Supplementing decisions

• Remember children’s adrenal glands have a zone in the cortex that is at rest (zona reticularis)
• Hence children will not produce DHEA and one should never supplement a child because DHEA can promote early puberty and would cause the epiphyseal plates to fuse ...which can lead to reduced height.
The adrenals are resilient and will usually re-calibrate and return individuals to optimal functioning (if possible) **within 2 years.**
**Stress Reducing Techniques**

Rapidly turn off overactive stress hormone release

**Exercise**
- Aerobic/Cardio 150min/week
- Weight-bearing
- Daily Stretching

**RELAX**
- Breathe deep and often
- Do something relaxing for 20 minutes DAILY!

**Sleep** - 8 hours of straight sleep nightly
Dietary guidelines

Prevent stress hormone surges associated with missing meals, comfort food cravings and overeating

Smart Eating Tips to Break the Stress Cycle

1. Eat a protein-rich breakfast every morning.
2. Low-glycemic, whole foods
3. Small, frequent meals
4. Finding new “comfort” foods
5. Eliminate refined sugars, artificial sweeteners and trans-fats

• 2007: $25 billion dollars were spent on antidepressants and antipsychotics

• 2009: US doctors wrote more psychiatric prescriptions than there were people in the USA

The rate of antidepressant use in the United States has increased nearly 400% over the last two decades.

Currently:

- 11% of Americans (over age 12) take antidepressant medication
- 23% of women aged 40-59 take antidepressants (more than any other age-sex group)


Relationship of the Endocrine Organs

Solid lines = Stimulates
Dotted lines = Inhibits
Numerous chief complaints/many functional conditions...
Where to begin?

• Treat root causes:
  • Neuroendocrine imbalances
    • Hormonal
    • Adrenal
    • Neurotransmitter
Neurotransmitters

Neurotransmitters are chemical messengers that regulate many physical and emotional processes including movement, stress response, cognition, emotions, energy, cravings, pain and more.
Medicalinsider.com
We test these basic Neurotransmitters:

- Serotonin
- Dopamine
- Norepinephrine
- Epinephrine
- GABA
- Glutamate
Neurotransmitter testing provides successful assessment and treatment interventions for:

- Anxiety
- Depression
- Fatigue
- Insomnia
- Addictions
- Weight loss
- Cravings and poor impulse control
- Cognitive impairment (poor memory, lack of mental clarity, inability to focus)
- Chronic pain
- Headaches
- IBS
Neurotransmitter pathways

Tryptophan
- Iron
- MTHF
- B6
- Vitamin C
- Vitamin D
  → 5-Hydroxytryptophan (5-HTP)
    - Tyrosine hydroxylase

Serotonin
- 5-HTP
  → TBHP
  - aromatic amino acid decarboxylase
  → N-acetyl transferase

Acetylserotonin
- SAMe
  → hydroxyindole-β-methyltransferase

Melatonin
- Glutamine
  → glutamate decarboxylase (GAD)

α-ketoglutarate
  → glutamate

Glutamate
glutaminase

GABA

KEY
PSF (pyridoxal 5-phosphate)-activated form of vitamin B6
MTHF = (methyltetrahydrofolate), active form of folate. MTHF is required for the production of tetrahydrobiopterin, a cofactor in this conversion.
MAO = monoamine oxidase
COMT = catechol-O-methyl transferase
SAMe = endogenous levels can be supported with Mg, MTHF, and methylcobalamin supplementation
Cofactors = Enzymes =
Treatment for neurotransmitter and Adrenal imbalances

• After evaluation, the best course of action is to target the imbalances with precursors and nutrients which remedy the problem.
  • Amino acids
  • Co-factors
  • Nervine and adaptogenic herbs
Amino acid precursors

- Taken on empty stomach at least 30 minutes away from food
- Cross the blood brain barrier and interact with HPA axis and neurotransmitter regulation

<table>
<thead>
<tr>
<th>Tryptophan</th>
<th>5-HTP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosine</td>
<td>Glutamine</td>
</tr>
<tr>
<td>GABA</td>
<td>L-theanine</td>
</tr>
<tr>
<td>Taurine</td>
<td></td>
</tr>
</tbody>
</table>

Mucuna pruriens (200-800 mg qd)

- Cowhage (mucuna pruriens) seeds have been used in traditional Ayurvedic medicine
- Contains small amounts of L-dopa, a precursor to dopamine
  - The bean portion of the plant has 3-6% L-dopa
  - Inner layer (endocarp) is 5.3% L-dopa
- Proven to lessen symptoms of Parkinson’s disease

St. John’s Wort

- Equivalent relief of depressive symptoms in mild/moderate depression compared to SSRIs.
- Clinical guidelines from the American College of Physicians-American Society of Internal Medicine suggest that St. John’s Wort can be considered an option along with antidepressant medications for short-term treatment of mild depression.
- Standard dose 300 mg tid.
- Caution: SJW causes many drug interactions. (Especially CYP P450 2C19 and 3A4)

Cofactors

• Cofactors are substances essential for the activity of an enzyme. For example, the conversion of dopamine to norepinephrine is driven by the enzyme dopamine b-hydroxylase, which requires vitamin C, copper and vitamin B3 (niacin) to fuel the conversion.

• Cofactors are often vitamins or minerals. B vitamins are especially important in neurotransmitter pathways.
Cofactors

- Clinically, cofactors become important when conversion is slow.
- For example, if norepinephrine is elevated, and epinephrine levels are low, there is likely an issue with the enzyme phenylethanolamine N-methyltransferase (PNMT). This will result in the N/E ratio being elevated.
- The cofactors in this conversion are SAMe, Mg and cortisol.
- Treatments might include supplementing with SAMe or Mg, and addressing adrenal gland dysfunction.
Adaptogenic herbs

- Adaptogens do exactly what their name would suggest...help the body resist and adapt to stress. To be officially called an adaptogen, a compound must be able to enhance the body’s physiology without any adverse side effects.
- They promote a normalizing action, tonifying adrenal glands and improving the body’s ability to handle stress.
- Adaptogens promote balance in the whole adrenal gland: the adrenal cortex which secretes cortisol, as well as the adrenal medulla which secretes norepinephrine, epinephrine, and a small amount of dopamine. Common adaptogens include:

<table>
<thead>
<tr>
<th>Rhodiola</th>
<th>Ginseng</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licorice</td>
<td>Ashwaganda</td>
</tr>
<tr>
<td>Eleutheroococcus</td>
<td>Astragalus</td>
</tr>
<tr>
<td>Gingko</td>
<td>Schizandra</td>
</tr>
</tbody>
</table>
Nervines

Nervine herbs provide a restoring and balancing action to the nervous system. Practitioners often prescribe sedative nervine herbs in the form of teas, tinctures, extracts or capsules to help patients cope with stress, anxiety, insomnia, and mild depression. Some common nervines include:

<table>
<thead>
<tr>
<th>Valerian</th>
<th>Hops</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passion flower</td>
<td>California poppy</td>
</tr>
<tr>
<td>Chamomile</td>
<td>Lavender</td>
</tr>
<tr>
<td>Lemon balm</td>
<td>Kava</td>
</tr>
<tr>
<td>Oats</td>
<td></td>
</tr>
</tbody>
</table>
Methylation support

• Possible supplements to support methylation include:
  • L-Methylfolate (NOT folic acid. It is recommended to avoid folic acid when a MTHFR defect is present, as the patient is unable to convert folic acid to methylfolate)
  • Methylcobalamin
  • Pyridoxal-5-phosphate
  • SAMe
L-theanine

- As we discuss treatments for high and low neurotransmitter levels, you will see that L-theanine is repeatedly recommended.
- Many functions
  - Acts as a GABA agonist (neuroinhibitory and parasympathetic)
  - Antagonistic effects on glutamate receptors
  - Can modulate serotonin, GABA and dopamine levels

L-theanine (100-500 mg bid)

- Amino acid found in green tea
- Produces a calming effect in the brain (boosts alpha waves)
- Helps modulate mood; creates a sense of well being
- Reduces mental and physical stress responses
- Improves cognition
- When combined with caffeine, has been shown to increase focus and attention. “Mindful alertness.”
- Recommend divided dosing as L-theanine has a short ½ life (4-6 hours)

Vitamin D

Calcitriol activates the gene expression of the enzymes tyrosine hydroxylase and tryptophan hydroxylase (the rate limiting steps in the production of serotonin and the catecholamines)

## Supporting Serotonin

### Low serotonin
- Tryptophan
  - 500-2,000 mg
- 5 HTP
  - 50-600 mg
- L-theanine
  - 100-500 mg bid
- Cofactors
  - Iron 25-50 mg (citrate or bisglycinate)
  - P5P 50-200 mg
  - Vitamin C 4,000-6,000 mg
  - Vitamin D 2,000-10,000 IU
  - MTHF

### High serotonin
- L-theanine
  - 100-500 mg bid
- Co-factors (to support metabolism and conversion)
  - Vitamin B2: 50 mg
  - Vitamin B3: 50 mg
  - Iron: 25-50 mg
  - SAMe: 250-500 mg

### Diagram

```
tryptophan hydroxylase

5-Hydroxytryptophan (5-HTP)

N-acetyltransferase

Acetylserotonin

S-adenosylmethionine (SAMe)

Melatonin
```
Dopamine

- Enhances the reward response, especially if the reward is perceived as greater than expected.
- Stimulates pleasure centers
- Enables us not only to see rewards, but to take action to move towards them
- Drive and motivation.
- Locomotion and coordination of movement
- Motivation
- Behavior and cognition
- Sleep
- Mood
- Attention and learning
- Inhibition of prolactin production (involved in lactation)

**Dopamine Deficit**

- Parkinson-like Symptoms
  - slow reaction time
  - anergia

- Anhedonia
  - "pleasure center" dysfunction

**Serotonin Deficit**

- OCD-like Symptoms
  - obsessive thoughts
  - compulsive behaviors

- Anhedonia
  - suicide/aggression
  - susceptibility to "cue triggers"

**Depression & Craving**

- Decreased synaptic DA
- Altered DA transporter function
- Postsynaptic receptor changes

- Decreased synaptic 5-HT
- Decreased 5-HT cell activity
- Decreased synaptic DA
Supporting Dopamine

**Low dopamine**
- N-acetyl l-tyrosine
  - 250-1,500 mg
- Macuna pruriens
  - 200-800 mg
- L-theanine
  - 100-500 mg bid
- Vitamin D
  - 1,000-10,000 IU
- Cofactors
  - Vitamin C 4-6 gm
  - Iron 25-50 mg
  - Vitamin B3 50 mg
  - P5P 50-200 mg
  - MTHF
  - Vitamin D 2,000-10,000 IU

**High dopamine**
- L-theanine
  - 100-500 mg bid
- Co-factors (to support MAO/COMT)
  - Vitamin B2: 50 mg
  - Vitamin B3: 50 mg
  - Iron: 25-50 mg
  - SAMe: 250-500 mg
- Co-factors (if Norepi low or low range)
  - Vitamin C: 4,000-6,000 mg
  - Copper: 0.5-1 mg
  - Vitamin B3: 50 mg
Norepinephrine and epinephrine

- Regulate flight or flight response
- Control attention and arousal
- Regulate heart rate and blood pressure
- Release glucose from energy stores
Excess levels of norepinephrine and epinephrine may lead to...

- **Physical symptoms**
  - Irritability
  - Anxiety
  - Agitation
  - Sleeplessness
  - Inability to relax
  - Lack of mental focus

- **Mood/Cognitive**
  - Palpitations
  - Tachycardia
  - Arrhythmia
  - Headache
  - Restlessness
  - Cold hands
  - Tremor
  - Hypertension
  - Acute pulmonary edema
Supporting Norepinephrine

Low norepinephrine
- N-acetyl l-tyrosine
  - 250-1,500 mg
- Macuna pruriens
  - 200-800 mg
- L-theanine
  - 100-500 mg bid
- Vitamin D
  - 1,000-10,000 IU
- Co-factors
  - Vitamin C: 4-6 gm
  - Copper: 0.5-1 mg
  - Vitamin B3: 50 mg

High norepinephrine
- L-theanine
  - 100-500 mg bid
- Co-factors (to support MAO/COMT)
  - Vitamin B2: 50 mg
  - Vitamin B3: 50 mg
  - Iron: 25-50 mg
  - SAMe: 250-500 mg
- Co-factors (if epi low or low range)
  - SAMe: 250-500 mg
  - Address hypoadrenia
Supporting Epinephrine

Low epinephrine
- N-acetyl l-tyrosine
  - 250-1,500 mg
- Macuna pruriens
  - 200-800 mg
- L-theanine
  - 100-500 mg bid
- Co-factors
  - Vitamin C 4-6 gm
  - SAMe 250-500 mg
  - Magnesium 150-500 mg
- Must address adrenal dysfunction (hypoadrenia)

High epinephrine
- L-theanine
  - 100-500 mg bid
- Co-factors (to support MAO/COMT)
  - Vitamin B2: 50 mg
  - Vitamin B3: 50 mg
  - Iron: 25-50 mg
  - SAMe: 250-500 mg
Glutamate

The most common excitatory neurotransmitter in the brain
High/Low

- **High glutamate**
  - Depression
  - Fatigue
  - Brain fog
  - Addiction/dependency
  - Slowed learning

- **Low glutamate**
  - Anxiety
  - Insomnia
  - ADHD/poor concentration
  - Seizure
  - ALS/MS
  - Autism
  - Alzheimer’s
Glutamate

We all know that MSG can increase glutamate levels, but there are many hidden sources of glutamic acid in the foods that we eat

<table>
<thead>
<tr>
<th>Ingredients that ALWAYS contain free glutamic acid</th>
<th>Ingredients that OFTEN contain or produce glutamic acid</th>
<th>Ingredients SUSPECTED of creating glutamic acid in sensitive people</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSG</td>
<td>Bouillon and broth</td>
<td>Corn starch, corn syrup</td>
</tr>
<tr>
<td>Yeast extract</td>
<td>Any “flavors” or “flavoring”</td>
<td>Dextrose</td>
</tr>
<tr>
<td>Anything “hydrolyzed”</td>
<td>Barley malt or malt extract</td>
<td>Rice syrup, Brown rice syrup</td>
</tr>
<tr>
<td>Textured protein (anything “protein”)</td>
<td>Soy sauce</td>
<td>Reduced fat milk (skim, 1%, 2%)</td>
</tr>
<tr>
<td>Soy or whey protein</td>
<td>Seasonings</td>
<td>Most things low fat or no fat</td>
</tr>
<tr>
<td>Gelatin</td>
<td>Carrageenan</td>
<td>Anything vitamin enriched</td>
</tr>
</tbody>
</table>
Supporting Glutamate

**Low glutamate**
- L-glutamine
  - 1,000-3,000 mg

**High glutamate**
- L-theanine
  - 100-500 mg bid
- Taurine (reduces glutamate toxicity)
  - 500-1,500 mg
- Co-Factors (to support metabolism and conversion)
  - Vitamin B3: 50mg
  - P5P: 50-200 mg
- Magnesium (reduces glutamate toxicity)
  - 150-500 mg
GABA

• The major inhibitory neurotransmitter in the brain
• Relaxing and calming
• Synthesized from glutamate and P5P
• Predominant receptor
  • GABA A
    • Utilized by neuroactive drugs like benzodiazepines
    • Often used to treat anxiety, seizures, act as sedative or muscle relaxant
Addressing GABA

**Low GABA**
- L-theanine
  - 100-500 mg bid
- GABA
  - 500-2,000 mg
- Phenibut
  - 250-1,000 mg bid
- Glutamine
  - 1,000-3,000 mg
- Co-factors
  - P5P: 50-200 mg

**High GABA**
- L-theanine
  - 100-500 mg bid
Sample NT test report

<table>
<thead>
<tr>
<th>Neurotransmitter Test</th>
<th>Result</th>
<th>Units</th>
<th>L</th>
<th>WR</th>
<th>H</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td>23.37</td>
<td>μg/gCr</td>
<td></td>
<td></td>
<td></td>
<td>74.13 - 111.19</td>
</tr>
<tr>
<td>GABA</td>
<td>0.01</td>
<td>μMol/gCr</td>
<td></td>
<td></td>
<td></td>
<td>2.76 - 4.14</td>
</tr>
<tr>
<td>Dopamine</td>
<td>103.37</td>
<td>μg/gCr</td>
<td></td>
<td></td>
<td></td>
<td>139.1 - 208.7</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>85.49</td>
<td>μg/gCr</td>
<td></td>
<td></td>
<td></td>
<td>28.07 - 42.11</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>18.30</td>
<td>μg/gCr</td>
<td></td>
<td></td>
<td></td>
<td>3.36 - 5.06</td>
</tr>
<tr>
<td>Glutamate</td>
<td>70.81</td>
<td>μMol/gCr</td>
<td></td>
<td></td>
<td></td>
<td>60.69 - 91.03</td>
</tr>
<tr>
<td>N/E Ratio</td>
<td>4.67</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;10.0</td>
</tr>
<tr>
<td>Creatinine</td>
<td>102.58</td>
<td>mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>1.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient Info:
Jane Sample NT
Age: 52  Gender: F
Menopausal Status:
Hysterectomy (Ovaries Not Removed)
9876 SW Balanced St
Billings, MO 64515

Sample Collection
Neurotransmitter
Date/Time
02/25/2012 0735
Wake Up Time
0700
Samples Arrived
02/29/2012
Results Reported
03/03/2012
Additional Monitoring

Women
- Clinical observation
- Saliva or Blood levels
  - Testosterone
  - Total Estrogen
  - Progesterone
  - Sex Hormone Binding Globulin
  - DHEA-S
  - Cortisol x 4 (saliva)
  - Cholesterol
  - Thyroid Panel
  - Vitamin D-25-OH

Men
- Clinical Observation
- Saliva or Blood Levels
  - Total and Free Testosterone
  - Estradiol
  - DHEA-S
  - Cortisol x 4 (saliva)
  - PSA
  - Cholesterol
  - Prolactin
  - Thyroid Panel
  - Vitamin D-25-OH
Importance of Supplement Quality

- GMP Certified
- Registered with the FDA
- 3rd Party Analysis
- Testing
  - Dissolution
  - Disintegration
  - Mass Spectroscopy
  - Liquid Chromatography
What are patients Reading?

- Dr. David Brownstein “The Miracle of Natural Hormones”
- Dr. John Mulhall, “Saving Your Sex Life”
- Dr. James Wilson, “Adrenal Fatigue”
- Pam Smith, M.D., “HRT: The Answers” and “What you Must Know about Women’s Hormones”
- Shawn Talbott, Ph.D., “The Cortisol Connection”
- Shawn Talbott, Ph.D., “The Cortisol Connection Diet”
- Billie Jay Sahley, Ph.D., “GABA The Anxiety Amino Acid”
- Michael Murray, N.D., “Glandular Extracts”
- C. Norman Shealy, M.D., Ph.D., “DHEA, The Youth and Health Hormone”
- Barbara Wexler, MPH., “Vitamin D”
- Bob Cooley, “The Genius of Flexibility”
How Do I Get Started?

- Read, research, and listen to your patients.
- Have your patients Complete a Patient Evaluation Form
- Have your patients call to schedule a personal consultation and/or Receive a Therapy recommendation
- Call/discuss with their health care provider.
- Prescription/supplements filled by Your Pharmacy.
- Practitioners—Collaborate with YOUR compounding Pharmacist
Obtaining CE

If you would like to receive continuing education credit for this activity, please visit:
http://pcca.cds.pesgce.com