Bioidentical Hormone Replacement as the “Standard of Care”

Hormone Myths vs. Scientific Evidence

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Objectives

1. Review the AMA Position Papers on Bioidentical Hormone Replacement

2. Present the Scientific Evidence for BHRT as the “Standard of Care.”

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

- 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.
- Current evidence fails to support the efficacy of hGH as an anti aging therapy
- 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
- DHEA as an antiaging supplement shows neither meaningful benefit nor serious adverse effects
No evidence currently suggests that custom CBHT formulations offer clinically relevant benefits.


PMCID: PMC3127562
American Association of Clinical Endocrinologists

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
Hypothalamus
Vasopressin
Oxytocin

Thyroid
Thyroid Hormones
Calcitonin

Thymus
Thymosins

Pancreas
Insulin
Glucagon

Liver
IGF-1

Pineal Gland
Melatonin
Epithalon

4 Parathyroid Glands
Parathormone

2 Adrenal Cortex
DHEA
Cortisol
Aldosterone

2 Kidneys
Erythropoietin

2 Testicles (Males)
Testosterone
Dihydrotestosterone (DHT)

2 Ovaries (Females)
Estrogens
Progesterone

Bio-identical Hormones
= human hormones (same molecular structure)
Non-Bio-identical Hormones

= synthetic derivatives of human hormones (different molecular structure)
True or False?

There Are No FDA Approved “Bioidentical Hormones.”

True or False?

There is no FDA Indication for Testosterone Use in Women.
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)
Just For Fun: “FDA Approved Treatment With “Credible Evidence” of Therapeutic Efficacy

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](http://www.huffingtonpost.com/2009/09/02/pfizer-pay-23b_n_275012.html)

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

“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.”
The AMA vs. Testosterone

- 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.

Testosterone supplements linked to heart attacks in new study

The New York Times

Don’t Ask Your Doctor About ‘Low T’

SANTA BARBARA, Calif. — A FUNNY thing has happened in the United States over the last few decades. Men’s average testosterone levels have

FDA

U.S. Food and Drug Administration

Protecting and Promoting Your Health

Drugs

FDA evaluating risk of stroke, heart attack and death with FDA-approved testosterone products

CBS EVENING NEWS

Testosterone supplements linked to heart attacks in new study

FORBES

FDA Evaluating Safety Of Testosterone Products

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

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;

Morgantaler vs Vigen

Conclusional: Delusional?
A Predetermined Outcome?

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

With T 5% Deaths vs. Without T 9% Deaths= T Caused Deaths?

YOU DON'T SAY
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."
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
Myth: Testosterone Causes 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


• Conclusion- Testosterone therapy in hypogonadal men does not increase the risk of prostate cancer.
Myth: Testosterone Causes 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.”


Testosterone and Depression

T has Antidepressant effect in Depressed Patients, esp. those w Hypogonadism.


Testosterone and Growth Hormone Improve Body Composition and Muscle Performance in Older Men

Supplemental T produced significant gains in lean mass, strength and aerobic endurance with significant reductions in whole body and trunk fat. GH further enhances outcome

Free & Total Testo => ↓ Alzheimer’s D.

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

Figure: 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)

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

Many levels within the ref. range

N = 434 consecutive male patients aged 50-86 yr

serum testosterone $\Rightarrow$ Mortality

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

SAFER when serum testo is in highest quartile

A man needs to have a serum testo $> \pm 600$ ng/dl

Insufficient testosterone levels $\Rightarrow$ Men die quicker

Mohr BA; Clin Endocrinol (Oxf). 2005 Jan;62(1):64-73

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

1. **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


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

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


- 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.
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.

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

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

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)


All Mortality with GH Use Decreased Post MI by Minimum 300%

“Current evidence fails to support the efficacy of hGH as an anti aging therapy.”
GH Improves Nutrition, QOL and CV Risk


GH, Longevity, and Efficacy of hGH as an Anti Aging Therapy

1. Increases albumin and prolongs survival in patients with chronic liver failure

2. Reduces neoplastic disease, modifies age-related pathology, increases life span

3. HGH is not associated with any increase in mortality.


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

1. Some degree of hypopituitarism is found in 35-40% of TBI patients.

2. Untreated TBI induced hypopituitarism contributes to the chronic neurobehavioral problems seen in many head-injured patients.

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.

The Elephant In The Room: Estrogen Causes Cancer
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
Estrone

Horse
Equilin

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

Transdermal E2 does not increase risk of VTE like oral E2

- 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 Replacement Prevents Alzheimer’s Disease

72% used Premarin® only

Hormonal Influence on Breast Cancer Risk

- Estrogen Excess
  - Oxidation of E₁, E₂
    - Lack of clearance
# 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

≠

Lawsuits
Provera® Prempro®
Yasmin®

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
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?

“Pimp” Question for the day:

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

What did it show?
Does Estrogen Cause Breast Cancer?

If you said “Women’s Health Initiative”
Then you are listening to gossip and propaganda
Open A Book, Your Eyes and Pay Attention
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
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<thead>
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<th>Vs.</th>
<th>E3N</th>
</tr>
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<td></td>
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<td>BHRT When Used in Balanced Combo – no increased risk</td>
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</table>
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

E2 plus progesterone: no increased risk of breast cancer!

Similar study: estradiol + progesterone 0.4; estradiol + synthetic progestin 0.94
Progesterone vs. Breast Cancer in menstruating women

6,000 women
5 yr. F/U

**Relative risk**

*Cl 95%*

of breast cancer

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
Estrogen, Progesterone and Breast Cancer

Never, Ever, Never, Ever Use Estrogen without Progesterone

Never, Ever

You All Have to Pinky Swear
PINKY SWEAR
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
HRT after breast cancer => ↓ mortality

Mortality

<table>
<thead>
<tr>
<th>Mortality (%)</th>
<th>Non hormone users (testosterone pellets, tamoxifen, &amp; progestogens)</th>
<th>Nonestrogen hormone users (testosterone, 45/50 + progestogens, often MDA)</th>
<th>Estrogen users (40/50 + progestogens, often MDA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 76 women with breast cancer</td>
<td>33.3% = 6/18 (n = 18)</td>
<td>12.5% = 1/8 (n = 8)</td>
<td>6% = 3/50 (n = 50)</td>
</tr>
</tbody>
</table>

Follow-up: 6 mo. to 10 yrs (mean = 4 yrs 2.5 mo.)
Follow-up: 2 to 11 yrs (mean = 6.0 yrs)
Follow-up 6 mo. to 32 yrs (mean = 6 yr 11.3 mo.)

Figure:
Estrogen replacement does not seem to increase either recurrences or mortality rates. Adding progestogens may even reduce recurrences.

Women with early breast cancer should be offered hormone replacement after full explanation (risks, benef., controv.).

Case Hx.-Breast cancer in remission x 2 years

(+) Hormone Sx Do you give hormones? Other options?

• Black cohosh

• Siberian rhubarb extract

Sweedish Sunflower Seeds

• Gabapentin, Clonidine, Paroxetine, Citalopram

Hormone options might include

• Vaginal Estriol 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)
Estrogen Use in the Presence of Breast Cancer

Estradiol is not completely contraindicated if Remission ≥ 2 years, (-) Mammo and clearance pathways have been evaluated.


Testosterone: For Males Only?

Testosterone- T is the most abundant active sex steroid in women throughout the female lifespan.

- Helps maintain muscle and bone strength, restores sex drive and libido.
- Improves overall feeling of well being, reduces “bad” cholesterol.
- Testosterone replacement leads to increase bone and muscle mass.
- Testosterone Deficiency leads to dry eyes, pale faces, thinning of inner 1/3 of eyebrow.

C. Dimitrakakis, J. Zhou, C.A. Bondy, Androgens and mammary growth and neoplasia, Fertility and Sterility, 77 (2002), pp. 26–33
**Myth: Testosterone's Only Role in Women is Sex Drive and Libido**

Pre and post-menopausal women, and aging men, experience symptoms of androgen deficiency:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphoric mood (anxiety, irritability, depression)</td>
<td>Sexual dysfunction</td>
</tr>
<tr>
<td>Lack of well being</td>
<td>Urinary complaints, incontinence</td>
</tr>
<tr>
<td>Physical fatigue</td>
<td>Hot flashes,</td>
</tr>
<tr>
<td>Rheumatoid complaints, pain,</td>
<td>Breast pain</td>
</tr>
<tr>
<td>Bone loss and Muscle loss</td>
<td>Changes in cognition, Memory loss, Insomnia</td>
</tr>
</tbody>
</table>

**Fact: Testosterone is essential for women's physical and mental health and wellbeing.**

More Myths: Testosterone and Women

1. Myth: Testosterone masculinizes females  Fact: T does not have a masculinizing effect on females.

2. Myth: Testosterone causes hoarseness and voice changes.  Fact: There is no evidence that T causes hoarseness or irreversible vocal cord changes in women.


4. Myth: Testosterone causes liver damage. Fact: Non-oral T does not adversely affect the liver or clotting factors.


Myth: Testosterone Increases the Risk of Breast Cancer

- 1268 pre and postmenopausal women
- 142/100,000 treatment groups
- 390/100,000 control groups

Fact: More than double the Risk of Breast Cancer W/O Testosterone

- $P < 0.001$

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 => Builds and protects against cortisol catabolism.

Decreases visceral & subcutaneous fat in elderly persons.

Reduces serum low density lipoprotein levels and body fat.

Improved Bone Density

Symptoms Relieved: Fatigue, Dry Eyes, Dry Skin

Regulates mood, Supports the immune system, Improves Insulin Sensitivity


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

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

- Inhibits Free Radical Formation-inhibits nuclear factor-kappaB-dependent transcription

- Improves Sexual Function

- Improves Skin Tone, Reduce 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

DHEA and Well-Ness (DAWN) Study.

Cognitive, life satisfaction and sexual function evaluated

- Healthy, normal cognitive
- Double blind placebo controlled with 50 mg daily of DHEA
- Increased testosterone (60%) and estrogen (40%) in women, not men
- No adverse effects

7 Keto DHEA

Weight loss without side effects (kalman)

- Improves Immune function; Useful in Raynaud’s, Autoimmune Dx.
- 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”

Hormone Therapies that ↑ Life span
Scientific Evidence

- Insulin
- Vasopressin
- Thyroid
- Cortisol
- Aldosterone
- DHEA
- Oxytocin
- Testosterone
- Estrogens

Growth hormone
IGF-1
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 Telomerase

4. **Pregnenolone, Estrogen, Progesterone, Testosterone, DHEA, Thyroid** - Lessen and/or prevent Psychiatric Disorders including Schizophrenia

5. **Aldosterone** - Hearing Loss, Balance, Tinnitus

(References at end of slide presentation)
Do You Agree? There is No Credible Evidence Exists on the Value of Bioidentical Hormones.

- 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.

- 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

- Current evidence 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
References Cited

In this Presentation 108 Peer Reviewed Studies Are Cited Refuting AMA Paper

In My Thyroid Module (available upon request) we cite 25 studies from peer reviewed medical journals.

A Grand Total of 133 “Non Credible” Evidence Published In Journals Endorsed by A Multitude of Mainstream Medical Societies
“Don't get your information from me, folks, or any newscaster. Get it from people with PhD after their names.”
Do You Agree?

Myth: There are no studies on bioidentical hormones.

Reality: Do you have the Scientific Evidence for BHRT as the “Standard of Care?”

Reality: Do You Now Have A Succinct Reference Source to the Age Old Refrain “My Doctor Says BHRT is No Good For Anything.”
You’re At The Watering Hole: DRINK!

Remaining Slides Contain References to:

Vitamin D

Melatonin

Telomeres

Sex Hormones and Psychiatric Disorders

Aldosterone
Lucy and I Thank You For Inviting Us Today!

Lucy and I Are Grateful For the Invitation and Chance To Speak Today.
Fact: Vitamin D and Infectious Disease

Vitamin D is an Effective in Preventing and Aborting the Spread of Influenza

Calcitriol induces production of human cathelicidin (LL-37) a polypeptide antimicrobial

LL-37 can fight bacterial and viral infections.

- Rosenau MJ. Experiments to determine mode of spread of influenza JAMA 1919, 73:311-313

Fact: Vitamin D and Infectious Disease

1. **1,25(OH)2D acts as an immune system modulator**

2. Prevents excessive expression of inflammatory cytokines and increases the 'oxidative burst potential of macrophages

3. Dramatically stimulates the expression of potent anti-microbial peptides, which exist in neutrophils, monocytes, natural killer cells, and in epithelial cells lining the respiratory tract.


Study: 1200 IU D3/day; Placebo, double blind, controlled

- Relative Risk getting Influenza A

- All treated children in study - .58  Not previously taking Vitamin D - .36 Started preschool > 3 y/o - .36

Urashima M et al. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr March 10, 2010710
Fact: Vitamin D and Cardiovascular Disease

- 18,000 men 45-75 without CV disease
- 10 year follow up
  - 25 (OH) < 15 ng/mL 2.5 x risk
  - 15-30 ng/mL 2.0 x risk
  - > 30 ng/mL 1.0

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

**Vitamin D References**


Rosenau MJ. Experiments to determine mode of spread of influenza JAMA 1919, 73:311-313

Urashima M et al. Randomized trial vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr March 10, 2010710 004.


Cannell, JJ. Vitamin D3 Treatment for Irritable Bowel Disease, [https://www.vitamindcouncil.org/blog/vitamin-d3-treatment-for-irritable-bowel-syndrome/](https://www.vitamindcouncil.org/blog/vitamin-d3-treatment-for-irritable-bowel-syndrome/)


Zhang X1, Nicosia SV, Bai W, Vitamin D receptor is a novel drug target for ovarian cancer treatment. Curr Cancer Drug Targets. 2006 May;6(3):229-44.

Myth: Melatonin is Only for Sleep

Fact: Manages circadian rhythm of inner clock - Controls sleep wake cycle

Low Melatonin associated with:

• Alzheimer's
• CV disease
• Insulin resistance
• Cancer
• Infectious disease
• Immune dysfunction
Fact: Melatonin is a Potent Free Radical Scavenger

1. More effective than Glutathione or Vitamin E
2. Protects Lipids, Protein, DNA, and against pro-oxidation effect of Fe
3. Protects DNA, Mitochondria from Injury,
4. Protects Against Ionizing Radiation
5. Aids Reperfusion of Ischemic Tissue
6. Inhibits tumor growth
7. Counteracts stress induced immunosuppression
8. Increases in CD4 cells, natural killer cells; Activates cytokine system,
9. Decreases pro-inflammatory cytokines

Nelson RJ Melatonin mediates seasonal changes in immune function Ann N Y Acad Sci 2000;917:404-15
Fact: Melatonin Delays Aging

Stimulates under basal immunosuppressive conditions

Anti-inflammatory under exacerbated immune response

Inflammation or autoimmune conditions.

Binds Free Radicals (Antioxidant)

Prolonged survival mice from 23.8 to 28.1 months; preserved youthful state


Fact: Melatonin Delays Aging, Decreases Visceral Fat

Melatonin prevented mitochondrial impairment associated with aging


Daily melatonin administration at middle age suppressed male rat intraabdominal visceral fat and plasma insulin to youthful levels.”

Wolden-Hanson T Daily melatonin administration to middle-aged male rats suppresses body weight, intraabdominal adiposity, and plasma leptin and insulin independent of food intake and total body fat Endocrinology 2000 Feb;141(2):487-97
Melatonin as an Analgesic

Chronobiotic, antioxidant, antihypertensive, anxiolytic and sedative

• Potent analgesic effects in a dose dependent manner.

• Fibromyalgia, irritable bowel syndrome, migraine

• Mechanism: melatonin receptors, opioid μ-receptors, GABA-B receptors, better sleep

Melatonin and Cancer

- Inhibits tumor growth in humans; Anti-mitotic activity, Downregulate activity of receptors

- Decreased Estrogen binding to cells in breast ca; Enhanced Immune Response, Free Radical scavenging, Anti-angiogenesis

- Improved outcome in glioblastoma, malignant melanoma, breast cancer
  - Used along with chemo, radiation, Protects against chemo/radiation toxicity
  - Large doses used 20-700 mg /day
Melatonin and Cancer

370 patient, with advanced solid CA, 20 mg orally at bedtime

• Chemotherapy alone vs chemo/melatonin

• Significant regression rate and survival in combination group

  • Lissoni P. Biochemotherapy with standard chemotherapies plus the pineal hormone melatonin in the treatment of advanced solid neoplasms. Pathol Biol (Paris). 2007 Apr-May;55(3-4):201-4

10 adjunctive or sole treatment studies of melatonin and solid tumors 1992-2003

• Melatonin reduced the risk of death at 1 year Relative risk: 0.66

• Conclusion: Great potential for melatonin and cancer therapy

Melatonin Facts

Protects Against:

Hypertension

B-Amyloid Formation

Stimulates Neural Stem Cell Proliferation in Hypoxic State

Counteracts Neurodegenerative Processes of Brain


Escames, G et al. The Role of Mitochondria in Brain Aging and the Effects of Melatonin Current Neuropharmacology, 2010, 8, 182-193
Melatonin Administration

1. Low dose lozenge - 2-3 hours before sleep: 0.3 mg SL

1. Combine 1-2 hours before bedtime:
   - Melatonin 3-30 mg
   - Magnesium Taurate 200-400 mg
   - Vitamin D 2000-5000 IU
AMA: “No Credible Evidence Exists of the Value of Bioidentical Hormones.”

Fact: Hormone optimization prevents Telomere shortening

Telomeres:

Region of repetitive nucleotide sequences (TTAGGG) at each end of the chromatid

• Protects the end of the chromosome from deterioration or from fusion with neighboring chromosomes

• Telomeres act as the cellular aging clock.

• Telomere loss is a Major Cause of Cellular Aging
Telomeres

Telomere length is dynamic and results from balance between:

– Erosion (Blackburn, 1991)

– Oxidative stress (Von Zglinicki, 2000)

– Restoration through telomerase activity, (Greider and Blackburn, 1985)

• Telomere length remains a key feature that indicates the viability of a cell.
Telomeres

Protects genomic integrity

• Prevents chromosome fusion

• Prevent genomic instability

• Necessary for cellular replication

• Protection from cellular senescence

• Protection from DNA mutations that can lead to cancer

Telomeres

Reverses some aspects of aging in old mice

– Brain, spleen and reproductive organs were rejuvenated
– Resulting in increased neurons and new viable sperm cells.
– Sense of smell returned.
– None of the mice developed cancer.

Telomere Length Determines Cellular Age

Somatic cells – Make up > 99% of the cells in the adult body – Have little or no telomerase and telomeres shorten as we age

• Telomere Length Shortening:
  – Conception: Telomeres start out 15,000 base pairs (bp) long.
  – By Birth the embryo has divided so many times that telomere length is down to 10,000 bp.
  – Over the rest of our lifetime we lose another 5,000 to 7,000 bp.
  – When telomere length gets to 3-5,000 bp, the genome is no longer protected from mutations, the cell can no longer divide, becomes senescent, metabolism slows down, and the cell dies.

Senescence-Associated Secretory Phenotype - inflammation
Telomeres Shorten When Cells Divide

"Short telomeres appear to be associated with increased risks for human bladder, head, neck, lung, and renal cell cancers”

• Fraternal twins with the shortest telomeres had a three times greater risk of death during the follow-up period than their co-twins with the longest telomere measurements


Chronic Diseases are Telomere Syndromes?

• Short telomeres are involved with almost all the diseases associated with aging

• Root cause of the disease?

What Can Be Done To Limit Telomere Shortening?

1. Limit inflammation
   a. Limit free radical damage
   b. Limit toxic environmental exposure

2. Restore Youthful Hormone Levels

3. Activate Telomerase

4. Lifestyle – Nutrition, Exercise, stress reduction, meditation

5. Nutraceuticals - Omega 3’s, resveratrol, Vitamin D

Limit Inflammation

Mediterranean Diet = Longer Telomeres

• Conclusion In this large study, greater adherence to the Mediterranean diet was associated with longer telomeres. P < .004

  Marta Crous-Bou et al. Mediterranean diet and telomere length in Nurses’ Health Study: population based cohort study BMJ 2014; 3 49

Exercise-VO2max associated with telomere length (3x/wk)


Limit Inflammation

**Stress Reduction**- Correlations between improvements in psychological distress, eating behavior, and metabolic health and increases in telomerase activity.

- Telomerase activity may be in part regulated by levels of both psychological and metabolic stress.

- Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study.

Cortisol and Telomeres

Greater cortisol responses to acute stressor associated with shorter telomeres

• Long-term consequences of frequent high stress reactivity include accelerated telomere shortening.


Depression associated with shortened telomeres.

• Shorter telomeres persist in individuals with lifetime depression

• CD8+ cytotoxic T cells and CD20+ B cells are particularly affected in depression.

Alexander Karampatziakis et al. Telomere shortening in leukocyte subpopulations in depression. BMC Psychiatry 2014, 14:192
Hormones and Telomeres

Androgen and Estrogen increase telomerase activity

- No effect from Cortisol
- Tamoxifen decreases telomerase activity

Lengthen Telomeres

Activate Telomerase – an endogenous enzyme that stabilizes telomere length by adding DNA repeats (TTAGGG) onto the telomeric ends of the chromosomes, compensating for the erosion of telomeres when cells divide.
Therapeutic Uses of Hormones in Psychiatry

- 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
- Antiglucocorticoid Medication for the Treatment of Depression
Severe hearing loss
=> -50% serum aldosterone within ref. range

SUBJECTS: 47 healthy men & women, ages of 58 & 84
RESULTS: people + severe hearing loss =>
• average about 1/2 serum aldosterone as their counterparts with normal hearing.
• aldosterone levels found in all the participants = considered normal
• direct link between blood levels of aldosterone & the ability of people to hear normally as they age. Depressed hormone levels => hurt hearing both in the inner ear & the part of the brain used for hearing

"The inner ear is especially sensitive to any disruption in potassium levels," said Robert D. Frisina, Ph.D., professor of Otolaryngology at the University of Rochester Medical Center and an adjunct professor at Rochester Institute of Technology. "We know that potassium levels in the inner ear seem to decrease as we age and that these falling levels play a role in age-related hearing loss, and we also know that blood levels of aldosterone generally decrease with age."
Need More Info?

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See Us at OMED on Oct 8, 2017 in Philadelphia
We will be presenting a 1 day workshop on BHRT