HAPPY HORMONES
PSYCHIATRY AND HORMONAL BALANCE

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*Dr. Bongiorno is a retained as a consultant for Douglas Laboratories.
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Suicide Deaths in The United States Continue to Increase

(Years 2000-2016)
Suicide Deaths Climb Dramatically in U.S., Nearly Double for Women

Experts say that the increase in suicides is related to a combination of factors, including undiagnosed mental illness.

By Rebecca Greenberg

Suicide rates in the United States have been increasing in recent years. According to data released by the Centers for Disease Control and Prevention (CDC), the findings, which were released last month in two reports, coincided with the suicides of celebrities Kate Spade and Anthony Bourdain.

One of the issues that we are grappling with in this country and in many other countries is suicide prevention. The CDC's report indicates that roughly 45,000 Americans died by suicide in 2017. Suicide became the leading cause of death among those aged 10 to 34 and the second leading cause among those aged 35 to 44. According to the report, the age-adjusted suicide rate among those aged 10 to 34 increased by 35% from 2015 to 2016.

The reports, released on June 7 and June 14, examined state and national suicide trends, respectively.

Holly Hedegaard, M.D., and colleagues from the CDC's National Center for Health Statistics published the final report indicating that roughly 45,000 Americans died by suicide in 2017. Suicide became the leading cause of death among those aged 10 to 34 and the second leading cause among those aged 35 to 44. According to the report, the age-adjusted suicide rate among those aged 10 to 34 increased by 35% from 2015 to 2016.

A PA member Patrice Harris, M.D., M.A., a former APA trustee and AMA board member, was elected president-elect of the American Psychiatric Association's House of Delegates meeting last month.

"I believe our American Psychiatric Association has well dedicated itself to the mental health care of our nation's people, and it is a privilege to serve as president-elect of the APA. Psychologists have an important role to play in helping to shape the future of mental health care in our country," said Harris.
• The number of people taking antidepressants has increased by 65 percent (between 1999 and 2014) according to the CDC (NCHS Data Brief No. 283, August 2017)
• 1 in 8 people are using these medications
• In the same time period, the annual rate of suicide increased from 10.5 to 13 people out of 100,000 – a 24% increase, which was the highest in almost three decades. (CDC - NCHS Data Brief No. 241, April 2016)
Testing testes

Arnold A Berthold
(1803-1861)

- In one of the first endocrine experiments ever recorded, Professor Arnold A. Berthold of Gottingen did a series of tests on roosters in 1849 while he was curator of the local zoo.
Hormone-specific psychiatric disorders: do they exist?

Margaret Altemus

Margaret Altemus, Department of Psychiatry, Weill Medical College, Cornell University, Box 244, 1300 York Ave, New York, NY 10065, USA, maltemus@med.cornell.edu; *Corresponding author.
Today’s Plan

• Hormones and Mental Health
• Key Ideas
• Testing
• Natural (Non Hormonal) Treatments
• Bio-identical Hormones
Hormone Classifications

**genomic hormones:** adrenal, reproductive and thyroid hormones

**amino acid chain hormones:** hypothalamic releasing hormones, pituitary trophic hormones, insulin, glucagon, IGF-I/II

**structurally modified amino acids:** neurotransmitters, neuropeptides, cytokines, endothelin, bradykinin, local acting (NO, eicosanoids)

- **biogenic amines:** norepinephrine, epinephrine, serotonin, dopamine and phenylethylamine.
FIGURE 11.1 Metabolism of select steroids.
Major Players

- Estrogen
- Progesterone
- Prolactin
- Oxytocin
- Testosterone
- DHEA
- Thyroid Hormone
- Cortisol
- Melatonin
Estrogen

• E1 (estrone):
  • reduces brain survival, dominant in Premarin
  • Benefits cardiovascular system $\rightarrow$ NO
  • oral hormones $\rightarrow$ estrone

• E2 (estradiol):
  • most associated with brain receptor activity and mood
  • Affects all NT’s, but serotonin preferentially

• E3 (estriol):
  • Can be anti-inflammatory, immune suppressive
  • Dominant in pregnancy
  • Agonizes B receptor in vagina (topical works)
Estrogen

- **Estrogens:**
  - ↓ MAOa → ↑ serotonin, ↑ DA production, melatonin
  - ↑ MAOb → ↑ epinephrine

- **Low estrogen:** → ↑ MAO activity → ↓ NT’s

- **Anxiolytic** via endogenous cannabinoids / anandamide

- **Highest density of receptors:** amygdala, hippocampus, hypothalamus

- **Men:** 6 – 8 times as much brain estrogen as women

- **Increases BDNF**
Estrogen sx$s

- **Estrogen excess:**
  - Angry, irritable, anxiety
  - Breast tenderness
  - Ovarian cysts, endometriosis, fibroids
  - Acne
  - Fibrinogen activation
  - Digestive issues

- **Estrogen deficiency:**
  - Angry, irritable, anxiety
  - Surgical menopause → OCD like behaviors
  - Vaginal dryness
  - Skin aging
  - Digestive issues
Microbiome Imbalance and Estrogen:

- **Dysbiosis** → ↑ beta-glucuronidase activity → reabsorption of excess estrogens
- **Candida** waste products → false estrogen → tricks the body into thinking it has produced adequate levels → body reduces estrogen
- **High estrogen levels** → increase vaginal candidiasis
- **Birth control pills / estrogen replacement** → greater risk of developing candida


Raising estrogen for better mood?


Effect of estrogen replacement therapy on symptoms of depression and anxiety in non-depressive menopausal women: a randomized double-blind, controlled study.

Demetrio FN¹, Rennó J Jr, Gianfaldoni A, Gonçalves M, Halbe HW, Filho AH, Gorenstein C.

Author information
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- non-depressive, hysterectomized, postmenopausal women
- 6 cycles with ERT
- no benefit: depression, anxiety improved similarly in active and placebo groups
Moderating Estrogen

- Caloric Restriction
- Exercise
- Weight loss
- **Protein:** Increases overall cytochrome P450 activity including cytochrome P450-1A2 which detoxifies estradiol
- **Lower saturated fat:** Promote 2-OH hydroxylation pathways
- **Fiber** → treating constipation
- **Liver support**‡
- **Calcium D Glucarate:** detoxification of estrogens by upregulating Phase I and Phase II enzymes‡
- **DIM / I3C:** Promote C-2 hydroxylation over C-16α and C-4 hydroxylation of estrogens‡

‡These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
• 25mg per day (versus 150mg – linked to endometrial hyperplasia) or placebo
• 87 women x 2 months
• Significantly alleviated symptoms of depression and insomnia in Japanese middle-aged women
## SOY FOOD ISOFLAVONE CONTENT

<table>
<thead>
<tr>
<th>Soy Food</th>
<th>Amount</th>
<th>Isoflavones (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Textured soy protein granules</td>
<td>¼ cup</td>
<td>62</td>
</tr>
<tr>
<td>Roasted soy nuts</td>
<td>¼ cup</td>
<td>60</td>
</tr>
<tr>
<td>Tofu (low fat and reg.)</td>
<td>½ cup</td>
<td>35</td>
</tr>
<tr>
<td>Tempeh</td>
<td>½ cup</td>
<td>35</td>
</tr>
<tr>
<td>Soy beverage powder</td>
<td>1-2 scoops</td>
<td>25 - 75 (varies with manufacturer)</td>
</tr>
<tr>
<td>Regular Soy Milk</td>
<td>1 cup</td>
<td>30</td>
</tr>
<tr>
<td>Low fat Soy Milk</td>
<td>1 cup</td>
<td>20mg</td>
</tr>
<tr>
<td>Roasted soy butter</td>
<td>2 tbsp</td>
<td>17</td>
</tr>
<tr>
<td>Cooked soybeans</td>
<td>½ cup</td>
<td>150</td>
</tr>
</tbody>
</table>

For daily diet, look for 50 to 80mg per day.
Progesterone:

- $\uparrow$ MAO type A $\rightarrow$ $\downarrow$ serotonin
- $\downarrow$ MAO type B $\rightarrow$ $\uparrow$ epinephrine

Allopregnanolone:

- regulator of GABA-A receptor (alcohol and benzodiazepines)
- $\downarrow$ serotonin availability (estrogen blocker)
- $\uparrow$ MAO activity $\rightarrow$ $\downarrow$ NT’s
- ($\uparrow$ cort $\rightarrow$ $\downarrow$ progesterone)
The neurosteroids allopregnanolone and dehydroepiandrosterone modulate resting-state amygdala connectivity.

Sripada RK\(^1\), Welsh RC, Marx CE, Liberzon I.
Low Progesterone sxs

- Overwhelm
- Intrusive, obsessive thoughts that **patient realizes** is irrational
- High estrogen symptoms
- Premenstrual anxiety, post partum anxiety
- Loss of lush and thick hair
- Hx of endometriosis or fibroids
- Low allopregnanolone → ANXIETY
Allergic to progesterone?

Sex hormone-sensitive gene complex linked to premenstrual mood disorder

Dysregulated cellular response to estrogen and progesterone suspected.

National Institutes of Health (NIH) researchers have discovered molecular mechanisms that may underlie a woman’s susceptibility to disabling irritability, sadness, and anxiety in the days leading up to her menstrual period. Such premenstrual dysphoric disorder (PMDD) affects 2 to 5 percent of women of reproductive age, whereas less severe premenstrual syndrome (PMS) is much more common.

“We found dysregulated expression in a suspect gene complex which adds to evidence that PMDD is a disorder of cellular response to estrogen and progesterone,” explained Peter Schmidt, M.D., of the NIH’s National Institute of Mental Health, Behavioral Endocrinology Branch. “Learning more about the role of this gene complex holds hope for improved treatment of such prevalent reproductive endocrine-related mood disorders.”

Schmidt, David Goldman, M.D., of the NIH’s National Institute on Alcohol Abuse and Alcoholism, and colleagues, report on their findings January 3.
Allergic to progesterone?

“PMDD is a disorder of cellular response to estrogen and progesterone”

“it establishes that women with PMDD have an intrinsic difference in their molecular apparatus for response to sex hormones – not just emotional behaviors they should be able to voluntarily control.”
Balancing Progesterone‡

- **Stress reduction‡**
- **Bladderwrack** *(fucus)* – supports cycle length, progesterone‡
- **Saffron** – for PMS, mood, relaxation‡
- **Vitex**
  - Supports progesterone and estrogen slightly‡
  - Supports luteinizing and plasma prolactin hormones²‡
- **Progesterone cream** *(natural, paraben free)*
- **Oral micronized progesterone** *hs*

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¹Skibola BMC Comp Alt Med 4 (2004):10
²These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Dehydroepiandrosterone - DHEA

- Inversely correlated with mood
- Low levels: higher cortisol SXS
- Supplementation: supports BDNF, 5-HT(2A) receptor expression in amygdala¹‡

- How to support DHEA levels
  - Work on stress
  - Address cortisol levels
  - DHEA supplementation ‡


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• High: aggression, impulsivity, compulsive, paranoia

• Mood benefits may be d/t ↑ estrogen in women

• ↑ insulin → ↑ T

• ↑ T → ↑ MAO, ↓ COMT, ↑ PMNT
Low Testosterone

- Mood swings, flat mood, anx
- Fatigue and depression
- Trouble staying asleep
- Can’t gain muscle
- Truncal fat
- Low libido

(Davis 2002) and men(Carnahan and Perry, 2004)
Supporting Testosterone

- Sleep
- Exercise
- DHEA
- Testosterone replacement
Testosterone reduces unconscious fear but not consciously experienced anxiety: implications for the disorders of fear and anxiety.

van Honk J¹, Peper JS, Schutter DJ.

Testosterone administration in 15 females reported reductions in unconscious fears in a placebo-controlled, double-blind crossover trial.

“the habitual vigilant emotional response to the masked fearful face observed in the placebo condition was significantly reduced after testosterone was administered, while the self-reported measures of anxiety remained unaffected.”
Supporting Testosterone‡

- Sleep
- Exercise
- Vitamin D
- TestoGain‡

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Thyroid Hormone

- Thyroid → affects estrogen utilization
- Excess thyroid → ↓ cortisol fxn
- ↓ cortisol → ↓ thyroid fxn (adrenal fatigue = thyroid fatigue?)
- Hypothyroidism and ↑CRP → ↑’s depression
- Progesterone supports thyroid receptor fxn
- Blood sugar regulation affects TBG fxn
- Caloric restriction: ↓ ‘s T3

Addressing the thyroid

To support thyroid hormone production:

- **Vitamin D** helps production‡
- **Selenium**: conversion of the thyroid hormone thyroxine (T4) to its more active form tri-iodothyronine (T3). Selenium improved mood and diminished anxiety (Shor-Posner et al., 2003 and Duntas et al., 2003) meat, fish, nuts (especially **Brazil nuts**), and garlic‡
- **Tyrosine‡**
- **Natural thyroid**: Armour/ NaturThroid

To moderate thyroid activity in cases with underlying immunological component

- **Food sensitivities and Gut healing work**
- **Selenium / Brazil Nuts**

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T3 augmentation of SSRI resistant depression

Gebrehiwot Abraham, Roumen Milev, J. Stuart Lawson
Cortisol

- Excess: fears, oversensitivity, foggy thinking
- Deficiency: adrenal fatigue, sound and light sensitivity,
- Dysregulated: tired and wired, day exhausted and can’t sleep, anx/depression mix
- Excess thyroid $\rightarrow \downarrow$ cortisol
Are you suicidal?
Are you suicidal?

Only in the morning.
Balancing cortisol

- Sleep
- Morning sunlight / light box
- “Adrenal supports”
Balancing Cortisol

- Magnolia, Phosphatidylserine
- Adrenal Glandular
- AM Licorice
- Melatonin

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Prolactin

• *Prolactin* regulator of both emotionality and HPA axis reactivity
  • ↑’s lactation
  • ↓’s ovulation
  • **Prolactin increases with anxiety** (Lennartsson AK 2011 Psychoneuroendocrinology. Nov;36(10):1530-9)
  • Dopamine - ↓’s prolactin

• High prolactin sxs:
  • men: ED, gynecomastia, headache, low T
  • Women: breast d/c, irregular cycles, low muscle mass, vaginal dryness, dyspareunia, acne, facial hair
Prolactin Balancing

• Manage stress
• Address thyroid
• Vitex:‡
  
  1-month study of 34 females
  - 30-40mg/day moderated prolactin in 80% of participants
  - Also supported clinical parameters related to menstrual cycle


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Oxytocin

- Neurotransmitter best associated with feelings of love, meaningful touch, cuddling,
- Reduces hyperactivity of the amygdala and helps block the perception of a threatening environment.
- Social anxiety disorder → dysregulated oxytocin
- Adults who were abused in early-life show lowered levels of oxytocin (Heim et al., 2009)
Intranasal administration of oxytocin has shown to substantially increase in trust among humans (Kosfeld et al., 2005).

Oxytocin preparations are currently being tested as an anti-anxiety drug in several clinical trials.
Natural ways to raise oxytocin

- Released by petting a dog
- Receiving a massage
- Hugging others and physical intimacy
- Cooking aromatic foods and then eating them
- Physical activity and exercise
- Community and social involvement
Melatonin

• Master hormone of circadian rhythm

• Higher levels positively associated with cellular health, sleep

• Endogenous melatonin and progesterone (allopregnolone) act at the GABAa receptor
Testing

Symptoms

Saliva Tests

Blood Tests

Urine
How did the hormone imbalance happen?

- Poor or Lack of Sleep
- Stress
- Foods
- Microbiome Imbalance
- Lack of Exercise
- Environmental Toxins
- Liver Challenges
Balancing Hormones for Mood

1. Primary recommendations
   • Sleep support
   • Stress support
     • Thought Work
     • Mind / Body Work
   • Food
   • Exercise
   • Hydrotherapy / Nature
   • Detoxification

2. Natural supplements

3. BIH Hormonal Supports
Liver Support

- Water
- Remove xenoestrogens
- Elimination diet
- Extra fiber
- Liver herbs
- Castor oil packs
- Colonics
- Sauna
- Meditation
Chinese Medicine and the Liver

• Organ of holding stress - “Qi constraint”
  • Organ of holding anger
• How to help the liver and immune system?

Rx:
1- Start RELAXING
2- Follow your PASSIONS
Natural Hormone Support‡ Hierarchy

- Adrenal
- Cortisol
- Thyroid
- DHEA
- Estrogen
- Testosterone

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Hormonal Replacement
Hormonal Supports

“Hormone replacement therapy should not be considered without a complete understanding of how all of the body’s hormones interact with each other.”
Hormonal Supports

“Hormone replacement therapy should not be considered without a complete understanding of how all of the body’s hormones interact with each other.”
BI hormones vs. Conventional?

Comparison of regimens containing oral micronized progesterone or medroxyprogesterone acetate on quality of life in postmenopausal women: a cross-sectional survey.

Fitzpatrick LA1, Pace C, Wiita B.

176 subjects: 80% experiences improvement in anx and dep sxs when switched from synthetic to oral micronized
BI hormones

Low estrogen:
- Bi-est (E3 (80%) and E2 (20%) of a transdermal cream (0.625 to 5mg)
- Post menopause: day 1-25 or qd

Low progesterone:
- Transdermal (25 - 50mg)
- Oral (50 - 150mg - to enhance GABA)
- Premenstrual: only during luteal phase
- Postmenopausal: day 1 -25 or on all days

DHEA:
- Topical: 5-20mg female
- Topical: 50-75mg male
- PO: 5 - 450mg

Low testosterone:
- Female: 1-5mg qd
- < 50yrs Male: 50 - 100mg
- >50yrs male: 25 -50mg

Pregnenolone: 5 to 25mg po

Notes:
“Dermal fatigue”: best to rotate inside of arms and wrists, back of knees

Transmucosal route: inner labia or anus (not as necessary to rotate)

Monitor: retest 2 - 3 months
Pregnenelone is the top of pile
Post Partum Depression

Original Article
May 2010

Elevated Brain Monoamine Oxidase A Binding in the Early Postpartum Period

Julia Sacher, MD, PhD; Alan A. Wilson, PhD; Sylvain Houle, MD, PhD; et al

Post partum

- PP Depression – 13% of women
- PP Anxiety – 17% of women
- Progesterone and estrogen deficiencies
- Often: low ferritin, carnitine
- Chinese herbals: Eight Treasures Decoction (Ba Zhen Tang) with Astragalus
Endnote: Primary Prevention

Accumulating evidence suggests that **hormonal exposures during gestation can impact psychiatric status in adulthood**

Fetal exposure to maternal **hypothalamic-pituitary-adrenal axis dysregulation, excessive glucocorticoids, and inflammation** with resulting **epigenetic changes at both the placental and fetal levels**

During the intrauterine period, **thyroid hormone is essential for normal brain development**
Balancing Hormones for Mood

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   - Stress support
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   - Food
   - Exercise
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3. BIH Hormonal Supports
Thank you

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