Introduction to Hormone Replacement

Hormone Myths vs. Scientific Evidence

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Introduction to Bioidentical Hormones

Objective # 1
- What’s All the Fuss?
- 1. What are Bioidentical Hormones?
- 2. What is all the Controversy?

Objective # 2
- Review the Position of:
  - AMA 2009, 2016
  - NAMS 2017
  - AACE

Objective # 3
- Review the Scientific Evidence, Pro and Con in Relation to the use of Bioidentical Hormones

Objective # 4
- Medium Pharma Gets It
- 4 Recently Released FDA Approved Bioidentical Hormones

Overriding Theme
- Participants Will Return Home Armed with Peer Reviewed-Evidenced Based Knowledge and References
- Confidently Prescribe Bioidentical Hormones
I Have No Conflicts of Interest germane to this Lecture

- Consultant: Nutrient Foods, Boston, MA.
Fuss # 1-You Prescribe Bioidentical Hormones?

OH MY G-D
THE HORRORS!
What’s All the Fuss?

1. What are Bioidentical Hormones?

- Bioidentical hormones are:
  - Plant-Based, derived from Soy or Yams
  - Contain the same molecular structure to those naturally produced in the body.

- Poorly Understood
  - Even by the “Experts”
“No medical or scientific evidence exists to support the idea that the adverse and/or beneficial effects found in the WHI resulted from the molecular structure of the synthesized hormones, nor is there any sound scientific evidence to show that a different or "customized" dose of hormones would have changed the outcome.”

Endocrine Society Position Paper on BHRT

● “No, they aren’t.”
  ○ Tatnai Burnett, M.D.

● Little or no scientific or medical evidence supports claims that bioidentical hormones are safer or more effective than more traditional FDA-approved therapies.
American Association of Clinical Endocrinologists-2011

For women who cannot control severe vasomotor symptoms, lifestyle changes should be implemented first.

Pharmacologic therapy:

a. Antidepressants-Venlafaxine (**Effexor**)

b. Antidepressants intolerant
   i. Clonidine (Catapress)
   ii. Megestrol (Synthetic Progesterone)
   iii. Gabapentin

Neil F. Goodman, MD, FACE; Rhoda H. Cobin, MD, MACE; Samara Beth Ginzburg, MD; Ira A. Katz, MD, FACE; Dwain E. Woode, MD, American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice, *Endocrine Pract.*, 2011(17)Supplement 6; 1-25
Recommendation: No previous recommendations from the 2011 menopause clinical practice guidelines have been reversed or changed.

Estrogen - No previous recommendations from the 2011 menopause clinical practice guidelines have been reversed or changed.

Estrogen - Transdermal as compared with oral may be considered less likely to produce thrombotic events.
American Association of Clinical Endocrinologists-2017

- **Progesterone** when necessary, micronized progesterone is considered the safer alternative.

- **Symptomatic at risk of use of HRT**-SSRI’s, Clonidine, Gabapentin

- **Bioidentical hormone therapy**-AACE does not recommend use

Patients receiving off-label therapies not backed by scientific evidence are more likely to experience adverse drug events. (15)


**Read the Study!-Admire Their Chutzpah!**

*Design Setting:* A cohort of 46,021 patients who received 151,305 incident prescribed drugs assembled from primary care clinics in Quebec, Canada.

*Results:* Off-label use lacking strong scientific evidence had a higher ADE rate (21.7 per 10,000 person-months) compared with on-label use (AHR, 1.54; 95% CI, 1.37-1.72).

However, off-label use with strong scientific evidence had the same risk for ADEs as on-label use. The risks for ADEs were higher for drugs approved from 1981 to 1995, patients receiving 5 to 7 drugs and patients receiving cardiovascular drugs.

NO MENTION OF HORMONES IN STUDY AT ALL!
Hey: AMA!

YOU'RE A LYING DOG-FACED PONY SOLDIER
No evidence currently suggests that BHRT formulations offer clinically relevant benefits.


PMCID: PMC3127562
Ms. Thomas has Hashimoto's. She also probably has untreated OSA, which is likely the driver of her symptom complex. Overall, I feel Dr. Clearfield is a shaman, preying on the placebo effect and some modest clinical side effects from drugs like T3 to "help" patients. In my opinion, its a shame he is a DO and he disgraces degree.

We reviewed there is NO legitimate peer reviewed literature supporting the use of androgens in women for any reason. She is only increasing her risk of hirsutism, and likely deriving no benefit.
Fuss # 2-FDA Approval

But Wait...

There’s MORE!
Fuss # 2 “FDA Approved”

Who Amongst Us Never Strays from the FDA’s Orthodoxy?

Who Never, Ever, Ever Prescribes Anything “Off-Label”
Just for Fun: “FDA Approved Treatment With “Credible Evidence” of Therapeutic Efficacy

1. Rofecoxib (Vioxx)
   - Maker: Merck
   - Recalled: 2004 (after five years on the market)
   - Financial damage: nearly $6 billion in litigation-related expenses alone
   - 140,000 incidents of premature coronary artery disease

2. Cerivastatin (Baycol)
   - Maker: Bayer
   - Hyperlipidemia
   - Recalled: 2001 (after four years on the market)
   - Financial damage: Litigation-related damages totaled $1.2 billion
   - 100,000 Deaths Due to Rhabdomyalysis
3. Oxycontin-Pain Relief

a. **Side Effects**- Highly Addictive, Easy Accommodation. Patients quickly need larger and larger doses to achieve same level of relief. Leading drug of abuse from 2004 on. 29,600 drug related fatalities due to overdose.

b. **Costs**- $38.5 Billion for abuse treatment, medical complications, productivity loss (minus mortality), and criminal justice. **Premature Death Cost** $63 B  **Life Years Lost** 29

c. **Sales**- $36 B  **Fine**- $600 million

August 14, 2015: FDA Approves Oxycontin for Children as Young as 11

OxyContin sales put Purdue's Sackler family on Forbes rich list

Ravi Katari and Dean Baker, Patent Monopolies and the Costs of Mismarketing Drugs; Center for Economic and Policy Research, April 2015; 1-18.

Purdue Pharma Files for Bankruptcy-3/4/2019
4. Risperidone

- FDA approved in autistic children for easing irritability, outbursts in ASD
- Side Effect: Elevated Prolactin
- 2003- Manufacturer of risperidone
  - “No link between elevated prolactin levels in boys and gynecomastia or other side effects that could result from excess prolactin (89)
  - FDA approval in 2006
    - Side effects including extreme weight gain and gynecomastia
    - The company agreed to a $2.2 billion dollar fine.
  - Data tables showing correlation between prolactin levels and gynecomastia withheld (90)
Fuss #2: 10 Most Common Off Label Use Drugs in USA

**SSRIs**
- Premature ejaculation, hot flashes, tinnitus (ringing in the ears)

**Prazosin**
- Post Traumatic Stress Disorder

**Amitriptyline**
- Fibromyalgia, migraines, eating disorders, pain after shingles infection

**Statins**
- Rheumatoid arthritis

**Clonidine**
- Smoking cessation, hot flashes, attention deficit/hyperactivity disorder (ADHD), Tourette’s Syndrome, RLS

**Aripiprazole**
- Dementia, Alzheimer’s Dx.

**Gabapentin, anti seizure**
- Peripheral Neuropathy esp. DM, Migraine H.A. Hot Flashes

**Topiramate-anti seizure**
- Bipolar disorder, depression, weight, alcohol dependence

**Risperidone**
- Alzheimer's disease, dementia, eating disorders, PTSD

**Trazodone**
- Insomnia, anxiety, bipolar dx.

**Propranolol**
- Stage Fright
What’s the Fuss 2?

AND...

Back to your Regularly Scheduled Programming...

1. Current evidence does not support the use of testosterone in older men with low testosterone levels.

2. Evidence of the value of testosterone as an antiaging therapy does not exist.

3. Current evidence fails to support the efficacy of hGH as an anti aging therapy.

4. The long term use of estrogens with or without progestins cause more risks than benefits.


5. The long term use of estrogens for the prevention of chronic conditions in postmenopausal women is not recommended

6. DHEA as an antiaging supplement shows neither meaningful benefit nor serious adverse effects

7. No evidence of long term changes in therapeutic doses of “anti aging hormones”

AMA, 2016: “No Credible Evidence Exists on the Value of Bioidentical Hormones.”

1. Current AMA policy supports the clinical decision-making authority of a physician to use an FDA-approved product off-label when such use is based upon sound scientific evidence or sound medical opinion.

2. **The Use of Compounded Hormone Therapies is not Supported by Evidence.**

3. Additionally, traditional compounding is recognized as a legal and important therapeutic approach when an FDA-approved drug product is not available or does not meet the clinical needs of individual patients.
AMA, 2016: “No Credible Evidence Exists on the Value of Bioidentical Hormones.”

4. However, in the case of many of the uses for compounded hormones, comparable FDA-approved therapies are available.

5. Further concern is prompted by the fact that compounding pharmacies are exempt from including specific and important safety information on labeled instructions. That lack of information may put some patients at risk.
“Ed Begley, Jr. Rule”

“Don't get your information from me, folks, or any newscaster. Get it from people with PhD’s after their names.”
A 15 Second Search for a Direct Comparison:

The Use of Compounded Hormone Therapies is Not Supported by Evidence.

Bioidentical 'Natural'
Hormone Evaluation in Early Menopause

Drisko, J., University of Kansas, 2006-2018

Bioidentical 'Natural' Hormone Evaluation in Early Menopause  
Drisko, J., University of Kansas, 2006-2018  

<table>
<thead>
<tr>
<th>Cholesterol</th>
<th>Prempro .45mg</th>
<th>Bi-est 2.6 mg</th>
<th>Estriol 2.5mg, Prog. 100mg</th>
<th>Estriol 2.5mg, Prog. 100mg</th>
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<td>223</td>
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<tr>
<th>Adverse Reactions</th>
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October 29, 2018 FDA Approved Bioidentical Capsule

- Company X Announces FDA Approval of TX-001HR: (Estradiol and Progesterone) Capsules for the Treatment of Moderate to Severe Vasomotor Symptoms Due to Menopause

- Brand Name is the First and Only FDA-Approved Hormone Therapy of Bio-Identical Estradiol in Combination with Bio-Identical Progesterone

- Fixed Doses: Estradiol 1 mg/Progesterone 100 mg

The Use of Compounded Hormone Therapies is not Supported by Evidence.
What’s all the Fuss 1?

- BHRT is Poorly Understood-Even by the Experts
  - 1st Entry in Google Search of Trade Name of TX-001HR is WebMD:
    - This medication contains 2 female hormones: an estrogen (such as conjugated estrogen, estradiol) and a progestin (such as medroxyprogesterone, norethindrone, norgestimate)
    - Women who have had their uterus removed do not need the progestin and therefore should not use this combination medication.

- Current evidence does not support the use of testosterone in older men with low testosterone levels.

- Evidence of the value of testosterone as an antiaging therapy does not exist.

Benefits of Testosterone

1) **Antidepressant**

2) **Increased muscle mass, strength, endurance, and increased exercise tolerance**

3) **Increased sense of well-being**

4) **Adequate memory**

5) **Elevates brain norepinephrine, enhancing memory and cognition**

6) **Increased sexual interest and sexual performance**

7) **Improved skin turgor**
Benefits of Testosterone

8. Decreases body fat
9. Maintains bone strength
10. Protects against osteoporosis
11. Reduced LDL cholesterol
12. Improves insulin sensitivity
13. Protects Against Diabetes
14. Involved in the making of protein and muscle formation
15. Improves oxygen uptake throughout the body
16. Needed for normal sperm development
17. Regulates acute HPA responses under dominance challenge
Coronary Heart Disease

• Men with coronary heart disease have significantly lower total testosterone, free testosterone, and bioavailable testosterone.
  — English, K., et al., “Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms,” Eur Heart Jour 2000; 21(11):890-4

• Low endogenous testosterone concentrations are related to mortality due to cardiovascular disease and other causes.

• Men with coronary heart disease under age 45 have total and free testosterone levels significantly lower than controls.
serum testosterone => ▼ Mortality

SAFER when serum testo is in highest quartile

A man needs to have a serum testo > ± 600 ng/dl

Insufficient testosterone levels => Men die quicker

N = 11,606 men aged 40 to 79 yrs; follow-up 6-10 yrs

Khaw KT. Circulation. 2007 Dec 4;116(23):2694-701 Cambridge UK

↑ mortality at serum total testo < 500 - 600 ng/dl

Serum Total Testosterone in apparently healthy men (ng/dl)

(Mohr BA; Clin Endocrinol (Oxf). 2005 Jan;62(1):64-73)
No Consistent Relationship has been Proven Between T Levels and Symptoms Associated with Low T.

Carotid Artery Disease

- Serum free testosterone levels is inversely related to carotid intima-media thickness (IMT) and plaque score.
  
  — Bhasin, S., et al., “Serum free testosterone is inversely related to carotid intima-media thickness (IMT) and plaque score,” Diabetes Care 2003; 26:1869-73.

- Low testosterone levels is associated with atherosclerosis in men.

### Prevalence of Concomitant Cardiometabolic Conditions in Men With Total Testosterone < 300 ng/dL

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Hypogonadism* Prevalence (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>52.4 (47.9-56.9)</td>
<td>2.38 (1.93-2.93)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>50.0 (45.5-54.5)</td>
<td>2.09 (1.70-2.58)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42.4 (39.6-45.2)</td>
<td>1.84 (1.53-2.22)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>40.4 (37.6-43.3)</td>
<td>1.47 (1.23-1.76)</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>43.5 (36.8-50.3)</td>
<td>1.40 (1.04-1.86)</td>
</tr>
<tr>
<td>Prostate disease</td>
<td>41.3 (36.4-46.2)</td>
<td>1.29 (1.03-1.62)</td>
</tr>
</tbody>
</table>

*Men with total testosterone < 300 ng/dL.
Facts: Testosterone and Heart Disease

- Low testosterone levels are associated with increased mortality, atherosclerosis, and incident coronary artery disease;

- Mortality is reduced by one half in testosterone-deficient men treated with testosterone therapy compared with untreated men;

Testosterone supplements linked to heart attacks in new study

The FDA said today that it was evaluating the cardiovascular safety of testosterone products. The investigation is prompted by two recent published studies that found a significant increase in cardiovascular events in men who received testosterone therapy.

The FDA said it had not concluded that testosterone is unsafe but recommended that “health care professionals should consider whether the benefits of FDA-approved testosterone treatment is likely to exceed the potential risks of treatment.” Testosterone is approved for use only in men who lack or have low testosterone levels in conjunction with an associated medical condition.
Current Evidence does not Support the Use of Testosterone in Older Men with Low Testosterone levels.

- Risk of non-fatal MI greater in the 3 months after testosterone Rx.
- ICD-9 study, patients not seen or interviewed
- No information on preparation, dose or interval of usage or if even used
- No info on fatal MI or cardiovascular mortality or all cause mortality
- No information on testosterone serum levels before or after therapy

Conclusional: Delusional?
A Predetermined Outcome?

With T 10% with Event vs. Without T 21% Events = T Caused Events?

With T 5% Deaths vs. Without T 9% Deaths = T Caused Deaths?
Testosterone and Heart Disease—Study Retracted

1. Authors improperly excluded 1132 men from analysis. Corrected to 128 subsequently.
   a. (Error rate 89%)

2. 100 women were identified among the study group.

3. Original group of 1132 individuals, meaning that one out of eleven “men” in the study were actually women.

4. More than 160 leading testosterone researchers and 29 medical societies from around the world joined ASG called for retraction of the study following revelation of the data errors, asserting that the magnitude and quality of the errors rendered the study "no longer credible."
Testosterone and Depression

Testosterone Levels Inversely Proportional to Degree of Depression

- Free testosterone in lowest quartile=highest incidence of depression

**Male**
- At Risk: 295 ng/dL Free T 6.0 ng/ml (Median 12-14 ng/ml)
- Depression: 147.5 ng/dL Free T 3.0 pg/ml

**Female**
- At Risk: 22 ng/dL (median 44 ng/dL); Free T 1.0 ng/dL (median 2-4 ng/dL)
- Depression: 11 ng/dL; Free 0.5 ng/dL

T Modulates Anorexia Nervosa

“No Consistent Relationship has been Proven Between T Levels and Symptoms Associated with Low T.”

• Low TT is predictive of hypertension

• TT is a biomarker for increased cardiovascular risk.

• Low TT = 📈 Mortality in CHF
TBI → Low T → Depression → Suicide

- 10th leading cause of death in US
  - (37,000 successful, 1 million attempts in 2009)
- Direct Relationship between Depression, Suicide, and Low Testosterone
- Men Have 4X Suicide Risk of Women
- Suicide Attempts are Inversely Related to Testo Levels
- Peak Years Men 80-90, Women 50-65
  - (UCSF-Attributed to Loss of Estrogen)

Testosterone and Anxiety

- Testosterone reduces anxiety, enhances cognition.
- Analgesic, anxiolytic, and cognitive effects
  - due to action on 5 alpha reductase metabolites in hippocampus effect

Edinger, KL; Frye, CA, *Testosterone’s analgesic, anxiolytic and cognitive-enhancing effect may be due in part to actions of its’ 5 alpha-reduced metabolites in the hippocampus*; Behav Neurosci; 2004 Dec;118(6):1352-64. Albany, NY

The presence of a LOW Prolactin level can be a tip-off in a patient with treatment resistant anxiety. Having a high dopamine (Prolactin inhibiting factor) will suppress the production of Prolactin from the Anterior Pituitary.)
Testosterone and Atherosclerosis

**Higher Total Testosterone & SHBG Inversely related to Carotid ASVD.**

Lowest to Highest Quartile

<table>
<thead>
<tr>
<th>Total SHBG</th>
<th>Total Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>62% Decrease in Carotid Intimal Thickness</td>
<td>52% Decrease in Carotid Intimal Thickness</td>
</tr>
</tbody>
</table>

No associations found between ASVD & estrone, DHEA-s, or androstenedione.


No Consistent Relationship has been Proven Between T Levels and Symptoms Associated with Low T.

- **Memory**

- Testosterone plays a major role in brain function.

- Low bioavailable T is a positive predictor of memory loss in men as they age.

- Low TT = Memory Loss
Testosterone and Alzheimer’s Disease

- **Dementia, Tremor and Gait Dysfunction Attributed to Low T**

- **Low bioavailable T = Correlate B memory loss/Alzheimer’s Dx**

- **Even subclinical androgen deficiency expresses amyloid-B-related peptides in vivo.**
Free & Total Testo => ↓ Alzheimer’s D.

Men + baseline ages
of 32 to 87 years

For each 10-nmol/nmol FTI increase
=> - 26% decrease in risk of Alzheimer’s disease

Figures: Increases in the FTI were assoc. w/ a decreased risk of Alzheimer’s disease. Calculated free testosterone conc. were lower in men who developed Alzheimer disease, & this difference occurred before diagnosis.

n = 574 men followed for a mean of 19.1 years (range, 4 - 37 years)

Testosterone’s Effects on Behavior

Testosterone down-regulates the production of Allopregnanolone (Allo-P is Calming) = Irritability, Impulsive Aggression, and Signs of Major Depression.

Graziano Pinna*, Erminio Costa, and Alessandro Guidotti, “Changes in brain testosterone and Allopregnanolone biosynthesis elicit aggressive behavior.,” PNAS, Feb 8, 2005, Vol. 102 No. 6 2135–2140 Psychiatric Institute, Dept of Psychiatry, College of Medicine, University of Illinois, Chicago, IL 60612
Serum Testost. within ref. range => ↓ vigor, libido, depression, type 2 diabetes, erectile dysfunction

INFO: the prevalence of psychosomatic symptoms & metabolic risk factors accumulated with ↓ androgen levels

THRESHOLDS: below which risk factors sign. increased

- 15 nmol = 432 ng/dl = 4320 pg/ml
- 10 nmol = 288 ng/dl = 2883 pg/ml
- 8 nmol/l = 231 ng/dl = 2310 pg/ml

Loss of vigor
Loss of libido
Depression & Diabetes mellitus type 2 (also in nonobese men)
Erectile dysfunction

N = 434 consecutive male patients aged 50-86 yr

Testosterone and Obesity

Restoration of Testosterone to Therapeutic Levels (6 Mo. Study)

Significant Reductions in:

- Weight (5.4%)
- Abdominal Fat (2.2%)
- Gluteal-femoral Fat (0.9%)
- Total Body Fat (2.1%)
- BMI (4.6%)

Myth: Testosterone Causes Prostate Cancer

Based on one report from 1941

- *No relationship of T, DHT, E2 to prostate Ca*
- *No reports of PC in men treated with T after radical prostatectomy*
- *Benefits from head to toe when hypogonadism treated*

Morgentaler A. Testosterone and Prostate Cancer: An Historical Perspective on a Modern AMA. Eur Urol. 2006 Jul 26
Testosterone therapy and the Risk of Prostate Cancer

- 3886 men with prostate cancer, 6438 controls

No associations were found between the risk of prostate cancer, Testosterone, calculated free testosterone, dehydroepiandrosterone sulfate, androstenedione, androstanediol, estradiol, calculated free estradiol

*Testosterone therapy in hypogonadal men does not increase the risk of prostate cancer.*

Testosterone Therapy and the Risk of Prostate Cancer

• “No compelling evidence at present suggests that men with higher testosterone levels are at greater risk of prostate cancer or that treating men who have hypogonadism with exogenous androgens increases this risk.

• In fact it should be recognized that prostate cancer becomes more prevalent exactly at the time in a man's life when testosterone levels decline.”


**BEFORE TESTOSTERONE:**

- Vasomotor symptoms?
- Dyspareunia?
- Incontinence?
- Pelvic Pain?
- Depression/anxiety?
- Relationship conflict?
- Medications?

**HRT/Lifestyle changes**

- Lubricants, moisturizers, low-dose vaginal Estrogen, DHEA
- Pelvic floor PT, devices, medication
- Treatment, medication, therapy
- Psychotherapy, counseling, meds
- Counseling, sex therapy
- Substitute for SSRI, psychopharm. consult
Benefits of Testosterone Therapy in Women

- Visceral Fat
- Fat Deposition
- Cellulite and Wrinkles
- Mental Fatigue
- Depression
- “Sore-Body” Syndrome
- Vaginal Dryness
- Moodiness and Irritability
- Vertigo, Lightheadedness
- LDL Cholesterol
Testosterone and Urinary Incontinence

- The pelvic floor musculature and fascia contain androgen receptors.
- Topical testosterone:
  - Increases levator ani hypertrophy
  - Improves stress incontinence
  - Strengthens pelvic musculature support around urethra
- Lowest quartile of serum testosterone resulted in 48% increased incidence of stress and 65% increased incidence of mixed incontinence compared with women not in the lowest quartile. (OR 1.45, 95% CI 1.03-2.12 and OR 1.68, 95% CI 1.23-2.22, respectively).

2.75X Risk of Breast Cancer Without Testosterone $P < 0.00$


Testosterone Novelties

- **Dry Eye Disease** - 0.3% Testosterone with 0.5% Progesterone in cyclodextrin base. Dawson, T.L., Testosterone eye drops: “A novel treatment for dry eye disease,” *Ophthalmology Times*, November 15, 2015


GROWTH HORMONE

Current evidence fails to support the efficacy of hGH as an anti aging therapy.

Rudman, 1991

- 8.8 percent increase in lean body mass
- 14.4 percent decrease in adipose-tissue mass
- 1.6 percent increase in average lumbar vertebral bone density
  - (P less than 0.05 in each instance)
- Skin thickness increased 7.1 percent.

RX: 0.03 mg of Biosynthetic HGH per kilogram of body weight SQ 3x/week

HUMAN GROWTH HORMONE BENEFITS

**BRAIN FUNCTION**
- Memory
- Dendritic formation of cortical neurons
- Cognitive function
- Improved mental function
- Alertness
- Motivation and Work Capacity
- Prevents Alzheimer's disease
- Concentration

**HEART**
- HGH enhances Cardiac Functions
- Stroke
- Heart Attack
- Irregular Heartbeat
- Shortness of Breath
- Numbness

**SKIN & HAIR**
- Thicker hair
- Growth in areas where hair was lost
- Increased collagen
- Skin thickening
- Smoother, firmer skin
- Of wrinkles, fine lines, and cellulite
- Decreased sagging

**BODY FAT**
- HGH accelerates metabolism

**SLEEP**
- HGH improves Your Sleep Quality

**BONE DENSITY**
- Reduced Risk of Osteoporosis
- HGH Increase Bone Healing

**IMMUNE FUNCTION**
- Stimulates bacteria fighting macrophages
- Increase production of T-cell and Interleukin2
- Increases erythropoiesis
- Increases maturation of neutrophils
- Increases and intensifies the production of new red blood cells
- Increases production of white blood cells that fight disease

**SEXUAL FUNCTION**
- Sexual function in men
  - Increased desire
  - Faster arousal times
  - Stronger erections
  - Longer lasting stamina
  - Increased pleasure

- Sexual function in women
  - Increased vaginal lubrication
  - Heightened arousal
  - Stronger desire
  - Improved endurance
  - Multiple orgasms
A Brief Primer on Growth Hormone (GH)

Single chain 191-amino acids linked in a specific manner, in a particular order.

Picture a Legos™ model snapped together to make a windmill or a car.

1. GH released in Spurts or Waves between 10PM and 4 AM
2. Stimulated by:
   a. Hypothalamus: GH releasing factor (GHRH)
   b. GI Tract: Ghrelin (GHRP)
3. Inhibited by: Somatostatin (GHIH)
4. Synthesized in the pituitary gland
## Growth Hormone Sufficiency vs. Deficiency

<table>
<thead>
<tr>
<th>Sufficient GH</th>
<th>Low GH</th>
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<tbody>
<tr>
<td><strong>Enhances:</strong></td>
<td></td>
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<tr>
<td>Cardiovascular function</td>
<td>● <strong>Memory</strong></td>
</tr>
<tr>
<td>Reduces IL-1, IL-6, CRP</td>
<td>● <strong>Concentration</strong></td>
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<tr>
<td>Concentration</td>
<td>● <strong>Mental clarity</strong></td>
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<tr>
<td>Memory</td>
<td>● <strong>OCD</strong></td>
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<tr>
<td>Mental stability</td>
<td>● Paranoia</td>
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<tr>
<td>In deficiency: OCD, paranoia</td>
<td>● Poor Concentration</td>
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<tr>
<td>Dark moods</td>
<td>● Impulse Control</td>
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<tr>
<td>Impulse control</td>
<td>● Anxiety</td>
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<tr>
<td>Sense of reality</td>
<td>● Lack of Socialization</td>
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<tr>
<td><strong>Executive Function</strong></td>
<td>● Inability to Plan</td>
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<tr>
<td>Energy</td>
<td>● Dark Moods</td>
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<tr>
<td></td>
<td>● <strong>Inability to Switch B Tasks</strong></td>
</tr>
</tbody>
</table>
1. GH-therapy of GH-deficient men **reverses early atherosclerotic changes**, namely the increased thickness of the intima media of the common carotid artery & the carotid bifurcation in 11 GH-deficient men (24-49 yr old) (Pfeifer M et al, J Clin Endocrinol Metab, 1999, 84 : 453-457)


Myth: GH Deficiency is Only Seen in Patients with Severe Multiple Pituitary Deficiencies since Childhood

Patients treated with GH experience significant improvements in concentration, memory, depression, anxiety and fatigue.

GH replacement therapy improves cognition and QoL in TBI patients with GHD, especially in those with severe disabilities.


Pituitary failure can occur even in minor head injuries and is poorly recognized.


AGHD is common and often not recognized after TBI and other brain insults.

• Evaluate all TBI, CVA patients within a year for AGHD. Treat if deficiency disease exists.
GH ➞ ↑ thyroid activity

% Change

Cortisol activity ➞ Plasma peak cortisol after intake ➞ Urinary cortisol metabolites ➞ Thyroid activity ➞ Androgen activity

- Cortisol production 2-6 PM
  - Study 1 (7 days): 8 healthy men
  - Study 2 (1yr): 14 GHD boys
- T3
  - Study 2 (1yr): 9 GHD adults
  - Study 3 (6 mo.): T3 +31% (P = 0.001)
- Testosterone stim. by CG
  - Study 4 (1yr): 11 adult men
  - Study 5 (1yr): 11 GHD boys
- SHBG
  - T3 +25% (P < 0.01)
  - SHBG +32% (P < 0.05)
GH therapy => prolongs life (↓ the increased mortality of) in GH deficient patients

Overall Mortality (vs normal population)

**GH-deficient patients**

- **All**
  - no GH
  - GH
  - 95% CI: 3.80 - 3.43
  - 0.84 - 1.76

- **Men**
  - no GH
  - GH
  - 95% CI: 3.36 - 2.93
  - 1.11 - 3.83

- **Women**
  - no GH
  - GH
  - 95% CI: 4.54 - 3.89
  - 0.00 - 5.26

**Figure:** Overall mortality & the rate of myocardial infarctions were increased in hypopituitary patients without GH replacement, GH replacement normalized the risk.

“Executive Function” Deficiencies in TBI and ASD =

**Growth Hormone Abnormality**

“Executive function” is one possessing the cognitive & mental capacities to achieve one’s goals.

“Executive functioning” is a hallmark of growth hormone sufficiency.
Executive Function

- Memory
- Task Initiation
- Planning and Prioritizing
- Organization
- Flexible Thinking
- Ability to Switch Between Tasks
- Completing Tasks
TBI and Growth Hormone Deficiency

- Correction of GHD:
- Tempers:
- Intensity of Outbursts
- Hostility
- Paranoid Ideation
- Anxiety, Phobia
- Somatization
- Obsessive Compulsive S/S

- Improves:
- Verbal and Non-Verbal Memory
- Cognition
- Mental Alertness
- Work Capacity

TBI and Growth Hormone Deficiency

- First and Most Common Deficiency

- Acute Injury Incidence rate: 20%.
- 12 month follow up rate increases to 35-40% of survivors.

1. Aimaretti, G; et al., Hypopituitarism and Growth Hormone Deficiency after TBI. Growth Hormone IGF Res 2004 June 14 Suppl A:S114-7
<table>
<thead>
<tr>
<th>TBI and Growth Hormone Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory</strong></td>
</tr>
<tr>
<td><strong>Concentration</strong></td>
</tr>
<tr>
<td><strong>Mental clarity</strong></td>
</tr>
<tr>
<td><strong>OCD</strong></td>
</tr>
<tr>
<td><strong>Dark moods</strong></td>
</tr>
<tr>
<td><strong>Paranoia</strong></td>
</tr>
<tr>
<td><strong>Poor Concentration</strong></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
</tr>
</tbody>
</table>
TBI and Growth Hormone Deficiency

Deficits in:

Rapid weight gain

Excessive anxiety

Depression along

Poor overall physical health and quality of life

Attention

Executive Functioning

Cognitive, Mental Ability to Achieve Goals

Memory

Emotion

Mood Anxiety/Depression
# Growth Hormone Deficiency vs. Autism

<table>
<thead>
<tr>
<th>S/S of GH Deficiency</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetitive behaviors</td>
<td>Repetitive Behaviors</td>
</tr>
<tr>
<td>Avoids Emotional Rec./Eye Contact</td>
<td>Avoids Emotional Rec. /Eye Contact</td>
</tr>
<tr>
<td>Aggression/Agitation</td>
<td>Aggression/Agitation</td>
</tr>
<tr>
<td>Hyperactivity/Impulsivity</td>
<td>Hyperactivity/Impulsivity</td>
</tr>
<tr>
<td>Anxiety/Stress/Depression</td>
<td>Anxiety/Stress/Depression</td>
</tr>
<tr>
<td>Mood swings</td>
<td>Mood swings/ “Meltdowns.”</td>
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<tr>
<td>OCD</td>
<td>OCD</td>
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<tr>
<td>Self-injurious behavior</td>
<td>Self-injurious behavior</td>
</tr>
<tr>
<td>Balance/Coordination</td>
<td>Balance/Coordination</td>
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<tr>
<td>Communication Deficits/Delays</td>
<td>Communications Deficits/Delays</td>
</tr>
<tr>
<td>Executive Function Impairment</td>
<td>Executive Function Impairment</td>
</tr>
<tr>
<td>Seizures</td>
<td>Seizures</td>
</tr>
<tr>
<td>Social Skills Impaired, Delayed</td>
<td>Social Skills Impaired, Delayed</td>
</tr>
</tbody>
</table>
IGF-1 and the Brain

- IGF1 expression levels decrease with aging
- Low-dose IGF1 treatment = neurons.
- Promotes adult hippocampal neurogenesis
- Exercise neurogenesis effect mediated through IGF1 signaling

Liver must convert GH to end-organ usable IGF-1 (IGF-2 Prenatal)
Sign. Inverse Assoc. of serum IGF-1 & Obesity

↑ Body mass index in normal boys at various stages of puberty & young adulthood (7-27 yrs) at lower 24-h serum GH & serum IGF-1 (Martha PM, J Clin Endocrinol Metab. 1992)

↑ Body mass index & obesity index in adolescent boys & girls (13-18 y) at lower serum GH (Molero-Conejo E, Arch Latinoam Nutr. 2006)

Optimal

BMI
↓ abd. fat


↑ Metabolic syndrome features at ↓ (lower) total serum IGF-1 almost linear rel. w/ the number of MetS components (Efstratiadis G, Angiology. 2006)

↑ risk of Obesity in nI men & women aged 30-64 y at lower serum IGF-1, & in women at lower GH (Maison P, Diabet Med. 2007)
GHD Patients = 9-fold incidence of cardiovascular mortality

Significant inverse association of serum IGF-1 and Cancer stage

**OPTIMAL**
- Less severe cancer
- No metastasis

↑ TNM (tumor-node-metastasis) stage at ↓ (lower) serum IGF-1 in breast cancer patients, despite a higher serum IGF-1 in BC patients vs controls, & after adjustment, the serum IGF-1 remained significantly & positively associated with breast cancer risk (odds ratio, 1.183; 95% CI: 1.167-1.201). (Agurs-Collins T, , Cancer Detect Prev. 2000)
To Remedy IGF-1 Deficiency

Improved:
- Mood, motivation
- Memory, attention
- Cognition.

Diminished:
- Hyperactivity
- Stereotypy
- Depression, anxiety
- OCD tendencies

Medications:
- hGH
- IGF-1
- Intranasal Insulin
- Low Dose Naltrexone
- Pioglitazone
- Statins
- Verapamil
- Tocilizumab
- Peptides

Supplements:
- EPA/DHA
- EGCG
- Vitamin C
- N-Acetyl Cysteine
- Quercetin
- Luteolin
- Rutin
- Zinc

IL-6 Antagonists
- IGF-1 Boosters
- Mast Cell Stabilizers

Improved:
- Mood, motivation
- Memory, attention
- Cognition.

Diminished:
- Hyperactivity
- Stereotypy
- Depression, anxiety
- OCD tendencies
Myth: “No Credible Evidence Exists on the Value of Bioidentical Hormones.”

- The long term use of estrogens with or without progestins cause more risks than benefits.

- The long term use of estrogens for the prevention of chronic conditions in postmenopausal women is not recommended.

Estrogen Has 400 Functions
Increases:

Heart/Circulation
- Metabolic Rate
- Artery Size
- Blood Flow to Brain
- HDL

Reproductive System
- Libido
- Sexual Performance
- Preparation for Pregnancy
- Breast Growth/Density

Miscellaneous
- Bone Density
- Insulin Sensitivity
- Skin Thickness

Neuro Effects
- Mood
- Energy
- Neurotransmitters
- Memory, Cognition
- Reasoning
- Anti-Psychotic
- Protective in TBI

Miscellaneous
- Mood
- Energy
- Neurotransmitters
- Memory, Cognition
- Reasoning
- Anti-Psychotic
- Protective in TBI
Estrogen Has 400 Functions
Decreases:

**Heart/Circulation**
- Carotid Arterial Plaque
- Blood Pressure
- Homocysteine
- LDL
- Heart Dx Risk 40-50%

**Reproductive System**
- Sexual Dysmorphia
- Vaginal Dryness

**Neuro Effects**
- Depression
- Anxiety
- Irritability
- Pain Sensitivity
- Alzheimer’s beta amyloid peptides
- Risk of PTSD

**Miscellaneous**
- Tooth Loss
- Colon Cancer
- Wrinkles

**Miscellaneous**
- Tooth Loss
- Colon Cancer
- Wrinkles
Symptoms of Low Estrogen

- Irregular or missed periods
- Mood swings
- Hot flashes
- Tenderness of breasts
- Headaches or worsening of migraines
- Depression
- Fatigue
- Trouble concentrating
- Decrease or absence of libido
- Pain during intercourse
- Lack of vaginal lubrication
- Vaginal loosening
The Elephant In The Room: Estrogen Causes Cancer
Does Estrogen Cause Breast Cancer?

Trick Question:

What is the LARGEST study ever done, exploring hormone use and breast cancer occurrence?

What did it show?
If You Said “WHI”CONCEPT

You Are Wrong!
E3N Vs. WHI

WHI – no Bioidentical hormone used

E3N – (+)Bioidentical and CEE + Progestins were used

# of women receiving “hormone” treatment

• WHI = 13,816 E3N = 29,420

Estrogen alone (CEE) both studies showed increase risk

Progestin’s in both studies showed GREATER risk

BHRT when used in balanced combo – no increased risk
Does Estrogen Cause Breast Cancer?

“No medical or scientific evidence exists to support the idea that the adverse and/or beneficial effects found in the WHI resulted from the molecular structure of the synthesized hormones, nor is there any sound scientific evidence to show that a different or “customized” dose of hormones would have changed the outcome.”

Endocrine Society Position Paper on BHRT

E3N-EPIC Study

TD-E2 = transdermal estradiol

Cohort study
55,000 women
8 years f/u
c/w WHI--
16,000, 6 yr. f/u

Relative risk* (CI 95%)

No HRT

Product used

TD-E2 alone

TD-E2 plus progesterone

TD-E2 plus progestins

(person-years)

(8,691)

(20,685)

(46,242)

E2 plus progesterone: no increased risk of breast cancer!

Int J Cancer. 2005 Apr 10;114(3):448-54

Similar study: estradiol + progesterone 0.4; estradiol + synthetic progestin 0.94

WHI Vs. E3N

# of women receiving “hormone” treatment

WHI = 13,816

E3N = 29,420

WHI – no Bioidentical hormone used

- Estrogen alone (CEE) both studies showed increase risk
- Progestin’s in both studies showed GREATER risk

E3N – Bioidentical and CEE + Progestins used

- Estrogen alone (CEE) both studies showed increase risk
- Progestin’s in both studies showed GREATER risk

BHRT When Used in Balanced Combo – no increased risk
AMA: Estrogen Use in Postmenopausal Women=

DON'T CROSS THE STREAMS
IT WOULD BE VERY, VERY BAD
2002 WHI Study—“HRT” is Dangerous!

- Premarin® alone given to older postmenopausal women caused adverse effects in the first year (strokes, blood clots)
  - Oral estrogens cause blood clots, transdermal estradiol does not

- Adding Provera® (Prempro®) caused more adverse effects (breast cancers, heart attacks, dementia)
  - Provera increases breast cancer and vascular inflammation. Progesterone does neither.

- Thousands of lawsuits pending; drug companies running a legal-protection propaganda campaign to paint all “hormones” as equally dangerous!
Premarin®
Conjugated Equine Estrogens

Human

Horse

Horse

Estrone

Equilin

Equilenin

CEE contains at least 10 estrogens, only 3 are human; also contains horse androgens and progestins.

Women Killers and Hormones

- Cardiovascular disease (CVD), osteoporosis, dementia and breast cancer are all rare before menopause.
- The first 3 are clearly related to estradiol deficiency; breast cancer is related to progesterone deficiency.
- Early removal of ovaries increases risk of heart disease, osteoporosis, and dementia.


- Youthful hormone levels protect women from these diseases.
Estradiol Restoration

- Protects against heart disease, dementia and osteoporosis.
- Improves insulin sensitivity—prevents diabetes
- Eliminates hot flashes, restores sleep
- Restores cognitive function and mood
- Maintains thickness, fullness of skin and hair
- Maintains genital/pelvic health—helps with vaginal lubrication, incontinence, bladder infections
- Protects against colon cancer and macular degeneration
Estradiol vs. Cardiovascular Disease

- Prevents the oxidation of LDL
- Improves lipid profile
- Reduces lipoprotein (a)
- Reduces blood pressure
- Improves endothelial function
- Reduces plaque formation
- Improves insulin sensitivity
FDA approved Estradiol-Progesterone Pill
DOES NOT ALTER COAGULATION FACTORS

**Activated Partial Thromboplastin Levels with**

**COMPARSED WITH PLACEBO**

- Baseline: 36.3, 36.5
- Month 12: 38.5, 39.2

**Fibrinogen Levels with**

**COMPARSED WITH PLACEBO**

- Baseline: 9.4, 9.5
- Month 12: 9.1, 9.1
Estrogen Replacement Prevents Alzheimer’s Disease

72% used Premarin® only

**Myth: E2 Replacement Increases Risk of Clots**

Transdermal E2 does not increase risk of VTE like oral E2

FDA approved Estradiol-Progesterone pill DOES NOT ALTER COAGULATION FACTORS

- Cardioprotective, decreased risk of AMI, Decreased risk of T2DM

- Internal Carotid Artery lumen widens by 224% when patient administered Estradiol > 6 months.

( Jonas HA et al, Ann Epidemiol, 1996, 6 (4) : 314-23)

Estrogen Dominance

- Allergies
- Autoimmune diseases
- Anxiety, moodiness
- PMS
- Bloating, fluid retention
- Fibrocystic breasts
- Heavy periods
- Endometriosis
- Breast cancer
- Ovarian cancer
- Uterine cancer
- Gallstones

Progesterone is the only effective treatment for estrogen dominance
Progestins ≠ Progesterone

Progesterone ≠ Medroxyprogesterone, Drospirenone

Confusion:
Progestins are often called “progesterone”, in the media and in scientific papers!
Scientific studies show that:

**Provera®** ≠ **Progesterone**

- Causes birth defects
- Can cause depression
- Insomnia, irritability
- Fluid retention
- Raises blood sugar
- Counteracts estrogen-induced arterial dilation
- Worsens lipid profile
- Causes heart attacks
- Increases estrogenic stimulation of breasts
- Causes breast cancer

- Maintains pregnancy
- Improves mood
- Improves sleep
- Diuretic
- No effect on blood sugar
- Maintains estrogen-induced arterial dilation
- Improves lipid profile
- No evidence of ↑ CVD
- Reduces estrogenic stimulation of breasts
- Prevents breast cancer
Who Needs Progesterone Supplementation?

- Irregular menstrual cycles
- No periods—amenorrhea
- Heavy bleeding
- Fibrocystic breast disease
- Endometriosis/adenomyosis
- Every woman in menopause
Progesterone vs. Breast Cancer in menstruating women

6,000 women
5 yr. F/U

Progesterone concentration (ng/ml)

<table>
<thead>
<tr>
<th>&lt; 9.01</th>
<th>&gt; 9.01 to 13.54</th>
<th>&gt; 13.54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk* (CI 95%)</td>
<td>1</td>
<td>0.40 (0.13-1.20)</td>
</tr>
</tbody>
</table>

More progesterone

*adjusted by age, BMI, length-of-cycle, days-from-sampling-to-next-menses, LH and FSH levels

P trend 0.005

Higher progesterone = lower risk of breast cancer
Novel Use of Progesterone: CVA, DM, BP and TBI

1. Progesterone inhibits ischemic brain injury
2. Progesterone reduces infarct volume and improves functional deficits following cerebral ischemic event.
3. Micronized P4 reduces risk of T2DM, does not increase risk of VTE, reduces BP
4. Dose: 8 mg/kg Progesterone best clinical results

- Ishrat T et al. Effects of progesterone administration on infarct volume and functional deficits following permanent focal cerebral ischemia in rats. Brain Res. 2009 Feb 27;1257:94-101
Does Estrogen Cause Breast Cancer?

“No medical or scientific evidence exists to support the idea that the adverse and/or beneficial effects found in the WHI resulted from the molecular structure of the synthesized hormones, nor is there any sound scientific evidence to show that a different or “customized” dose of hormones would have changed the outcome.”

Endocrine Society Position Paper on BHRT

Myth: The Women’s Health Initiative Saved Lives by Demonstrating the Dangers of HRT.

10 years of randomized treatment

• Oral HRT (estradiol, norethindrone) early after menopause

• Significantly reduced risk of mortality, heart failure, myocardial infarction

Without any apparent increase in risk of: Cancer, venous thromboembolism and stroke.

• Schierbeck et al Effect of hormone replacement therapy on cardiovascular events in recently postmenopausal women: randomised trial. BMJ 2012;345
Hormone Replacement After Breast CA

Long Term (Avg 11.6 yr.) Survival Rate In Patients Taking Bioidentical E2 Post Breast Cancer

Estrogen replacement does not increase recurrence or mortality. Adding progesterone decreases recurrences.

Estrogen, Progesterone and Breast Cancer

Never, Ever, Never, Ever Use Estrogen without Progesterone

Never, Ever

You All Have to Pinky Swear
Does Estrogen Cause Breast Cancer?

“No medical or scientific evidence exists to support the idea that the adverse and/or beneficial effects found in the WHI resulted from the molecular structure of the synthesized hormones, nor is there any sound scientific evidence to show that a different or “customized” dose of hormones would have changed the outcome.”

Endocrine Society Position Paper on BHRT

Endocrine Society Position Paper on BHRT
Estrogen Use in the Presence of Breast Cancer

Estradiol is not completely contraindicated if Remission x2 years, (-)
Mammo and clearance pathways have been evaluated


Case Hx.-Breast cancer in remission x 2 years

(+) Hormone Sx; Other options?

- Black cohosh
- Siberian rhubarb extract
- Swedish Sunflower Seeds
- Gabapentin, Clonidine, Paroxetine, Citalopram

Localized Hormone options might include:

- Vaginal DHEA, Estradiol, Testosterone to address dryness
- Progesterone to modulate estrogen receptors
Interventions to Improve Estrogen Balance

- Cruciferous vegetables = DIM & Allium (garlic, onion)
- Iodine – promotes Cyp-1A1 enzyme
- Flax seed meal – lignans (never OIL)
- High Protein Diet, Exercise
- Omega 3 fatty acids, NAC, ALA
- Folic acid, B6, B12 support pathway and promote COMT
- Soy – always organic, whole (not fractionated)
- Kudzu - isoflavone (daidzein)
Progesterone After Hysterectomy

- BONE HEALTH
- HOT FLASHES
- SEDATING EFFECTS
- MOOD & DEPRESSION

Myth: “No Credible Evidence Exists on the Value of Bioidentical Hormones.”


- **Pregnenolone**- aids in stress reduction, memory loss, Alzheimer’s disease, fatigue and energy production. Improves immunity.

- **Prolactin**- Milk letdown hormone has 400 functions in body. High levels = Pituitary adenoma until proven otherwise. Low levels = treatment resistant depression/anxiety.
Myth: “No Credible Evidence Exists on the Value of Bioidentical Hormones.”

- DHEA as an antiaging supplement shows neither meaningful benefit nor serious adverse effects

DHEA as an Antiaging Supplement shows Neither Meaningful Benefit nor Serious Adverse Effects

DHEA =>

Counters cortisol excess.

Decreases visceral & subcutaneous fat in elderly persons.

Reduces LDL and body fat.

Improves Bone Density

Symptoms Relieved: Fatigue, Dry Eyes, Dry Skin

Regulates mood, immune system, Improves Insulin Sensitivity


DHEA as an Antiaging Supplement shows Neither Meaningful Benefit nor Serious Adverse Effects

Reduces of atherosclerotic plaques; Inhibits Platelet Aggregation (Similar to Aspirin)

Inhibits Free Radical Formation- inhibits NF-kappaB-dependent transcription

Improves Sexual Function

Improves Skin Tone

Reduces Vulvar Vaginal Atrophy Postmenopausal with no Systemic Side Effects


DHEA as an Antiaging Supplement shows Neither Meaningful Benefit nor Serious Adverse Effects

Low levels associated with:

- All cause mortality, Cardiovascular mortality, Obesity, Type 2 diabetes
- Immune dysfunction, Autoimmune disease, Cancer, Hypertension, CV Disease
- Depression and loss of well-being, Low libido, Erectile dysfunction, Osteoporosis


FDA Approved DHEA Vaginal Insert

DHEA Insert indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.
7 Keto DHEA

Weight loss without side effects (Kalman)

- Improves Immune function; Useful in Raynaud’s, Autoimmune Dx.
- Decreases Estrone Levels by up to 50 % in 4-6 weeks
- Improves lipids
- Improves memory in rats
- Dose: 50-200 mg in AM

Myth: “No Credible Evidence Exists of the Value of Bioidentical Hormones.”

- No evidence of long term cognitive changes in therapeutic doses of “anti aging hormones”

No Evidence of Long Term Changes with Therapeutic Doses of “Anti Aging Hormones”

1. **Vitamin D**- Infections Dx Protection, CV Disease Risk (<25=2.5x risk), IBS, Ovarian Cancer, Dementia, Keloids
2. **Melatonin**- Free Radical Scavenger, Delays Aging, Anti-inflammatory, inhibits Tumor Growth, Hypertension, Neuroprotective
3. **Telomeres**- Deterioration accelerates aging, Anti neoplastic, Can restore organ function with Telemerase
4. **Pregnenolone**- Memory loss
5. **Aldosterone**- Hearing Loss, Balance, Tinnitus
References

**Vitamin D**

- Rosenau MJ. Experiments to determine mode of spread of influenza JAMA 1919, 73:311-313
- Urashima M et al. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr March 10, 2010 710
References

- **Melatonin**
References

Telomeres


• Marta Crous-Bou et al. Mediterranean diet and telomere length in Nurses’ Health Study: population based cohort study BMJ 2014; 349

References

• Journal “Psychiatric Annals” devoted entire issue in 2000:30(2)1-76
  • Reviewed Male Hypogonadism and Therapeutic Implications in Psychiatry
  • Effects of Estrogens on Mood and Cognition in Aging Women
  • The role of DHEA in Psychiatry
  • Use of Thyroid Hormones in Mood Disorders
  • Anti-glucocorticoid Medication for the Treatment of Depression

• Aldosterone
## Is it HORMONES?
**Ask Your Doctor Symptom Chart**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Adrenals</th>
<th>Estrogen</th>
<th>Testosterone</th>
<th>Thyroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
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<tr>
<td>Arthritis</td>
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<tr>
<td>Bladder Symptoms</td>
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<tr>
<td>Breakthrough Bleeding</td>
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<tr>
<td>Breast Tenderness</td>
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<tr>
<td>Cramps</td>
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<td>Decreased Sex Drive</td>
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<tr>
<td>Depression</td>
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<tr>
<td>Dry Skin/Hair</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Fibrocystic Breast</td>
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<tr>
<td>Fluid Retention</td>
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<tr>
<td>Hair Loss</td>
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<tr>
<td>Harder to Reach Climax</td>
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<tr>
<td>Headaches</td>
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<tr>
<td>Heavy / Irregular Menses</td>
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<tr>
<td>Hot Flashes</td>
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<tr>
<td>Irritability</td>
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<tr>
<td>Loss of Memory</td>
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<tr>
<td>Mood Swings</td>
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<tr>
<td>Night Sweats</td>
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<tr>
<td>Insomnia</td>
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<tr>
<td>Vaginal Dryness</td>
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<tr>
<td>Weight Gain</td>
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Do You Agree?

No Credible Evidence Exists on the Value of Bioidentical Hormones.

- Current evidence does/does not support the use of testosterone in older men with low testosterone levels.

- Evidence of the value of testosterone as an antiaging therapy does/does not exist.

- The long-term use of estrogens with or without progestins cause more/less risks than benefits.

- The long-term use of estrogens for the prevention of chronic conditions in postmenopausal women is/is not warranted.

Do You Agree?

No Credible Evidence Exists on the Value of Bioidentical Hormones.

- Current evidence supports/fails to support the efficacy of hGH as an anti aging therapy.

- DHEA as an antiaging supplement shows neither meaningful benefit nor serious adverse effects.

- There is/ or no evidence of long-term changes in therapeutic doses of “anti-aging hormones”

New FDA Approved Bioidentical Hormone Preparations

- **Estradiol-Progesterone Bioidentical Pill (1.0 mg/100 mg)**
  - Moderate to severe vasomotor symptoms due to menopause in women with a uterus.

- **Estradiol Vaginal Insert**
  - Indicated after menopause to treat moderate to severe painful intercourse.

- **Bremelanotide Injectable**
  - Indicated for acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women.

- **DHEA Vaginal Insert**
  - Indicated after menopause to treat vulvar and vaginal atrophy.
“We’ve visited with Folks w the PhD’s after their names.”
The Introduction to Bioidentical Hormones referenced

141 Peer Reviewed-Evidence Studies Cited

Fuss #1: Are BHRT Safer than Synthetics?
Fuss #2: You vs. Your Peers and BHRT:
   Can You Answer the Call?
Lucy and I Thank You For Inviting Us Today!
Take That Ya Lying Dog Faced Pony Soldier
The American Osteopathic Association of Rheumatic Diseases

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