A NEUROENDOCRINE CONNECTION TO WOMEN’S HEALTH.

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Faculty Disclosure

- **Faculty:** Dr. Penny Kendall-Reed

- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** Honoraria to be received for participation in this conference
  - **Consulting Fees:** Dr. Kendall-Reed serves as a paid medical advisor to Douglas Laboratories
  - **Other:** none
Disclosure of Commercial Support

• Honoraria for speaking and travel provided by Diversified Communications

• This program has not received additional financial support

• This program has not received additional in-kind support

• No Potential for conflicts of interest
Learning Objectives

- Describe the impact of stress on women’s health
- Review the relationship between hypothalamic–pituitary–adrenal (HPA) axis hormones and stress
- Evaluate the benefits of natural herbs and supplements, exercise, and relaxation techniques in reducing and preventing stress
Impact of Stress

- 79% to 90% of all visits to primary health care practitioners in NA are due to stress-related illnesses.
  

- 68% of women say they are chronically stressed, yet only 25% say they are doing anything about. (Statistics Canada)

- 11% of Americans age 12 or older report taking antidepressants. (CDC data)
Impact of Stress

- Within 30 mins of rising, women have higher peaks of cortisol than men, especially on week days.
  (Kunz-(Ebrecht, Sabine et al, Differences in cortisol awakening response on work days and weekends in women and men from the Whitehall II cohort, J of Pyschoneuroendo, May 2004 Vol 29, Issue 4, pg 516-528)

- Women experience more somatic symptoms and psychological distress for the same stressors when compared to men.
Both effects increase HPA stimulation and result in greater hippocampal and amygdala atrophy, biphasic alterations in structure increasing swings from depression to anxiety in woman as compared to men. (without clinical diagnosis of bipolar).

What is Stress?

- Necessary for our survival!
- Anything that stimulates the fight or flight response in the body.
- Real, perceived, psychological or physical stress = same response.
- Aging
- Food, alcohol, coffee, other stimulants, working long hours, lack of bonding.
FAMILY DAY
The Central Nervous System

- **Parasympathetic Nervous System - Campfire**
  - Stimulates digestion (enzymes, peristalsis, nutrient absorption), regulates sleep (stage 4), stimulates sex organs (libido/fertility).

- **Sympathetic Nervous System – Hunting**
  - Responsible for states of heightened awareness- Fight or Flight response. Increases heart rate, increases blood flow to extremities, diverts sugar to the blood, increases immunity, and parasympathetic stimulation
Diagram shows the secretion of cortisol and its feedback loop.

HYPOTHALAMUS

CORTICOTROPIC
RELEASING
HORMONE (CRH)

ANTERIOR
PITUITARY

ADRENO-
CORTICOTROPIC
RELEASING
HORMONE (ACTH)

ADRENAL
GLANDS

CORTISOL

[Symbolic representation of the hormonal interactions]
“Traditional” Stress – Prehistoric Caveman

- Single stressor - life in danger
- Stimulates the HPA axis to prepare body for action. (sympathetic nervous system)
- Resolution of stressor
- Negative feedback to the hypothalamus and return to “normal” daily routine (parasympathetic nervous system)
HUNTING, GATHERING.... IT'S SO HARD TO PRIORITIZE!
“Modern” Stress – Downtown Man

- Multiple stressors – sleep deprivation, hypoglycemic, traffic, fight with spouse….
- Each event stimulates HPA axis
- Continual stimulation of SNS, hypothalamic receptor saturation, loss of negative feedback, no resolution of stressor, No return to PNS
- Unable to identify and handle stress!
HPA Axis Hormones

- **Adrenaline and Noradrenaline**
  - Short acting (few minutes), responsible for the initial stages of the fight or flight response = increased breathing and heart rate, increased sweating, fluid retention, dilated pupils, increase fat breakdown.

- **Cortisol**
  - Prolonged stress response (hours), responsible for the later stages of the stress response, increased sugar delivery to blood, increased blood clotting, increased inflammation.

- **Corticotropin Releasing Hormone (CRH)**
  - Hormone produced and released from the hypothalamus. Stimulates the pituitary release of ACTH, to stimulate the adrenal release of corticosteroids, and control the strength of the sympathetic nervous response.
Normal Cortisol Cycle

Daily Cortisol Cycle

- Normal 6-8 am Peak

Cortisol Level

Time

Midnight  2am  4am  6am  8am  10am  Noon  2pm  4pm  6pm  8pm  10pm  Midnight
Chronic Stress Cortisol Cycle

Daily Cortisol Cycle with added stressors

Cortisol Level

Time

Midnight, 2am, 4am, 6am, 8am, 10am, Noon, 2pm, 4pm, 6pm, 8pm, 10pm, Midnight

Abnormal 2-4am Peak

Stuck in Traffic

Work Deadline

Family Crisis
Exposure to pollutants, such as PCBs, stimulate the adrenal cortex and the synthesis of cortisol.

Exposure to organic pollutants during fetal and suckling period caused altered cortisol levels in animals, and increased risk of diabetes, CV disease from altered cortisol levels in humans.

(Persistent Organic Pollutants Affect The Stress Hormone Cortisol. Karin Zimmer, Endocrinology Jan 2011)
The gene GLO-1 (Glyoxalase I) degrades cytotoxic byproducts of glycolysis, especially Methylglyoxal, (MG).

MG stimulates GABA-A receptors, calming the brain and body.

Studies in Journal of Clinical Investigation, found that animals with multiple copies of the GLO-1 gene were more likely to exhibit anxiety-like behavior due to lowered MG levels.
Genetic Causes of Anxiety

- Injections of MG decreased anxiety within 10 minutes of administration.

- MG also demonstrated sedative effects at high doses – the hallmark of GABA receptor activity.

- Research for drugs/supplements that can moderate the GLO1/MG underway for anxiety treatment.

- (Anxiety Disorders And Cellular Metabolism Linked, Grace Rattue, Journal of Clinical Investigation, Chicago, May 2012)
Hormone-Gene Interaction

Direct Gene Activation

- Receptor/hormone Complex
- mRNA
- Protein
- Phosphorylation
- Translation
- Transcription

Aldosterone
Cortisol
Testosterone
Estrogen
Progesterone
Thyroxine

www.freelivedoctor.com
Acute stress slows DNA methylation of glucocorticoid receptors in infants and young animals who have received less nurturing from their mothers >> increased sensitivity to emotional stress.

2 genes, oxytocin receptor (the “trust” or “anti-stress gene”) and Brain-Derived Neurotrophic Factor (BDNF), were examined under stress.
76 people were observed during fictitious job interviews and while solving arithmetic problems as stressors. Blood samples were taken before the test, ten and ninety minutes afterwards.

No effect on the BDNF gene was seen with stress.

Methylation greatly increased in the first 10 mins, then dropped below the original level 90 mins after the stress test.

Coincided with increased anxiety and glucocorticoids at 90 mins.

(Control Of Gene Activity Altered By Acute Stress, E.Unternaehrer et al, J of Pysch, Aug 2012)
Stress and Reproduction

[Diagram showing the relationship between stressors and reproductive outcomes.]

- **Stressors**:
  - Unknown factors
  - Alcohol
  - Smoking
  - Antioxidant nutrients, antioxidants, other antioxidant phytochemicals
  - Ionizing radiation & other environmental exposures
  - Infections
  - Physical activity

- **Reactive Oxygen Species**
  - Free Radicals
  - Lipid Peroxides

- **DNA & Tissue Damage, Mutagenesis, Cell Death**
  - **Males**
    - Sperm count↓
    - Sperm motility↓
    - Abnormal sperm
  - **Females**
    - Delayed conception
    - Fertilization↓
    - Oocyte penetration↓
    - Oocyte function↓
    - Viability↓
    - Implantation or Loss of implanted embryo

- **Biomarkers of oxidative stress**

- **Pregnancy Outcome**
Hypothalamic Gonadal Axis
Infertility affects more than 10 million North American women. 15% cause unknown.

Reproduction is controlled by pulsed secretions of GnRH leading to FSH/LH release, ovulation and egg maturation.

If fertilized, egg and uterus produce sufficient estrogen and progesterone to maintain pregnancy.

Estrogen and progesterone provide negative feedback to the hypothalamus and the pituitary to inhibit FSH/LH and GnRH.
<table>
<thead>
<tr>
<th>Hypothalamus</th>
<th>Pituitary</th>
<th>Uterus/Ovaries</th>
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</thead>
<tbody>
<tr>
<td>GnRH</td>
<td>FSH</td>
<td>Estrogen</td>
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<tr>
<td></td>
<td>GnRH</td>
<td>Progesterone</td>
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<tr>
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<td>LH</td>
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</table>
Stress and Reproduction

- responsiveness and pulsing of GnRH, especially during the follicular phase.

- gonadotropin release (FSH, LH, hCG and cCG) disrupting ovarian cyclicity.

- Altered LH surging especially during follicular phase >> abnormal estrogen and progesterone ratios.
Cortisol and GnRH

- Effects of cortisol on GnRH during follicular phase in sheep were tested via monitoring pituitary portal blood after stressors.

- Acute rise in cortisol (6 hrs) did not affect GnRH pulsing, continued exposure (27 hrs) lowered GnRH pulsing by 45% and delayed LH surging.

- Sustained release of cortisol lowers GnRH by up to 70%.

Stress and GnIH

- Cortisol levels of gonadotropin-inhibitory hormone, or GnIH.

- GnIH or RFamide-related peptide (RFRP), directly inhibits GnRH in the dorsal medial hypothalamus.

- Double whammy – cortisol inhibits GnRH and cortisol increases GnIH.

- Low GNRH reduction in FSH, LD, estradiol and testosterone.

- Increased HPA stimulation also directly increases testosterone production through the adrenals.
Most wild birds and vertebrates will not mate in captivity.

Testing this, researchers confined female rats for 3 hrs a day for 18 days, with 4 days off - paralleling the typical rat estrus cycle (akin to the human 28 days).

By the end of the stress-free 4 day hiatus, cortisol levels had returned to normal, yet RFRP remained elevated lowering GnRH release.
Stress and Reproduction

- **Decrease** in pregnancy rates was seen even after cortisol normalized from 80% to 20%.

- **Increase** in miscarriages was also observed.

- A virus inserted into the rat’s brains to block the RFRP gene and reduce the inhibitory peptide by 75% during periods of stress, produced normal mating and pregnancy rates.

- *(Blocking hormone could reduce stress induced infertility. Robert Sanders, Berkley News Center, Berkley University, Jan 2015.)*
Stress and GnIH
Stress and Reproduction

- Acute stress in rats upregulated RFRP for several hours but levels return to normal the next day.

- Chronic stress led to continual release of RFRP levels in the dorsal medial hypothalamus (even months after resolution of the stressor).

- When the adrenals of male rats were removed, and rats exposed to stress, RFRP levels remained normal.

- Showed that RFRP neurons expressed receptors for glucocorticoids and called stress the largest factor in “unexplained” infertility.

- (National Science Foundation. UC Berkeley’s Department of Integrative Biology. Kaufer, 2010.)
Stress and Reproduction

- Prolactin should be low in non-pregnant women to signal fertility, and rise at fertilization to inhibit GnRH.

- Stress increases prolactin in non-pregnant women, thereby decreasing ovulation, and prolactin in pregnant women decreasing pituitary feedback and increasing risk of miscarriages.
Stress and Reproduction

- Sympathetic stimulation initiates abnormal prolonged spasms of the fallopian tubes, increasing risk of egg destruction as it travels down the tubes.

- Cortisol also greatly increases the release of prostaglandins in the uterus, heightening inflammation and increasing cramping, spasms and miscarriages.
Stress and Amylases

- Amylases - salivary enzymes that breakdown starches into maltose and dextrin, or the pancreatic enzymes that breakdown amylose into dextrin, maltose or maltitriose.

- Genetic variations with duplications in the amylase gene increases amylase production and activity as well as infertility.

- Stress increases both cortisol and alpha amylase production but at different times.
Women with high levels of alpha-amylase have a harder time getting pregnant.

Saliva samples from 274 women over 6 menstrual cycles revealed that those with the highest enzyme concentrations were 12 percent less likely to conceive than were women with the lowest levels, even with no prior history of infertility.

Research shows that female children with higher alpha amylase production displayed more social/emotional problems following stressors (listening to arguments) and had future health and fertility issues.

Male children with higher levels were more aggressive and had heightened cognitive problems.

Irregular Menstruation and Early Menopause

- Approximately 30% of women in their reproductive years experience abnormal bleeding from HPA dysfunction.  

- The most common causes of anovulatory cycles include polycystic ovary syndrome (PCOS), premature ovarian failure, and hyperprolactinemia: all of which display versions of hypothalamic dysfunction.  
Irregular Menstruation and Early Menopause

- Chronic stress ↓ GnRH and ↑ GnIH.

- Altered FSH and LH surging, and subsequent alteration of estrogen and progesterone ratio, decreasing the buildup and shedding of the endometrium.

- As this continues, menses is altered in both timing and bleeding, with eventual anovulation and early menopause.

- Increase in insulin production increasing adipose deposition, inflammation and PCOS.
Irregular Menstruation and Early Menopause

The graph illustrates the probability of being in a fertile window during the menstrual cycle for both regular and irregular cycles. The x-axis represents the day of the menstrual cycle, ranging from 0 to 35, and the y-axis represents the probability of being in a fertile window, ranging from 0 to 0.6. The red line indicates the usual cycle in regular menstruation, peaking around day 14, while the blue dashed line represents an irregular cycle, showing a shift in the peak probability.
Stress and GABA

- Arcuate nuclei in the hypothalamus receives feedback via GABA as to a person’s emotional state.
- GE mice (blocked all GABA production) gained weight immediately with no change in diet.
- Gains were far greater when these mice were stressed.
- Discovered that expenditure through Brown Adipose Tissue is entirely due to GABA release from the Arcuate nuclei.
Stress and Ghrelin and Dopamine

- Ghrelin, appetite-stimulating hormone produced by the stomach when fuel sources are low.

- Ghrelin receptors (GHSR1a) are broadly distributed in the brain.

- Dopamine receptor subtype-2 (DRD2) is adjacent to GHSR1a, to turn off ghrelin stimulation once food has been consumed.

- Cortisol downregulates dopamine production and induces mutations in DRD2 that inhibit dopamine signaling and maintain ghrelin binding, increasing hunger and food consumption. (*Appetite Accomplice: Ghrelin Receptor Alters Dopamine Signaling*, R Smith and A Kern, J Neuron, Jan 2012)
Stress and Leptin

- Cortisol blocks the release of leptin from adipose tissue.

- Leptin stimulates alpha MSH, and inhibits NPY in the hypothalamus at the end of meal, to inhibit hunger and food cravings, initiate metabolic pathways and increase the rate of fat burning.

- Blocking leptin continual foraging for food, a reduction in the rate of fat burning from 92% to 35% and increased cravings in between and after meals.
Stress and Adipocyte Metabolism

- Cortisol and CRH ↑ the rate of lipogenesis following a meal >> disproportionate amount of food stored as fat.

- Cortisol triples insulin release to all grains, starches, fruits, sweets and alcohol.

- Abdominal adipose tissue has 30% more cortisol receptors than adipose tissue in other locations of the body.
Infections cause inflammation, which raises our cortisol level.

Ordinary, everyday stress also raises our cortisol level.

**Insulin resistance**

Cortisol reduces the amount of glucose (blood sugar) that liver and muscle cells can draw out of our bloodstream.

Since our liver and muscle cells can’t take as much glucose out of the blood as they should, glucose and insulin levels rise. This is insulin resistance.

**Metabolic Syndrome**

Insulin resistance increases the levels of fatty acids in our blood.

Some of the extra fatty acids make us more insulin resistant. This starts a vicious cycle that will keep us insulin resistant for months or years after our cortisol levels are corrected. This is metabolic syndrome.

Metabolic syndrome leads to obesity & type 2 diabetes.
## Chronic Stress

<table>
<thead>
<tr>
<th>Reproductive Affects</th>
<th>Metabolic Affects</th>
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<tbody>
<tr>
<td>Decreases GnRH</td>
<td>Alters Ghrelin reception</td>
</tr>
<tr>
<td>Increases GnIH</td>
<td>Inhibits dopamine production and binding</td>
</tr>
<tr>
<td>Alters FSH and LH</td>
<td>Inhibits Irisin</td>
</tr>
<tr>
<td>Alters Est/Prog/test ratio</td>
<td>Increases Leptin resistance</td>
</tr>
<tr>
<td>Increases prolactin</td>
<td>Increases Insulin resistance</td>
</tr>
<tr>
<td>Increases Prostaglandins</td>
<td>Increases lipogenesis and inhibits lipolysis</td>
</tr>
<tr>
<td>Increases fallopian tube spasticity</td>
<td>Increases food cravings</td>
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</tbody>
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Treatment

- Natural supplements
- Diet
- Massage Therapy
- Exercise
- Yoga
- Relaxation Techniques
“That pill they advertise all the time on TV. I’m not sure what it is, but I want it!”
Alpha-S1-Casein Tryptic Hydrolysate (Lactium)

- Bioactive tryptic decapeptide isolated from milk with a specific linking to GABA(A-1) receptor, and not the PBR site.

- PBR, peripheral-type benzodiazepine binding site, is the second BDZ-binding site with a predominantly mitochondrial localization, and accounts for the sedating and groggy side effects of benzodiazepines.

The alpha 1 casein peptide is estimated to be about 10 times more active than diazepam in vivo.

Less side effects due to the partial binding (no PBR binding).

(Characterization of α-casozepeine, a tryptic peptide from bovine αs1-casein with benzodiazepine-like activity. Laurent Miclo* Emmanuel Perrin. The FASEB Journal June 2001)
the sensitivity of the hypothalamus to cortisol. (re-establishes feedback loop).

cortisol and CRH during acute and chronic stress.

Alpha-S1-Casein Tryptic Hydrolysate (Lactium)

- 42 male subjects (DBRC) given 200 mg of casein peptides, 3 times, 12 hours apart, or a skim milk placebo.

- Serum cortisol, BP, and HR were measured at the start, during (IV catheter and BP cuff) and after the “stressors”.

- Significant decrease in BP (avg increase of 15 versus 25) and significant decrease in cortisol (3.39% versus 20.69%) in casein treated group.

Alpha-S1-Casein Tryptic Hydrolysate (Lactium)

- Double-blind, randomized, placebo-controlled, crossover study
- 63 females suffering from a disorder that may be related to stress such as anxiety, sleep problems, and general fatigue randomly allocated to receive either s1-casein hydrolysate or placebo at the dose of 150 mg/day for 30 days
- The 30-day treatment by s1-casein hydrolysate in females with stress-related symptoms reduced their symptoms, particularly in digestion ($P<0.01$), cardiovascular ($P<0.05$), intellectual ($P<0.01$), emotional ($P<0.05$) and social problems ($P<0.05$)

Theanine

- Non protein amino acid extracted from Green Tea that crosses the blood-brain barrier to increase alpha waves.

- Randomised, placebo-controlled, crossover study comparing placebo, 50mg and 200mg of L-theanine showed a dose dependant increase in the alpha frequency band (8-13Hz) of the (EEG) across parietal and occipital sites after approximately 40min

- (L-theanine, a natural constituent in tea, and its effect on mental state, Anna C Nobre PhD2 Asia Pac J Clin Nutr 2008;17 (S1):167-168)
Animal neurochemistry studies suggest that L-theanine increases brain serotonin, dopamine, GABA levels and has an antagonistic effect on AMPA, Kainate and NMDA receptors.

Behavioural studies in animals suggest improvement in learning and memory.

GABA

- Gamma Amino Butyric Acid.

- Stress inhibitory neuromodulator in hypothalamus and posterior amygdala nuclei, and a stress excitatory neuromodulator in medial and cortical amygdala nuclei.

- GABA supplementation reduces stress-induced glucocorticoid secretion in both rats and humans.

- GABA increases alpha and decreases beta waves.

  \[\text{(Neurocircuitry of stress: central control of the HPA axis: J Herman and W Cullinan, Neurosci (1997) 20, 78-84)}\]
Main active ingredients are magnolol, honokiol, beta-eudesmol and bornyl acetate all possess anxiolytic properties.

K+ added to bovine adrenal cells as a stressor (depolarization of the cell membrane) and catecholamine production monitored. All 4 ingredients were added. Catecholamine inhibition was seen, with honokiol and bornyl acetate producing the largest inhibitions.

(Effects of extracts and ingredients isolated from Magnolia obovota thunberg on catecholamine secretion from bovine adrenal chromaffin cells. Tachikawa et al, Biochem Pharmacol 2000;60(3):433-4)
Magnolia

- Decreases the excess release of cortisol, adrenaline and noradrenaline from the adrenal glands.

- Has been shown to increase DHEA in those who are deficient.

- Precaution in hormonally related cancers???
Schizandra Chinesis

- Adaptogenic herb that decreases the release of cortisol and helps regulate glucose levels.

- 34 rats were placed into 1 of 3 gps, non stress (a), stress (b) and schizandra supplemented stress grp (c).

- For 10 days they were put under physical (HIT and floating) stressors, and psychological distress and then measured serum testosterone, cortisol, LH and glucose.
Both glucose and cortisol levels were significantly reduced in Group C in comparison with B. Testosterone levels were reduced in Group B, but not in A or C. No significant differences were found in serum LH levels among the three groups. Study shows GC reducing affect of Schizandra but with no direct known mechanism of action.

No studies showing efficacy in humans.

Withania Somnifera is an adaptogenic herb.

Male rats given random foot shocks for 21 days, then put into 4 gps: 25mg or 50mg or 100 mg/kg of body weight of WS 1 hour before foot shocks, or given no supplementation.

Foot shock induced significant hyperglycaemia, glucose intolerance, increase cortisol, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression.

All these effects were attenuated in a dose dependant manner by WS supplementation.

Withania Somnifera - Ashwagandha

- WS mimics GABA like effects and has been shown to promote the new formation of dendrites and neural repair.  

- Prevents gastric ulcers and decreases joint inflammation – although exact mechanism is not known.

LH secretion and the luteal phase.

This stimulates increased formation of the corpus luteum, which in turn stimulates progesterone.

Studies show that 86% of women taking Vitex have increased progesterone levels.

(Romm, Aviva. Botanical Medicine for Women’s Health. 2010)
(The Genus Vitex – A review Pharmacognosy Reviews 2013, 7(14);188-198)
Dioscorea or Wild Yam is a phytosterol that increases progesterone activity without increasing progesterone itself.

Diosgenin, is a phytoestrogen that gets converted into progesterone in lab, but not in the body, and yet still has several properties of bioidentical progesterone such as anti-spasmotic, anti-inflammatory and antiproliferative in vivo.

Black Cohosh

- Black Cohosh or Cimicifuga Racemosa helps to balance estrogen and serotonin levels.

- Used in hormonal imbalanced induced hot flashes, insomnia and depression. (Warneke, G; Influencing of menopausal complaints with a phytodrug: Successful Therapy with Cimicifuga. Medizinische Welt 36:871-874 1985)

- BC appears to function like estradiol in the body, but not in the uterus or breast, increasing its safety against cancer.

Isoflavones

- Soy isoflavones have been shown in some clinical studies to be significantly more effective than placebo in reducing the frequency and severity of hot flashes.
  - (Taku et al, Menopause 2012, 19(7):776-790)

- There is strong evidence that soy isoflavones are safe to use. The North American Menopause Society recommends ongoing study.
Isoflavones

- Pueraria lombata (kudzu root) induces cytochrome P450 enzymes 1A1 and 1A2 which push estrogen through the 2-hydroxylation pathway.
  

- Trifolium pratense (red clover) and soy isoflavones change the way estrogens are metabolised and increase the C-2 hydroxyestrone over the C-16, altering the ratio.
  
Exercise

- 30-45 minutes of cardiovascular work – NO MORE!
- 30 minutes of weight training
- Deep breathing and stretching afterwards.
- Choose a type of exercise that you enjoy.
Relaxation Techniques

- Yoga, pilates, and dancing.
- Reflexology
- Shiatsu
- Acupuncture
- Deep breathing, meditation and relaxation tapes.
"I'm learning how to relax, doctor—but I want to relax better and faster! I WANT TO BE ON THE CUTTING EDGE OF RELAXATION!"
“This is my relaxation tape—it’s the sound of ocean waves crashing onto the shore, snatching my boss’s body off his beach chair and carrying him out to sea.”
Clinical Experience

Select case studies
Case Study 1

- 35yr old female, 2 miscarriages in the past year at 7 and 9 weeks, trying for last 2 yrs.
- Follicular levels: LH (3), FSH (4), progesterone (3nmol/L), DHEA-S (7.8 umol/L), prolactin (25ug/L)
- OBP was +33, reported anxiety and palpitations, scanty but regular periods.
- Sereniten Plus (combination of Lactium casein decapptide L-Theanine and Vitamin D) 2 BID for 2 wks, then 1 BID with Adrenomend (herbal extract blend containing Schisandra chinensis and magnolia) 1 BID, Progestomend (herbal combination including and Dioscorea villosa and Vitex) 2 BID, EFA’s 3000 mg/day, coQ10 200 mg a day
- 3 months later pregnant, carried to full term.
Case Study 2

- 22 year old female with cystic acne on the chin and back, smaller comodones over the nose that worsened with stress and slightly before her period.
- She woke between 3-4 am most nights, ate a primal style diet, exercised regularly.
- Testosterone (2.1pmol/L) and estradiol (1400) were high, ESR (28), OBP =+41.
- Sereniten Plus (combination of Lactium casein decapeptide L-Theanine and Vitamin D) 2 BID, a herbal blend 2 BID, Schizandra 550 mg BID, melatonin 6 mg PR, HA 40 mg
- 3 weeks later 40% reduction in acne, sleeping through the night.
- 2 months later all acne cleared, less emotional PMS and easier periods.
58 yr old post menopausal (7 years ago) female with hot flashes, sweats and racing thought at 2:30 am.

Husband was dx with cancer 6 weeks before the onset of symptoms.

Sereniten Plus (combination of Lactium casein decapeptide, L-Theanine and Vitamin D) 1 BID, GABA 500 mg BID, Black Cohosh 40 mg BID, L-theanine 150 mg on waking.

48 hours later - less racing thoughts, 3 weeks later sweats and flashes reduced by 65%, 5 weeks later completely gone and sleeping through the night.
Case Study 4

- 42 yr old female, CEO of a large company, mother of 2 and travelled a great deal for work.
- Lost her period 8 months ago, exhausted all the time, lightheaded on standing or quick movements, central weight gain with no change in diet.
- Sereniten Plus (combination of Lactium casein decapeptide L-Theanine and Vitamin D) 2 BID, Adrenoplus (containing adrenal and adrenal cortex extract) 1 BID, melatonin 3 mg reg and 3 mg PR before bed.
- 3 weeks later lightheadedness was gone, and energy 50% better.
- 6 weeks later period returned, energy back to normal and had dropped 6 of the 9lbs.
Supplemental Summary

- Reset and maintain the HPA axis
  - Lactium and L-theanine
- Maintain adrenal health
  - Magnolia, GABA, Schizandra, Ashwaganda, Adrenomend, Adrenloplus
- Support reproductive hormones
  - Vitex, Black Cohosh, I3C, DIM, Dioscorea, Isoflavones, Estromend, Estroquench, Progestomend, Testoquench for women
- Support Metabolic pathways
- L-Carnosine and L-Tyrosine
Balance

☐ Balance is key to management of the weight lost, disease and control of stress hormones.

☐ Never eliminate anything forever (unless allergic), especially chocolate!

☐ May require temporary avoidance of a specific food to retrain the metabolism and “de-sensitize” the body to those foods or short term use of supplements.