoxy-E1
COMT
methylation (protective)
4.6
0.9
14.4
2-OH-E1


STRESS
Hypothalamus
Pituitary
Pineal
CRH
ACTH
Stress (or inflammation) causes the brain to release ACTH, which stimulates the adrenal glands to make hormones
Reference Range Limit (low)
your result
Reference Range Limit (high)
10.0
6.4
50.0
Melatonin* (Waking)
Total DHEA Production
Age Range
20-30 1000-3000
30-40 800-2000
40-60 530-1550
>60 400-1350
Adrenal Gland
DHEA
400.0
1090.0
3000.0
Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)
A patient's catabolic vs anabolic balance can be estimated by observing relative DHEA (anabolic) vs cortisol (catabolic) production
Cortisol
Cortisol Metabolism
Circul-ing Free Cortisol
2750.0
4140.0
5400.0
Metabolized Cortisol (THF+THE)
(Total Cortisol Production)
Daily Free Cortisone Pattern
Cortisone (ng/mg)
High Range Limit
Patient Values
Low Range Limit
Waking (A)
Morning (B)
Afternoon (C)
Night (D)
Note: "Waking" samples reflect overnight production
Daily Free Cortisol Pattern
Cortisol (ng/mg)
Cortisol and Cortisone interconvert (11b-HSD) and are metabolized to THF & THE for excretion
220.0
280.0
400.0
24hr Free Cortisone
(A+B+C+D)
80.0
99.0
185.0
24hr Free Cortisol
(A+B+C+D)
NOTE: The balance between free cortisol and free cortisone reflects the kidney's conversion of cortisol to cortisone. See below for the overall preference between cortisol and cortisone.
More cortisone metabolites (THE)
More cortisol metabolites (THF)
NOTE: This 11b-HSD index measures the balance of cortisol and cortisone metabolites which best reflects the overall balance of active cortisol and inactive cortisone systemically.

Support Her Brain and Libido, Resolve Sexual Pain and Low Energy

- **Gut:** Dysbiosis and Yeast overgrowth - antimicrobial herbs
- **Can't absorb nutrients and LOW ATP/ oxidative stress (mitochondria) -** Digestive enzymes, hypochlorhydria?, leaky gut?, antioxidants (coQ10, lipoic acid, vitamin D, colorful fruits and veggies)
- **Low-normal corisol** (good rhythm = good sleep)**, high metabolites** (likely related to inflammation) Licorice (other adaptogens, but high metabolites, so think lowering inflamm/ oxidative stress first… WHY is SHE stressed?)
- **Low sex hormones -** Where is the juice in her life?
- **Low methylation -** Difficulty with detox, support with B-vitamins, cruciferous veggies, etc.

Support Her Brain and Libido, Resolve Sexual Pain and Low Energy

- **Do you have a lot of women in your life/ your practice like this?**
- **How can you support them?**
  - New mom identity retreat
  - Sensual/ powerful/ restorative fitness programs
  - Group coaching
  - Vision retreat/ Desire mapping
  - Mindful eating “cleanse”
  - Invite speakers re: sexuality/ sensuality in midlife/ after baby, relationship experts, career experts - is her work/ volunteering in alignment with fun/ purpose?

SUMMARY

- Create programs to help your clients find their inner pleasure/ purpose/ joy —> align with their fitness, nutrition, sleep, career, and relationships.
- You will be doing a GREAT SERVICE to the women in your community… literally preventing osteoporosis, heart disease, and dementia.

THANK YOU!

LEARN MORE…

http://integrativewomenshealthinstitute.com/opt/3-steps-webinar/

Opportunity for Women's Health Coach Certification (Nutrition + Coaching)