Introduction to Hormone Replacement

Hormone Myths vs. Scientific Evidence

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Introduction to Bioidentical Hormones

November, 2020 here! November, 2020

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

Disclosures

I Have No Conflicts of Interest Germane to this Lecture

- **Consultant:**

Nutrient Foods, Boston, MA.

Fuss # 1-You Prescribe Bioidentical Hormones?

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”

“HORMONES = CANCER”

What's All the Fuss # 1: Estrogen Causes 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

(2006, 2009, 2011)

http://www.menopause.org/docs/default-document-library/bioidenticalht_endosoc7FEEC6FE637F.pdf?sfvrsn=3799660e_2

Fuss # 1A-BHRT is "Safer" than Conventional HRT

- ***"No, they aren't."***
  - Tatnai Burnett, M.D.
    - https://www.mayoclinic.org/diseases-conditions/menopause/expert-answers/bioidentical-hormones/faq-20058460 *(Mayo Clinic Proceedings, Nov. 2019)*

- Little or no scientific or medical evidence supports claims that bioidentical hormones are safer or more effective than more traditional FDA-approved therapies.
  - The Endocrine Society, 2006, 2009 (http://www.menopause.org/docs/default-document-library/bioidenticalht_endosoc7FEEC6FE637F.pdf?sfvrsn=3799660e_2)

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

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AMERICAN COLLEGE OF ENDOCRINOLOGY

POSITION STATEMENT ON MENOPAUSE–2017 UPDATE

- **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

Rhoda H. Cobin and Neil F. Goodman (*2017*) AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT ON MENOPAUSE–2017 UPDATE. Endocrine Practice: July 2017, Vol. 23, No. 7, pp. 869-880.https://doi.org/10.4158/EP171828.PS

American Association of Clinical Endocrinologists-2017

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- **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*

- Cobin RH, Goodman NF; AACE Reproductive Endocrinology Scientific Committee. **AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT ON MENOPAUSE-2017 UPDATE.** Endocr Pract. 2017 Jul;23(7):869-880. doi: 10.4158/EP171828.PS.

Fuss # 1-BHRT is “Safer” than Conventional HRT

Specifically Cited:

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

(15) Eguale T, Buckeridge DL, Verma A, et al. Association of off-label drug use and adverse drug events in an adult population. JAMA InterMed. 2016;176(1):55-63.

Read the Study!-Admire Their Chutzpah!

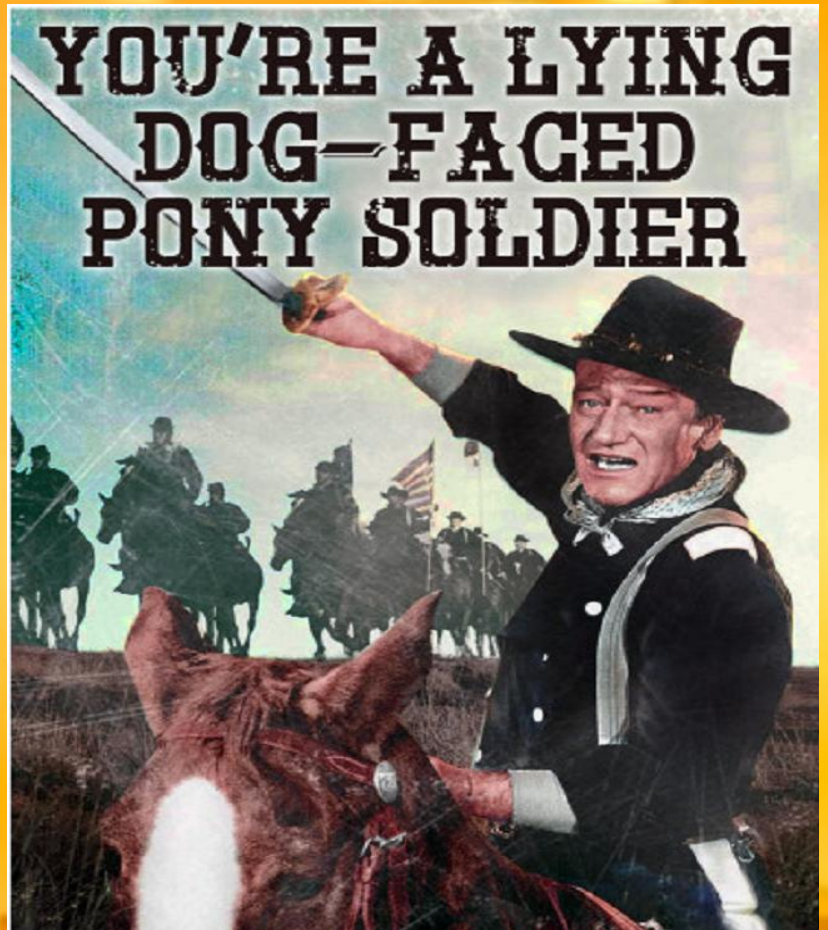
Design Setting: A cohort of 46,021 patients who received 151,305 incident prescribed drugs assembled from primary care clinics in Quebec, Canada.

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!



Mayo Clinic

No evidence currently suggests that BHRT formulations offer clinically relevant benefits.

Julia A. Files, MD, Marcia G. Ko, MD, and Sandhya Pruthi, MD, Bioidentical Hormone Therapy, *Mayo Clin Proc. 2011* Jul; 86(7): 673–680.

PMCID: PMC3127562

Fuss # 1B-They Do Not Love Us Out There

- **Marie Goes to the Endocrinologist-5/10/2017**

Ms. nas Hashimotos. She also probably has untreated OSA, which is likely the driver of her sympto complex. Overall, I feel Dr. Clearfield is a shaman, preying on the placebo effect and some modest clinica 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

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 cornary 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

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

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

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

Purdue Pharma Files for Bankruptcy-3/4/2019

Just for Fun : "FDA Approved Treatment With "Credible Evidence" of Therapeutic Efficacy

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.**
Propranol	**Stage Fright**

What's the Fuss 2?

AMA, 2009: "No Credible Evidence Exists on the Value of Bioidentical Hormones."

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.**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for "anti aging": A review of efficacy and safety. ***Report 5 of council on science and public health (A-09).*** **2009:1-17.**

AMA, 2009: "No Credible Evidence Exists on the Value of Bioidentical Hormones."

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"**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for "anti aging": A review of efficacy and safety. ***Report 5 of council on science and public health (A-09).*** **2009:1-17.**

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

https://clinicaltrials.gov/ct2/show/results/NCT00302731?term=bioidentical+hormones&rank=2&sect=X430126

Bioidentical 'Natural' Hormone Evaluation in Early Menopause

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

https://clinicaltrials.gov/ct2/show/results/NCT00302731?term=bioidentical+hormones&rank=2&sect=X430126

	Prempro .45mg Provera 1.5mg	Bi-est 2.6 mg Prog. 100mg	Estriol 2.5mg, Prog. 100mg	Estriol 2.5mg, Prog. 100mg
Cholesterol	221.5	221.5	223	165.5
Endometrial Thickness	13	10	2.5	3.1
Mammogram	0	0	0	0
Bone Density	0	0	0	0
Adverse Reactions	0	0	0	0

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

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**

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.***
  - https://www.webmd.com/drugs/2/drug-176851/bijuva-oral/details

AMA, 2009: "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.**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for "anti aging": A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

Benefits of Testosterone

1) **Antidepressant**
    1) Zarrouf, FA, Artz S., F=Griffith J, et al. Testosterone and Depression:Systematic review and meta-analysis. J. *Psychiatric Pract.* 2009 Jul;15(4):289-305.
2) **Increased muscle mass, strength, endurance, and increased exercise tolerance**
    1) Sattler FR, Castaneda-Sceppa C, Binder EF, et al. Testosterone Growth Hormone Improve Body Composition and Muscle Performance in Older Men. *J. Clin Endocrinol Metabol.* 2009 Jun;94(6):1991-2001.
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

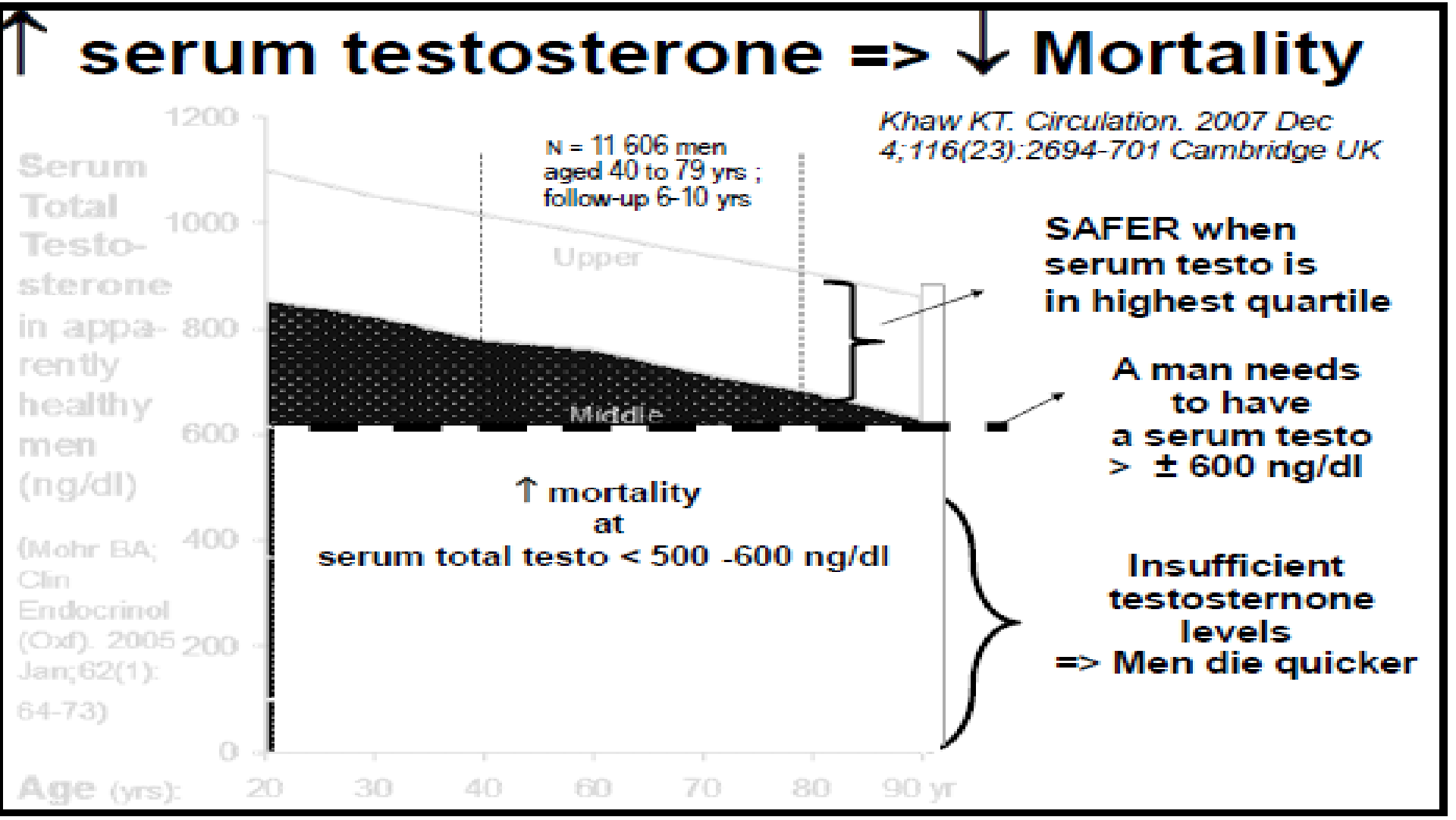
8. Decreases body fat
9. Maintains bone strength
10. Protects against osteoporosis
11. Reduced LDL cholesterol
12. Improves insulin sensitivity
13. Protects Against Diabetes
14. Involved in the making of protein and muscle formation
15. Improves oxygen uptake throughout the body
16. Needed for normal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

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

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.**
  - Vermeulen, A., "Androgen replacement therapy in the aging male---a critical evaluation," Jour Clin Endocrinol Metabol 2001; 86:2380-90.
  - Malkin, C., et al., "Low serum testosterone and increased mortality in men with coronary heart disease," Heart 2010; 96:1821-25
- **Men with coronary heart disease under age 45 have total and free testosterone levels significantly lower than controls.**
  - Turhan, S., et al., "The association between androgen levels and premature coronary artery disease in men," Coronary Artery Dis 2007; 18(3):159-62.

↑ serum testosterone => ↓ Mortality



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.**
  - Svartberg, J., et al., "Low testosterone levels are associated with carotid atherosclerosis in men," Jour Int Med 2006; 269(6):576-82.

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

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

*Men with total testosterone <300 ng/dL.
Adapted from Mulligan T, et al. Int J Clin Pract. 2006;60(7):762-769.

MMI METABOLIC MEDICAL INSTITUTE

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, A et al. Testosterone Therapy and Cardiovascular Risk:Advances and Controversies. Mayo Clin Proc. February 2015;90(2):224-251 18

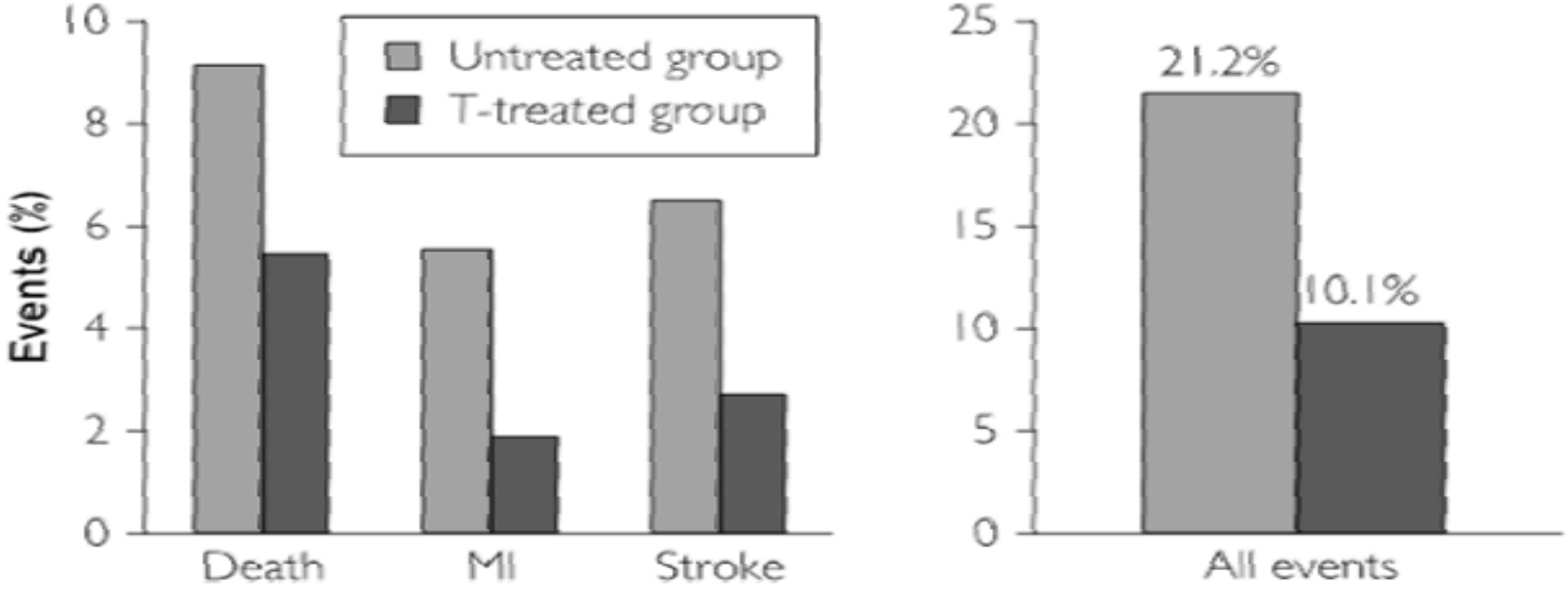

The New York Times
The Opinion Pages | OP-ED CONTRIBUTOR
Don't Ask Your Doctor About 'Low T'
By JOHN LA PUMA FEB. 3, 2014
SANTA BARBARA, Calif. — A FUNNY thing has happened in the United States over the last few decades. Men's average testosterone levels have
U.S. Food and Drug Administration
Protecting 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
By JONATHAN LAPOOK | CBS NEWS | January 29, 2014, 7:16 PM
TESTOSTERONE SUPPLEMENTS
FROM CBS NEWS
Forbes
FDA Evaluating Safety Of Testosterone Products
Larry Husten, Contributor
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.
LARRY HUSTEN'S POPULAR POSTS
MORE FROM LARRY HUSTEN

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**

Vigen R et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. JAMA. 2013 Nov 6;310(17):1829-36

Morgantaler vs Vigen



Morgantaler, A et al. Testosterone Therapy and Cardiovascular Risk:Advances and Controversies. *Mayo Clin Proc*. February 2015;90(2):224-251

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?

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

Craft, S; et. al. Androgen Effects on Cognitive Function, William Brenner Geriatric Research, Education and Clinical Center, VA Puget Sound Health Care System, Seattle, Washington, 2007

"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.**
  - Torkler, S., et al., "Inverse association between total testosterone concentrations, incident hypertension and blood pressure," Aging Male 2011; 14(3):176-82.

- **Low TT = ⬆ Mortality in CHF**
  - Guder, G., et al., "Low circulating androgens and mortality risk in heart failure," Heart 2010; 96:504-09.
  - Jankowska, E., et al., "Anabolic deficiency in men with chronic heart failure: prevalence and detrimental impact on survival," Circulation 2006; 114:1829-37.

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)**

Sher L , **Low testosterone levels may be associated with suicidal behavior in older men while high testosterone levels may be related to suicidal behavior in adolescents and young adults: a hypothesis.** Int J Adolesc Med Health. 2013;25(3):263-8. doi: 10.1515/ijamh-2013-0060.

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 Neuroscie; 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

Total SHBG	Total Testosterone
62% Decrease in Carotid Intimal Thickness	52% Decrease in Carotid Intimal Thickness

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

Golden SH, Maguire A, Ding J, Crouse JR, et al. Endogenous postmenopausal hormones and carotid atherosclerosis: a case-control study of the atherosclerosis risk in communities cohort. Am J Epidemiol. 2002 Mar 1;155(5):437-45.

Worboys S, Kotsopoulos D, Teede H, McGrath B, Davis SR. Evidence that parenteral testosterone therapy may improve endothelium-dependent and -independent vasodilation in postmenopausal women already receiving estrogen. J Clin Endocrinol Metab. 2001 Jan;86(1):158-61

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

- ***Memory***

- **Testosterone plays a major role in brain function.**
  - Filova, Barbora & Ostatníková, Daniela & Celec, Peter & Hodosy, Julius. (2013). The Effect of Testosterone on the Formation of Brain Structures. Cells, tissues, organs. 197. 10.1159/000345567.

- **Low bioavailable T is a positive predictor of memory loss in men as they age.**
  - Morley, J., et al., "Potentially predictive and manipulable blood serum correlates of aging in the healthy human male: progressive decreases in bioavailable testosterone, dihydroepiandrosterone sulfate, and the ratio of insulin-like growth factor 1 to growth hormone," Proc Natl Acad Sci USA 1997; 94:7537-42.

- **Low TT = Memory Loss**
  - **Flood, J., et al., "Age-related decrease of plasma testosterone in SAMPS mice: replacement improves age-related impairment of learning and memory," Physiol Behav 1995; 57:669-73.**

Testosterone and Alzheimer's Disease

- **Dementia, Tremor and Gait Dysfunction Attributed to Low T**
  - Okun, MS;, Delong, MR, Hanfelt, J. et al. Plasma testosterone levels in Alzheimer's and Parkinson Diseases Neurology. 2004; (62(3):411-3 Gainesville, Fl.

- **Low bioavailable T = Correlate B memory loss/Alzheimer's Dx**
  - Chu, L., et al., "Bioavailable testosterone is associated with a reduced risk of amnestic mild cognitive impairment in older men," Clin Endocrinol 2008; 68:589-98.

- **Even subclinical androgen deficiency expresses amyloid-B-related peptides in vivo.**
  - Gillett, M., et al., "Relationship between testosterone sex hormone binding globulin and plasma amyloid beta peptide 40 in older men with subjective memory loss or dementia," Jour Alzheimer's Dis 2003; 5:267-69.

↑ Free & Total Testo => ↓ Alzheimer's D.

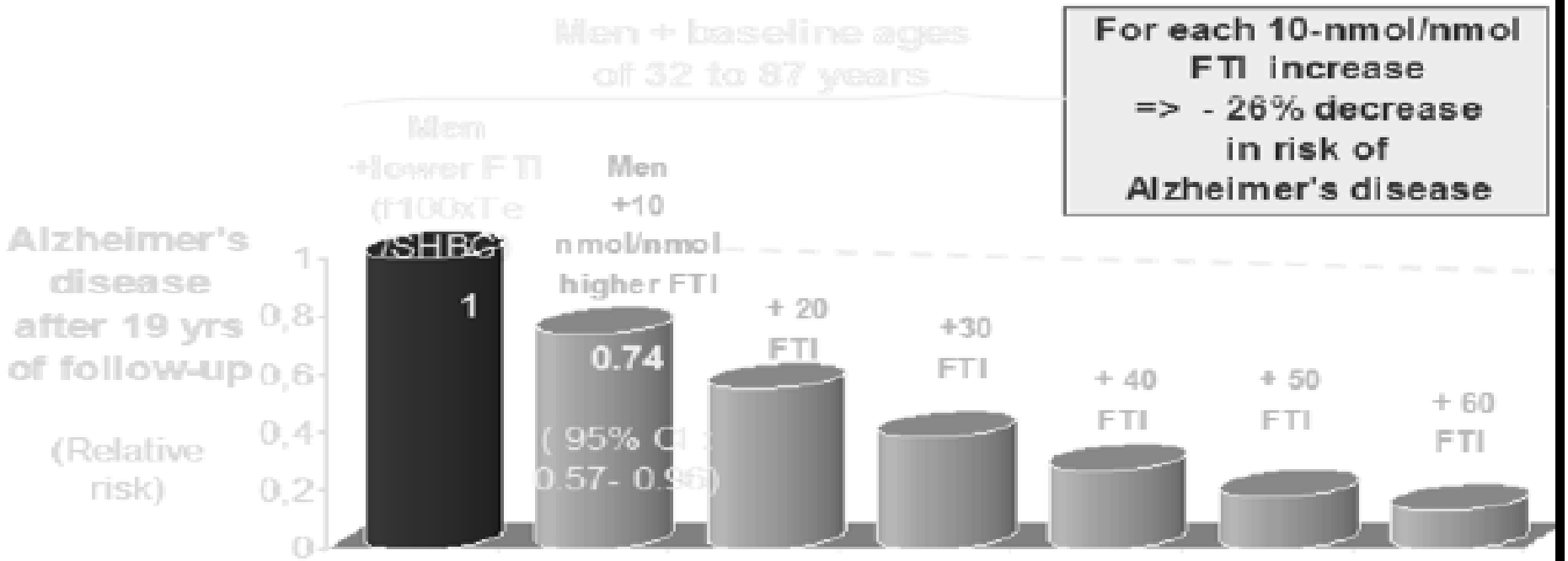


Figure: Increases in the FTI were assoc. w/ a decreased risk of Alzheimmer's disease Calculated free testosterone conc. were lower in men who developed Alzheimer disease, & this difference occurred before diagnosis

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

Moffat SD, Zonderman AB, Metter EJ, Kawas C, Blackman MR, Harman SM, Resnick SM. Free testosterone and risk for Alzheimer disease in older men. : Neurology. 2004 Jan 27;62(2):188-93

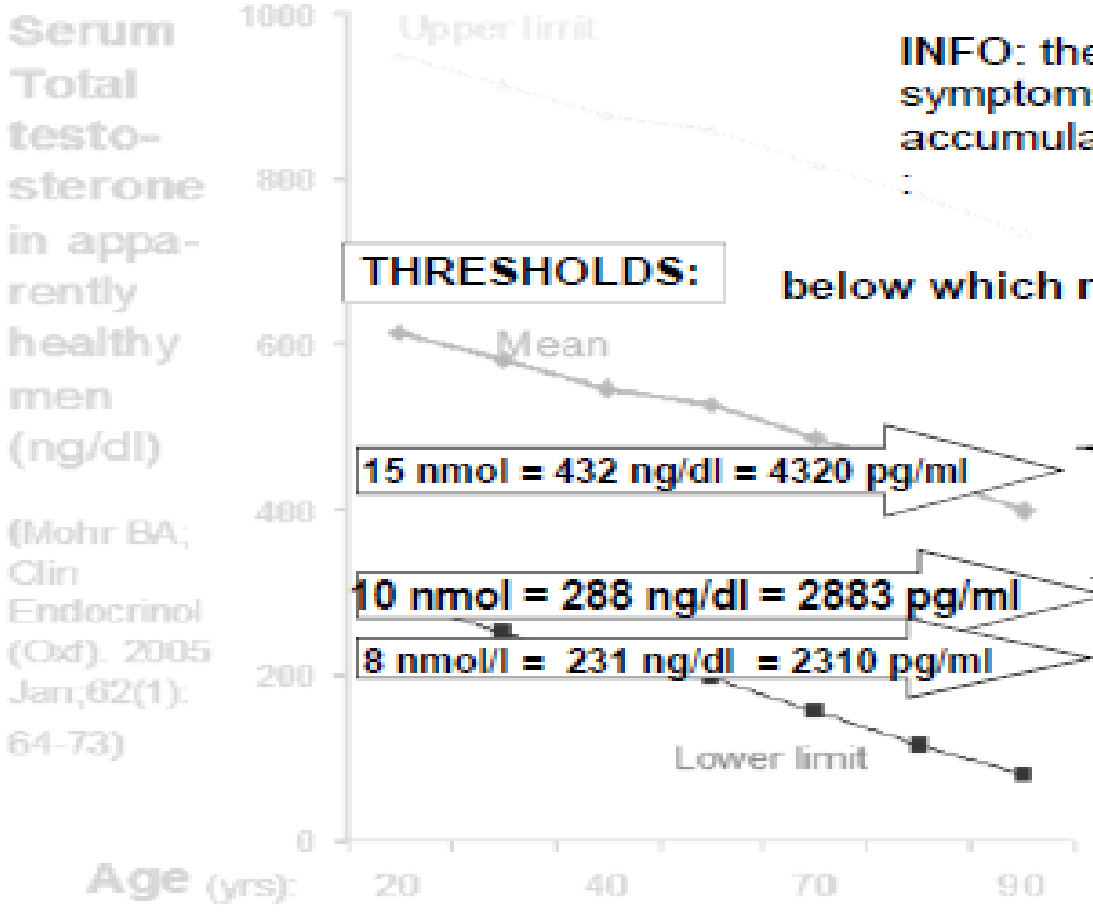
Testosterone's Effects on Behavior

Testo **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
- Loss of vigor
- Loss of libido

10 nmol = 288 ng/dl = 2883 pg/ml
- Depression &
- Diabetes mellitus type 2 (also in nonobese men)

8 nmol/l = 231 ng/dl = 2310 pg/ml
- Erectile dysfunction

Many levels within the ref. range

N = 434 consecutive male patients aged 50-86 yr

Zitzmann M, et al. J Clin Endocrinol Metab. 2006 Nov;91(11):4335-43

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%)

Van Kesteren PJ, Asscheman H, ...Gooren LJ. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clin Endocrinol (Oxf). 1997 Sep;47(3):337-42. Harvard Medical School, Boston n=13

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.

Endogenous Sex Hormones and Prostate Cancer: A Collaborative Analysis of 18 Prospective Studies Endogenous Hormones and Prostate Cancer Collaborative Group . **J Natl Cancer Inst 2008 100: 170-183 51**

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.**"

Rhoden E et al. "Medical Progress: Risks of Testosterone Replacement Therapy and Recommendations for Monitoring." **N Engl J Med** 2004; Jan 29; 350:482-492

• Bassil et al, "The benefits and risks of testosterone replacement therapy: a review," **Therapeutics and Clinical Risk Management** 2009: 5 427-448

•Morgentaler A Testosterone therapy and prostate risks: where's the beef**? Can J Urol.** 2006 Feb;13 Suppl 1:40-43

William Clearfield D.O.
F.A.A.F.R.M, F.A.A.M.A. , D.A.B.M.A.

April 26, 2018

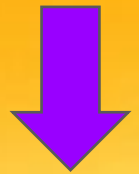
GYN Recommendation NOMA Winter 2020 Lecture

BEFORE TESTOSTERONE:

Vasomotor symptoms?	HRT/Lifestyle changes
Dyspareunia?	Lubricants, moisturizers, low-dose vaginal Estrogen, DHEA
Incontinence?	Pelvic floor PT, devices, medication
Pelvic Pain?	Treatment, medication, therapy
Depression/anxiety?	Psychotherapy, counseling, meds
Relationship conflict?	Counseling, sex therapy
Medications?	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

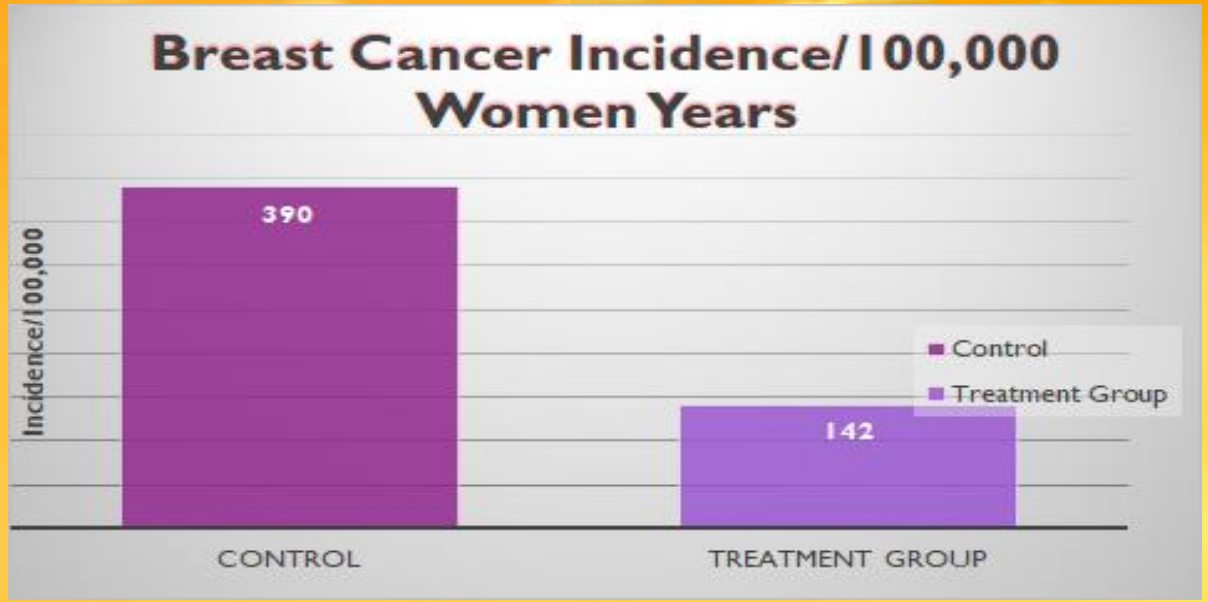
Testosterone and Urinary Incontinence

- **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).**

Kim MM[1], Kreydin EI[2,] **The Association of Serum Testosterone Levels and Urinary Incontinence in Women.** J Urol. 2018 Feb;199(2):522-527. doi: 10.1016/j.juro.2017.08.093. Epub 2017 Aug 26.

Testosterone and Breast Cancer Risk

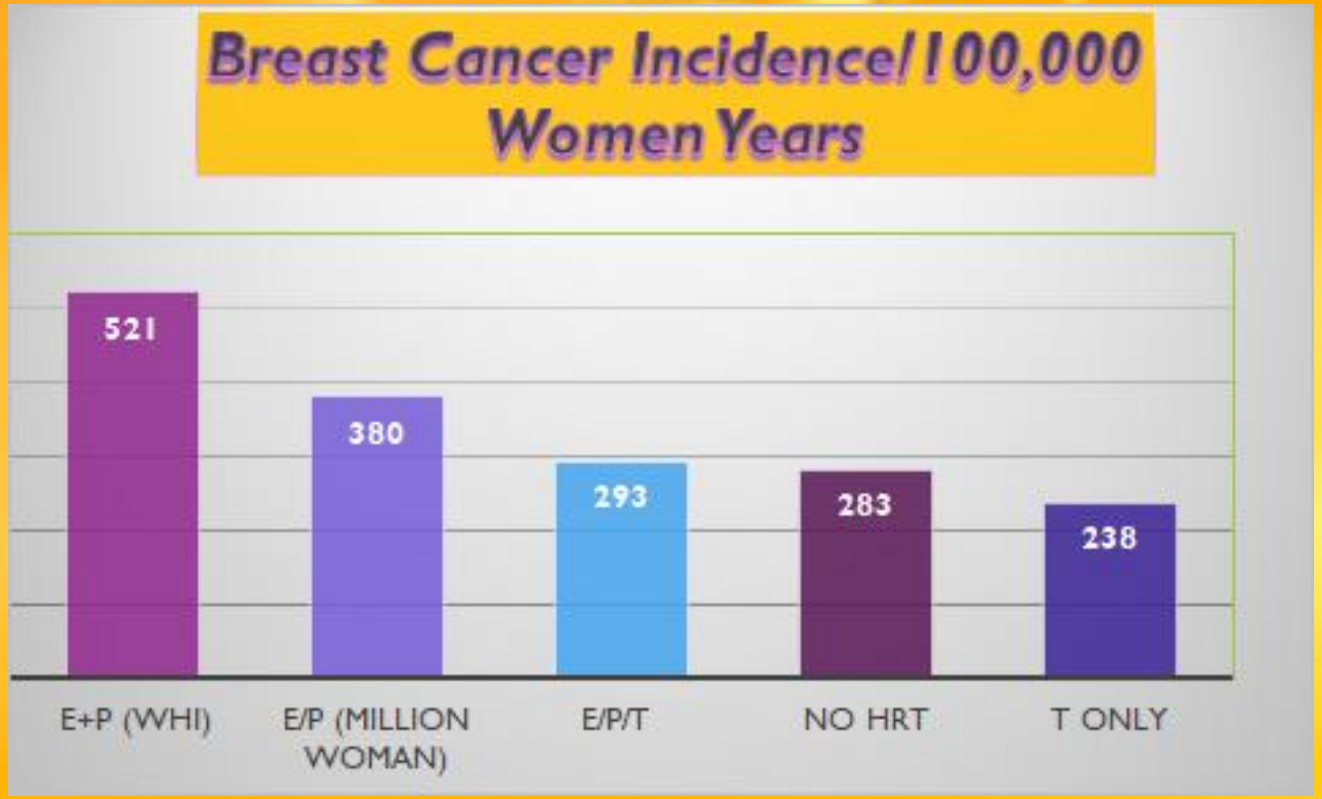


2.75X Risk of Breast Cancer Without Testosterone P < 0.00

Glaser and Dimitrakakis. Reduced Breast cancer incidence in women treated with subcutaneous testosterone, or testosterone with anastrozole: a prospective, observational study. Maturitas 2013 Dec;76(4): 342-9

Dimitrakakis C, Jones RA, Liu A, Bondy CA. Breast cancer incidence in postmenopausal women using testosterone in addition to usual hormone therapy. Menopause. 2004 Sep-Oct;11(5):531-535

Lowest Risk of Breast Cancer is in T Treated Patients



Dimitrakakis C, Jones RA, Liu A, Bondy CA. Breast cancer incidence in postmenopausal women using testosterone in addition to usual hormone therapy. Menopause. 2004 Sep-Oct;11(5):531-535.

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," *Opthalmology Times,* November 15, 2015

- **Chronic Pain in Fibromyalgia-**White, H.,Robinson T.; "A novel use for testosterone to treat central sensitization of chronic pain in fibromyalgia patients," *International Immunopharmacology*, Volume 27, Issue 2, August 2015, Pages 244–248

- **Chronic Non Radicular Low Back Pain-**Dubick MN, Ravin TH, Michel Y, Morrisette DC; Use of localized human growth hormone and testosterone injections in addition to manual therapy and exercise for lower back pain: a case series with 12-month follow-up, *Dove Press*, 23 June 2015 Volume 2015:8 Pages 295—302

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

Rudman D, Feller AG, Cohn L, Shetty KR, Rudman IW, Draper MW. Effects of human growth hormone on body composition in elderly men. Horm Res 1991;36 Suppl 1:73-81

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

Positive Results

- 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

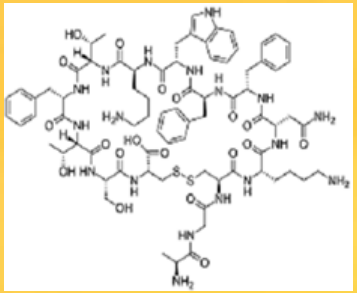
Sexual function in women

- 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.

t.

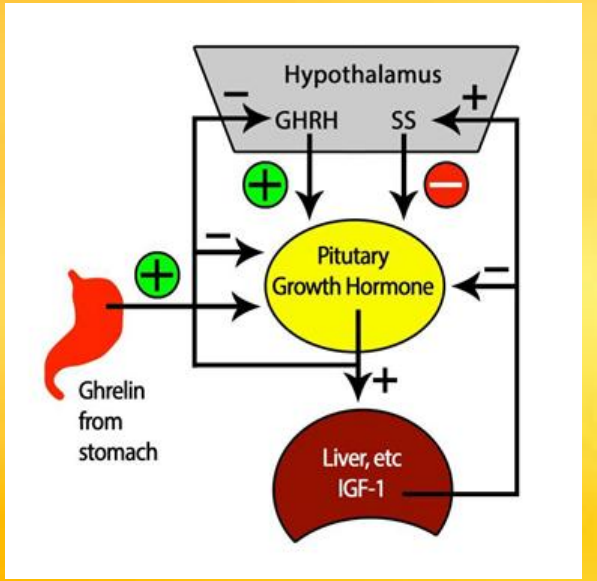


Picture a Legos ™ model snapped together to make a windmill or a car.

GH Prime Directive: Stimulate cell and growth reproduction.

Growth Hormone Physiology

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

Sufficient GH

Enhances:

Cardiovascular function

Reduces Il-1, Il-6, cRP

Concentration

Memory

Mental stability

In deficiency: OCD, paranoia

Dark moods

Impulse control

Sense of reality

Executive Function

Energy

Low GH

- ***Memory***
- ***Concentration***
- ***Mental clarity***
- ***OCD***
- **Paranoia**
- **Poor Concentration**
- **Impulse Control**
- **Anxiety**
- **Lack of Socialization**
- **Inability to Plan**
- **Dark Moods**
- ***Inability to Switch B Tasks***

“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)
2. **Decrease in Oxidative Stress** (free radical formation) **by 50%** Evans LM, Davies JS, Anderson RA, Ellis GR, Jackson SK, Lewis MJ, Frenneaux MP, Rees A, Scanlon MF. The effect of GH replacement therapy on endothelial function and oxidative stress in adult growth hormone deficiency. Eur J Endocrinol. 2000 Mar;142(3):254-62. Section of Endocrinology,Diabetes and Metabolism, University Hospital of Wales, Cardiff, UK.
3. **Increases thyroid & androgen activities, but decreases cortisol.** 1) Vierhapper H, Nowotny P, Waldhausl W. Treatment with growth hormone suppresses cortisol production in man. Metabolism 1998 Nov;47(11):1376-8 ; 2) Rodriguez-Arnao J, Perry L, Besser GM, Ross RJ. Growth hormone treatment in hypopituitary GH deficient adults reduces circulating cortisol levels during hydrocortisone replacement therapy. Clin Endocrinol (Oxf) 1996 Jul;45(1):33-7 ; 3) Weaver JU, Thaventhiran L, Noonan K, Burrin JM, Taylor NF, Norman MR, Monson JP. The effect of growth hormone replacement on cortisol metabolism and glucocorticoid sensitivity in hypopituitary adults. Clin Endocrinol (Oxf) 1994 Nov;41(5):639-48 ; 4) Carani C, Granata AR, De Rosa M, Garau C, Zarrilli S, Paesano L, Colao A, Marrama P, Lombardi G.The effect of chronic treatment with GH on gonadal function in men with isolated GH deficiency. Eur J Endocrinol 1999 Mar;140(3):224-30 ; 5) Belgorosky A, Martinez A, Domene H, Heinrich JJ, Bergada C, Rivarola MA .High serum sex hormone-binding globulin (SHBG) and low serum non-SHBG-bound testosterone in boys with idiopathic hypopituitarism: effect of recombinant

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.

Kozlowski O et al. Growth hormone replacement therapy in patients with traumatic brain injury. Neurotrauma. 2013 Jan 16.

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

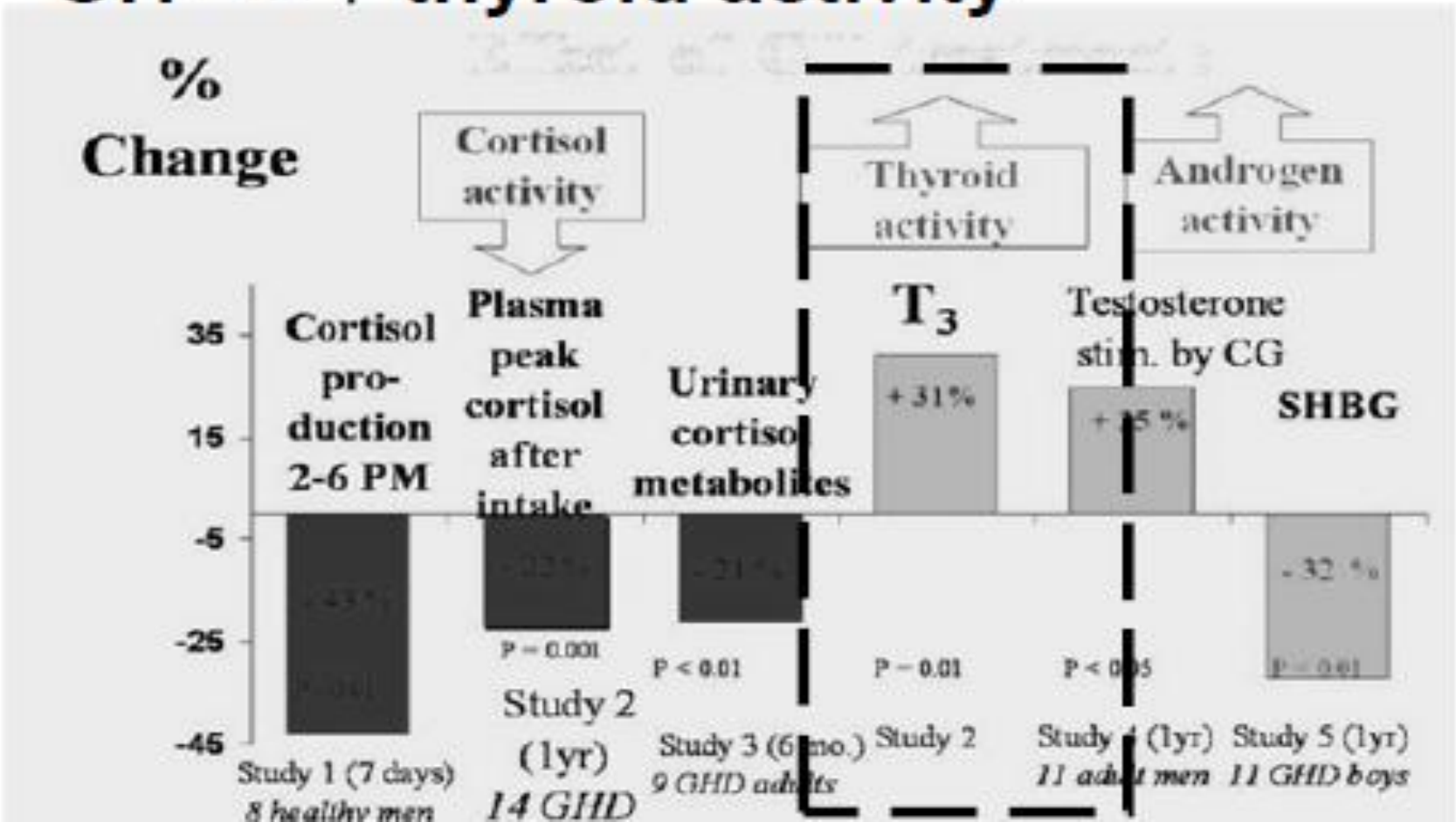
Rothman MS, The neuroendocrine effects of traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2007 Fall;19(4):363-72.

Behan LA et al. Neuroendocrine disorders after traumatic brain injury. J Neurol Neurosurg Psychiatry. 2008 Jul;79(7):753-9

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



GH therapy => prolongs life (↓ the increased mortality of) in GH deficient patients

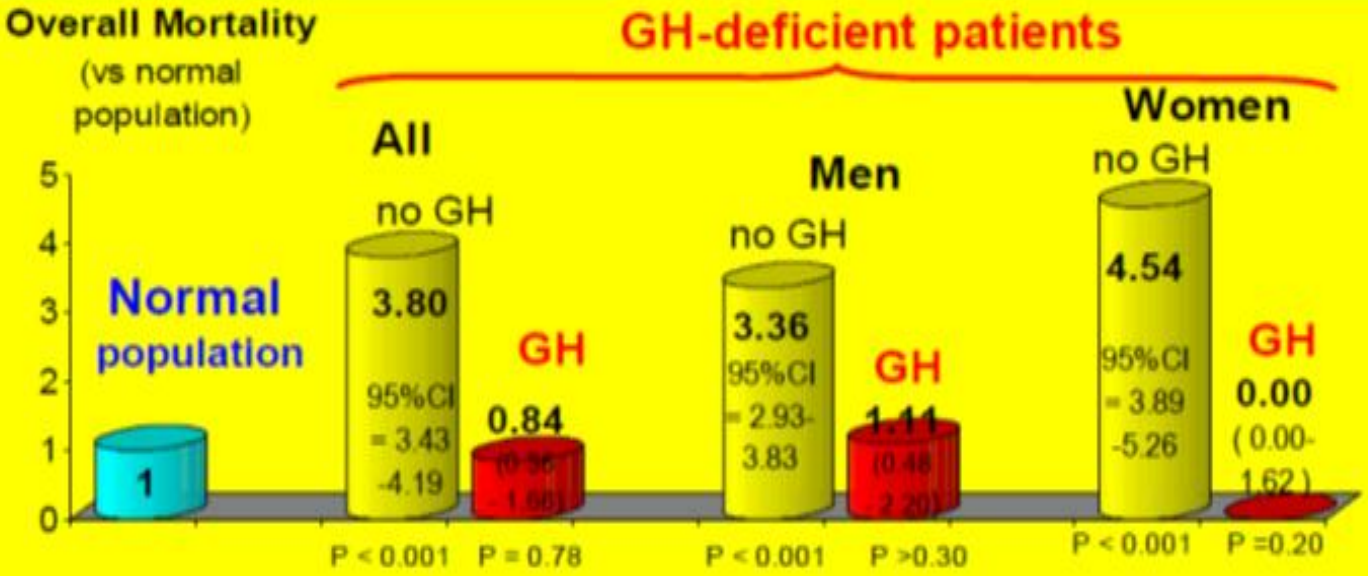


Figure: Overall mortality & the rate of myocardial infarctions were increased in hypopituitary patients without GH replacement, GH replacement normalized the risk.

J. Svensson, B.-Å. Bengtsson, T. Rosén, A. Odén, G. Johannsson. Malignant Disease and Cardiovascular Morbidity in Hypopituitary Adults with or without Growth Hormone Replacement Therapy . J Clin Endocrinol Metab. 2004 Jul;89(7):3306-12

Ah Ha! I Should Have Had A V-8”

“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

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
-

- Cook, D. Yuen, K, et. al., Medical Guidelines for Clinical Practice for Growth Hormone Use in GHD Adults and Transition Patients. American Academy of Clinical Endocrinologists, 2009

-

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
2. Agha A. Phillips J. Thompson C.J. Hypopituitarism following traumatic brain injury (TBI) Br. J. Neurosurg. 2007;21:210–216.
3. Kelly DF, McArthur DL, Levin H, et al. Neurobehavioral and quality of life changes associated with growth hormone insufficiency after complicated mild, moderate, or severe traumatic brain injury. *J Neurotrauma.* 2006 Jun;23(6):928-42.
4. Leon-Carrion J, Leal-Cerro A, Cabezas FM, et al. Cognitive deterioration due to GH deficiency in patients with traumatic brain injury: a preliminary report. *Brain Inj.* 2007 Jul;21(8):871-5.
5. Rothman MS, The neuroendocrine effects of traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2007 Fall;19(4):363-72.
6. Behan LA et al. Neuroendocrine disorders after traumatic brain injury. J Neurol Neurosurg Psychiatry. 2008 Jul;79(7):753-9

TBI and Growth Hormone Deficiency

Memory

Concentration

Mental clarity

OCD

Dark moods

Paranoia

Poor Concentration

Anxiety

TBI and Growth Hormone Deficiency

Rapid weight gain

Excessive anxiety

Depression along

Poor overall physical health and quality of life

Deficits in:

Attention

Executive Functioning

Cognitive, Mental
Ability to Achieve Goals

Memory

Emotion

Mood Anxiety/Depression

Growth Hormone Deficiency vs. Autism

S/S of GH Deficiency	Autism
Repetitive behaviors	Repetitive Behaviors
Avoids Emotional Rec./Eye Contact	Avoids Emotional Rec. /Eye Contact
Aggression/Agitation	Aggression/Agitation
Hyperactivity/ Impulsivity	Hyperactivity/Impulsivity
Anxiety/Stress/Depression	Anxiety/Stress/Depression
Mood swings	Mood swings/ “Meltdowns.”
OCD	OCD
Self-injurious behavior	Self-injurious behavior
Balance/Coordination	Balance/Coordination
Communication Deficits/Delays	Communications Deficits/Delays
Executive Function Impairment	Executive Function Impairment
Seizures	Seizures
Social Skills Impaired, Delayed	Social Skills Impaired, Delayed

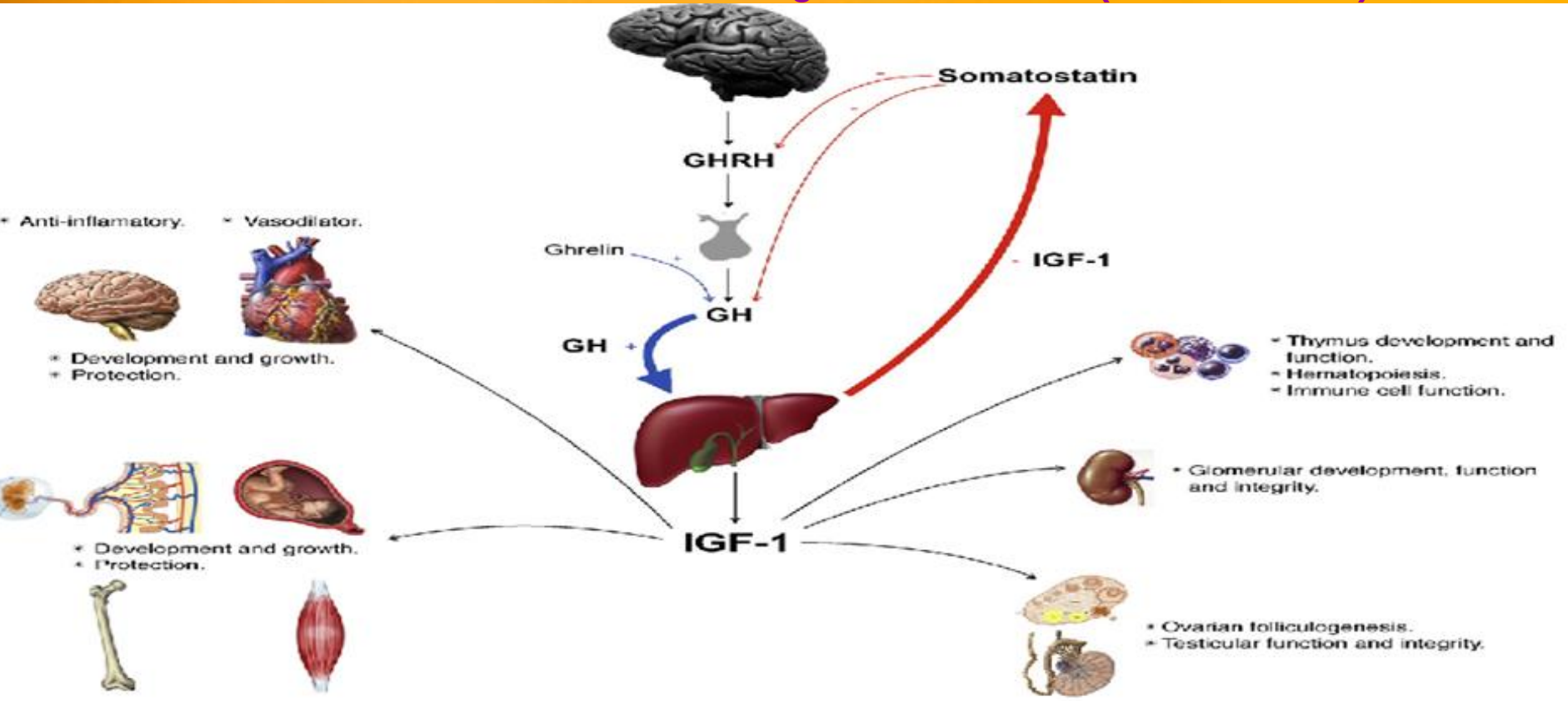
IGF-1 and the Brain

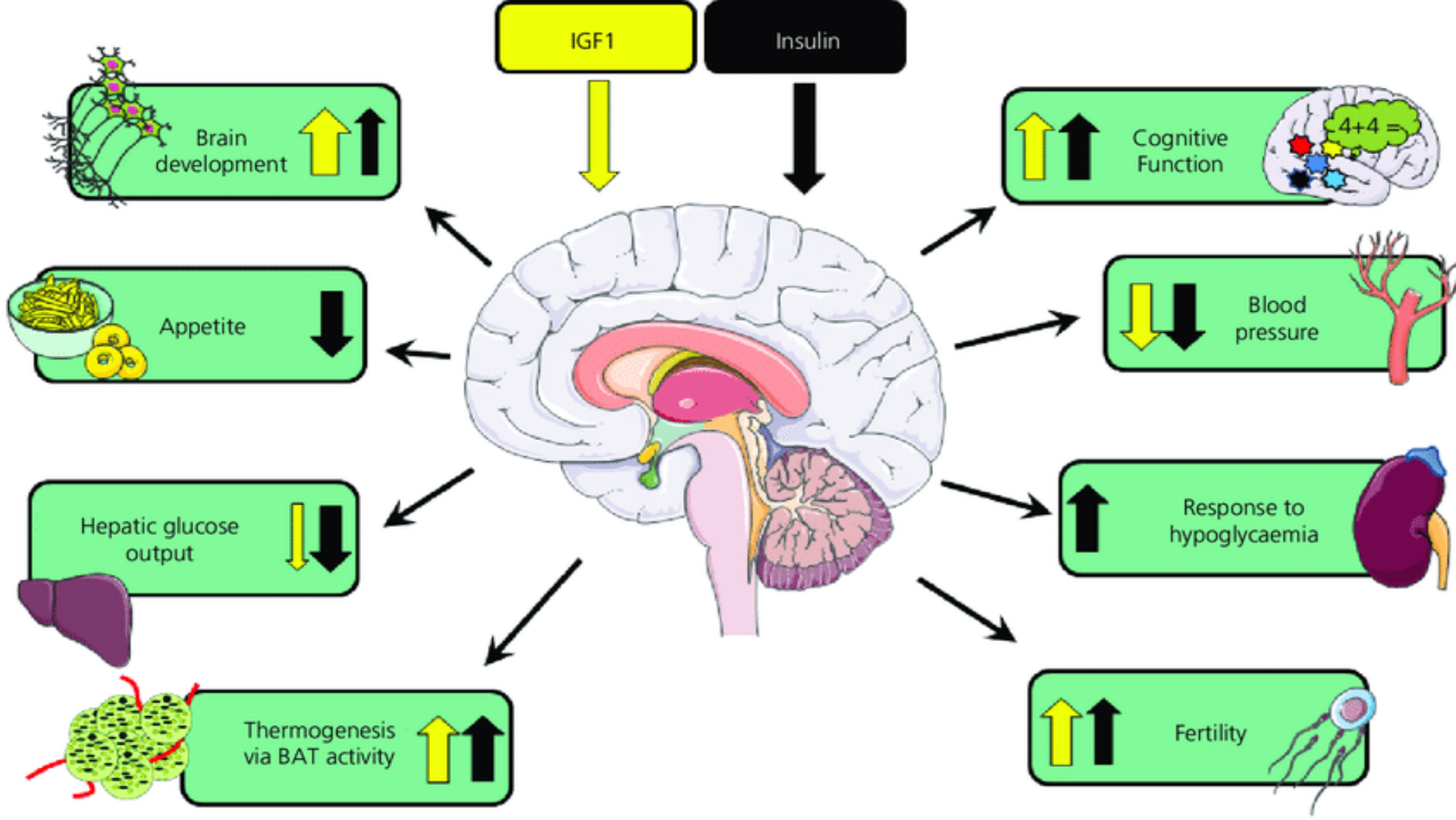
- IGF1 expression levels decrease w aging
- Low-dose IGF1 treatment = ⇧ neurons.
- Promotes adult hippocampal neurogenesis
- **Exercise neurogenesis effect** mediated through IGF1 signaling

- .*Fernandez AM, Torres-Aleman* The many faces of insulin-like peptide signaling in the brain *Nat Rev Neurosci. 2012 Mar 20; 13(4):225-39.*

Growth Hormone Physiology

Liver must convert GH to end-organ usable IGF-1 (IGF-2 Prenatal)




IGF1
Insulin
Brain development
Appetite
Hepatic glucose output
Thermogenesis via BAT activity
Cognitive Function
4+4 =
Blood pressure
Response to hypoglycaemia
Fertility

Sign. Inverse Assoc. of serum IGF-1 & Obesity

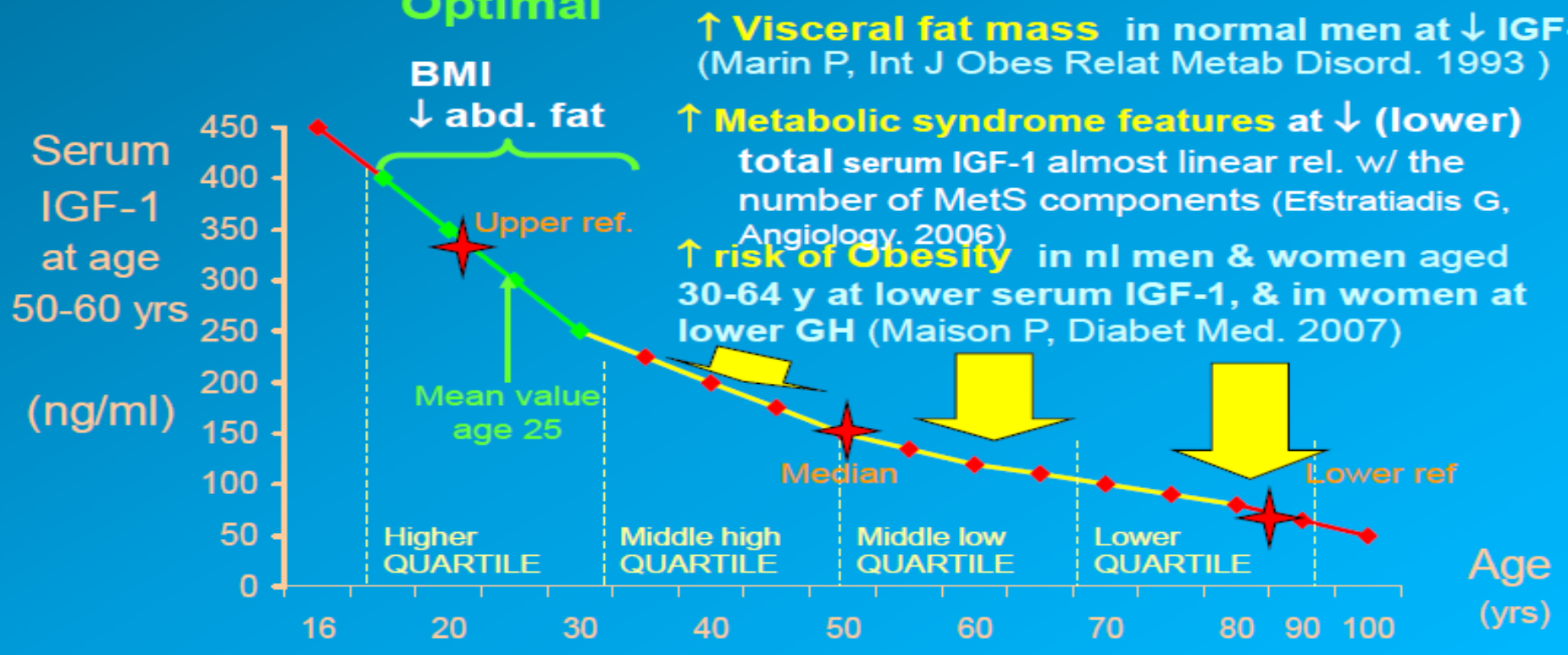
↑ **Body mass index** in normal boys at various stages of puberty & young adulthood (7-27 yrs) at lower 24-h serum GH & serum IGF-1 (Martha PM, J Clin Endocrinol Metab. 1992)

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

↑ **Visceral fat mass** in normal men at ↓ IGF-1 (Marin P, Int J Obes Relat Metab Disord. 1993)

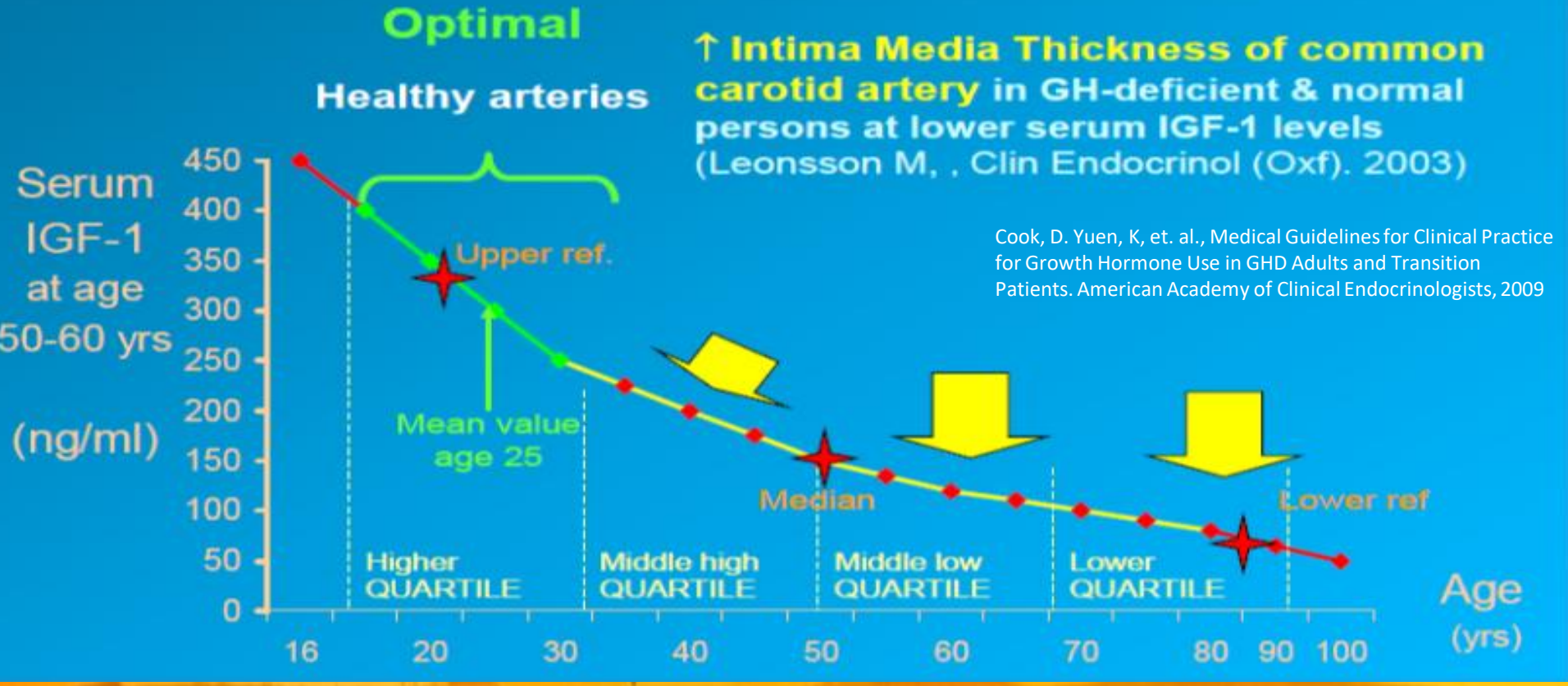
↑ **Metabolic syndrome features** at ↓ (lower) **total** serum IGF-1 almost linear rel. w/ the number of MetS components (Efstratiadis G, Angiology. 2006)

↑ **risk of Obesity** in nl men & women aged 30-64 y at lower serum IGF-1, & in women at lower GH (Maison P, Diabet Med. 2007)



Sign. Inverse Ass. of serum IGF-1 & Atherosclerosis

GHD Patients = 9-fold incidence of cardiovascular mortality



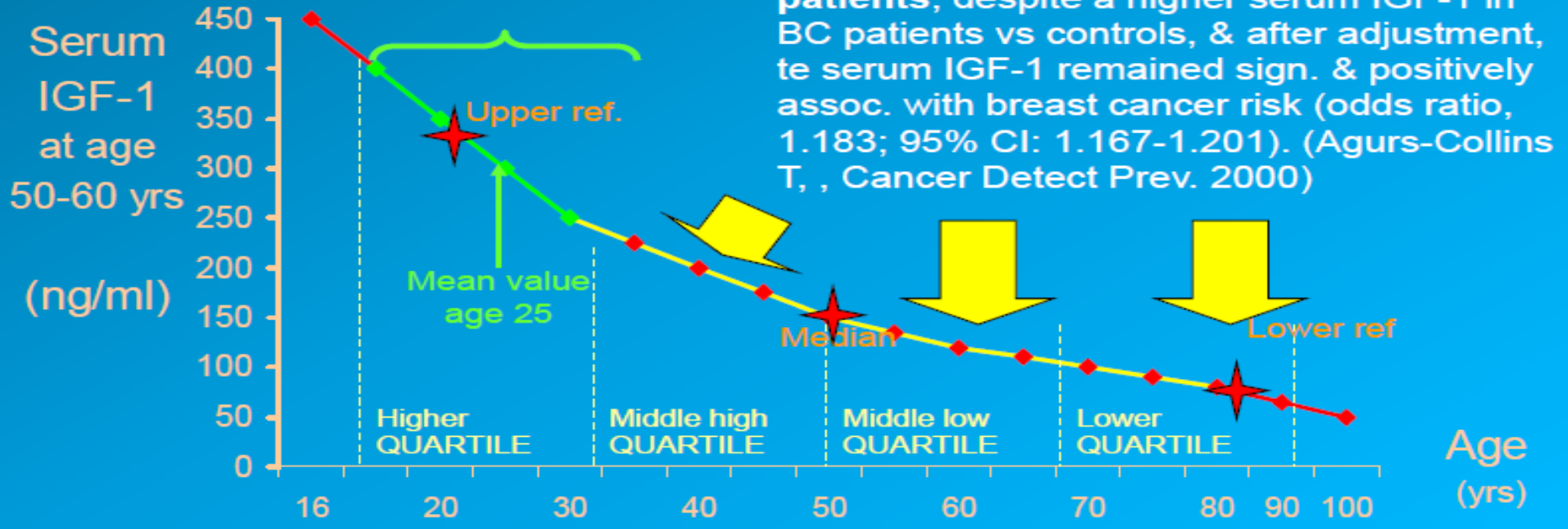
Cook, D. Yuen, K, et. al., Medical Guidelines for Clinical Practice for Growth Hormone Use in GHD Adults and Transition Patients. American Academy of Clinical Endocrinologists, 2009

Sign. inverse Assoc. of serum IGF-1 & Cancer stage

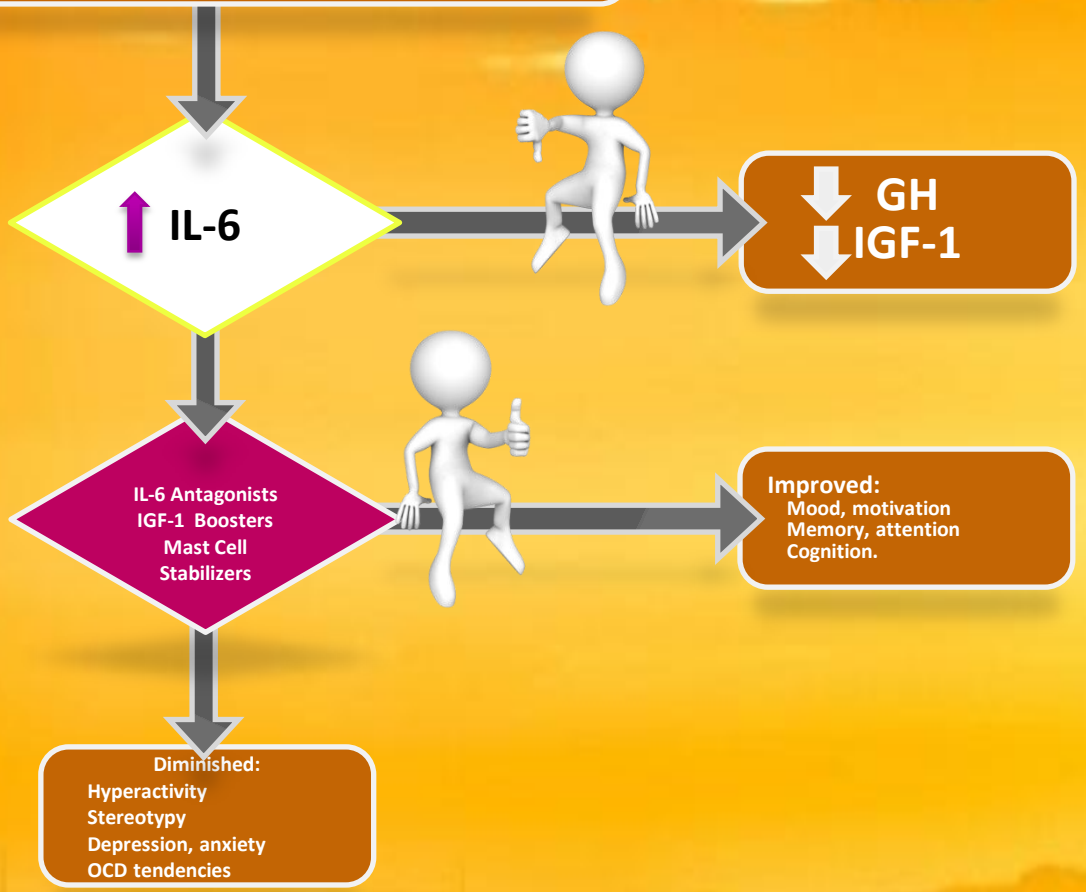
OPTIMAL

- 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, te serum IGF-1 remained sign. & positively assoc. 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



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

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**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for “anti aging”: A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

Estrogen Has 400 Functions Increases:

Heart/Circulation

Metabolic Rate
Artery Size
Blood Flow to Brain
HDL

Neuro Effects

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

Reproductive System

Libido
Sexual Performance
Preparation for Pregnancy
Breast Growth/Density

Miscellaneous

Bone Density
Insulin Sensitivity
Skin Thickness

Estrogen Has 400 Functions Decreases:

Heart/Circulation

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

Neuro Effects

Depression
Anxiety
Irritability
Pain Sensitivity
Alzheimer's beta amyloid peptides
Risk of PTSD

Reproductive System

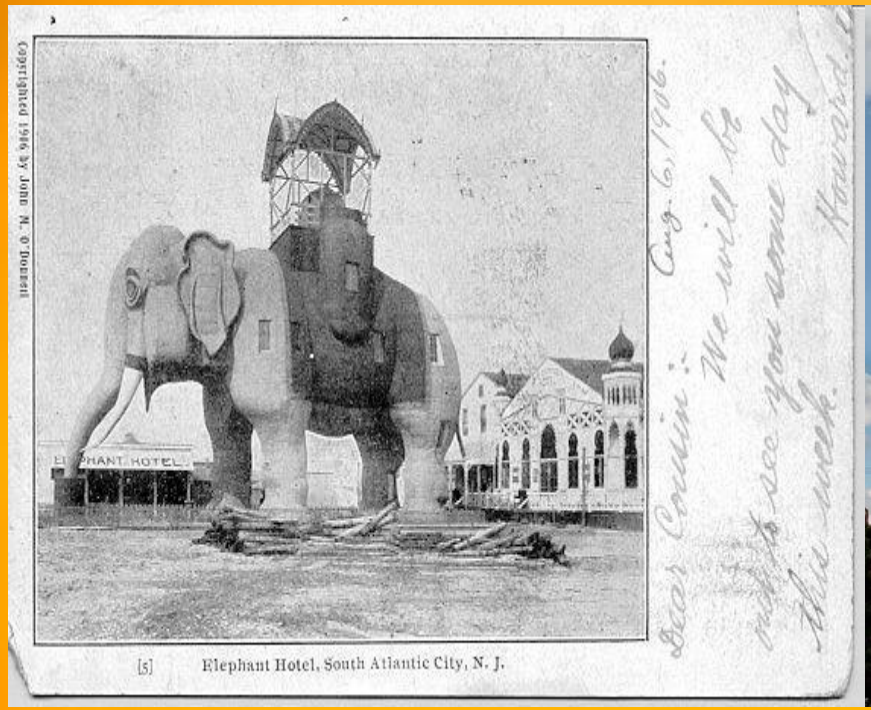
Sexual Dysmorphia
Vaginal Dryness

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."

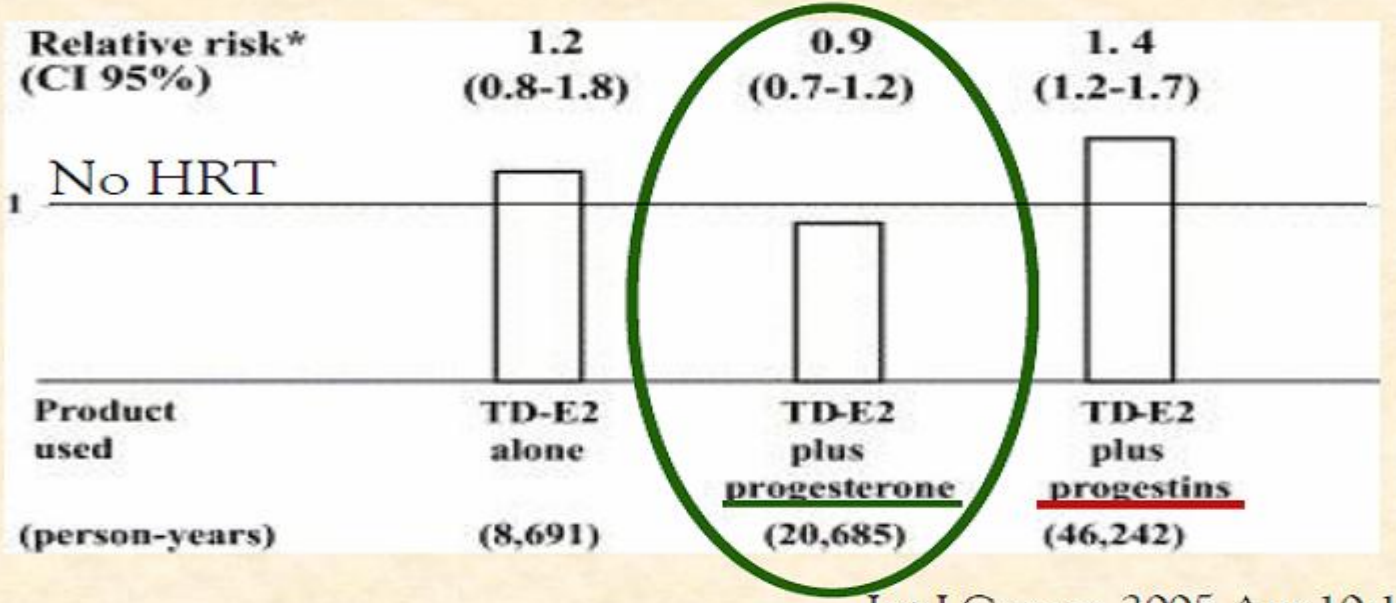
Endocrine Society Position Paper on BHRT

http://www.menopause.org/docs/default-document-library/bioidenticalht_endosoc7FEEC6FE637F.pdf?sfvrsn=3799660e_2

E3N-EPIC Study

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

TD-E2 = transdermal estradiol



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

E2 plus progesterone: no increased risk of breast cancer!

Similar study: estradiol + progesterone 0.4; estradiol + synthetic progestin 0.94
Espié, Gynecol Endocrinol. 2007 Jul;23(7):391-7.

WHI Vs. E3N

# of women receiving “hormone” treatment

WHI = 13,816

WHI – no Bioidentical hormone used

•Estrogen alone (CEE) both studies showed increase risk

Progestin’s in both studies showed GREATER risk

# of women receiving “hormone” treatment

E3N = 29,420

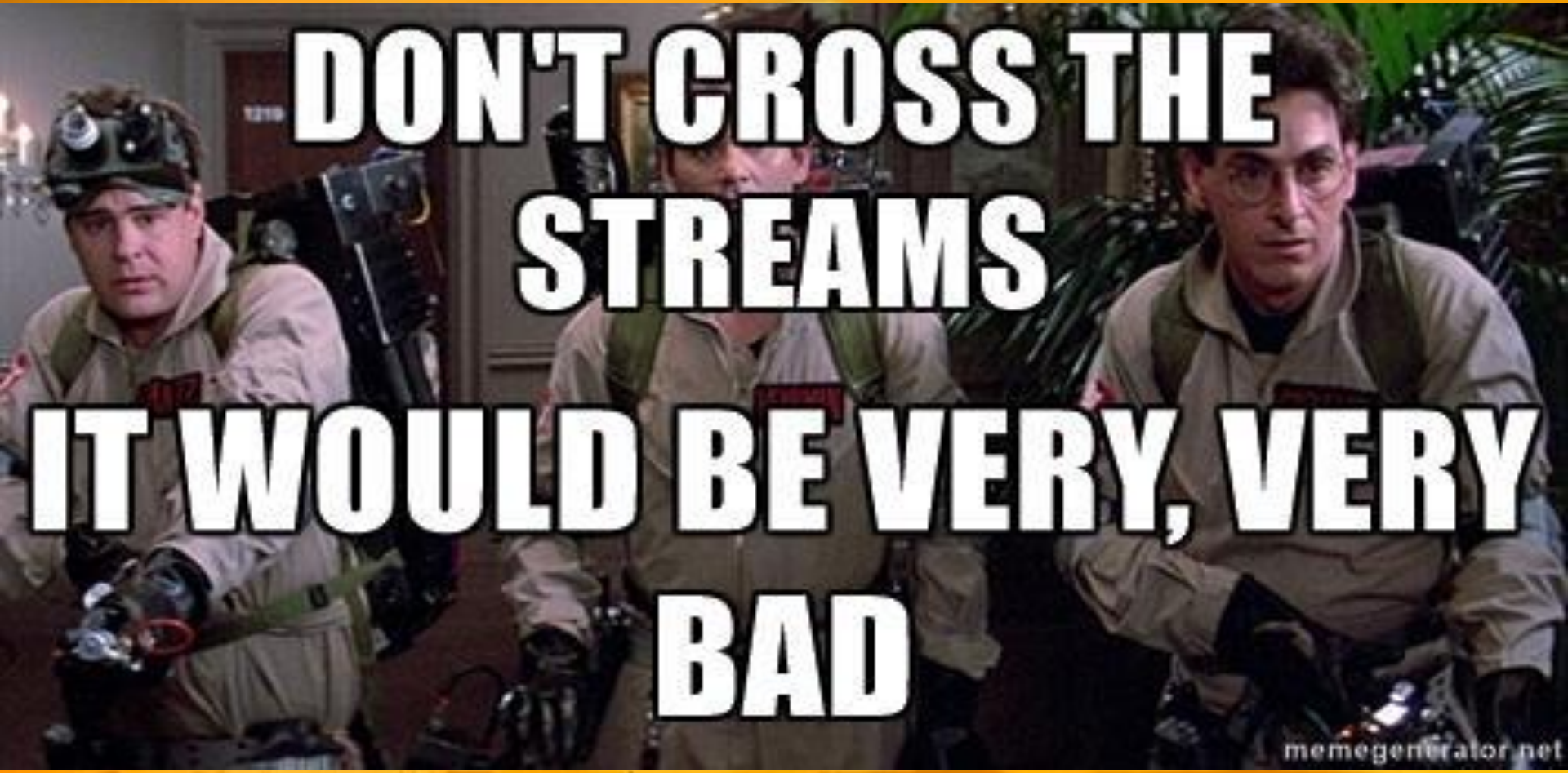
E3N – Bioidentical and CEE + Progestins used

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 Postmenopusal Women=

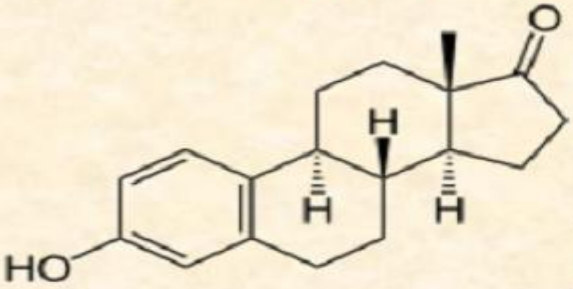


2002 WHI Study—"HRT" is Dangerous!

- 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!

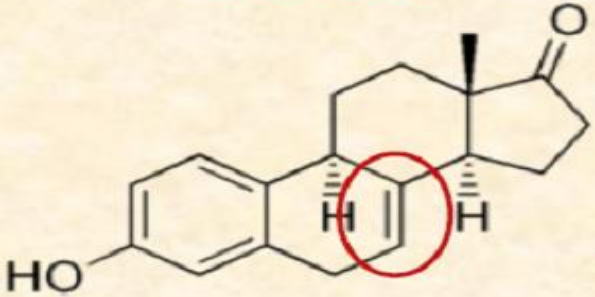
Premarin®
Conjugated Equine Estrogens

Human



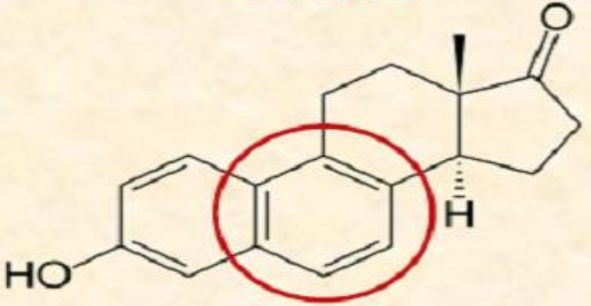
Estrone

Horse



Equilin

Horse



Equilenin

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

Klein R The Composition of Premarin. 1998 Int J Fertil 43:223

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.

  Parker WH, Womens Health (Lond Engl). 2009 Sep;5(5):565-76
- **Youthful hormone levels protect** women from these diseases.

Estradiol Restoration

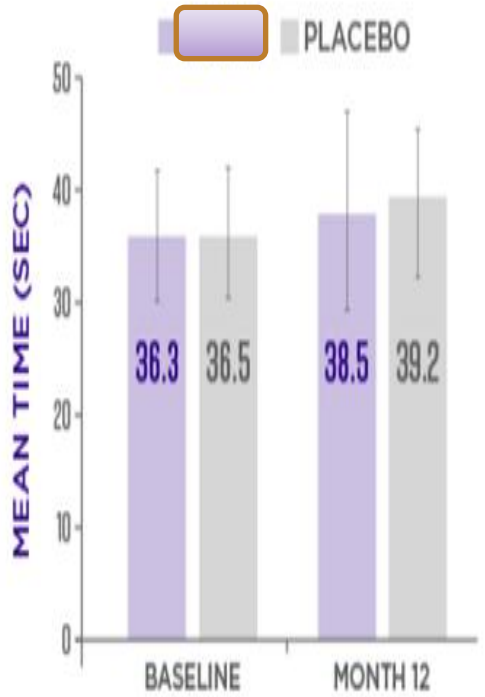
- Protects against heart disease, dementia and osteoporosis.
- Improves insulin sensitivity—prevents diabetes
- Eliminates hot flashes, restores sleep
- Restores cognitive function and mood
- Maintains thickness, fullness of skin and hair
- Maintains genital/pelvic health-helps with vaginal lubrication,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

Estradiol vs. Cardiovascular Disease

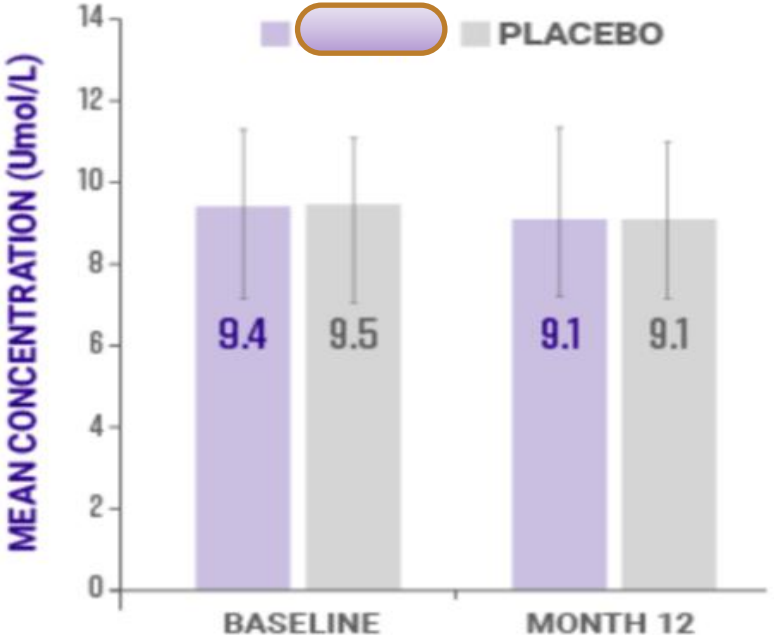
- Prevents the oxidation of LDL
- Improves lipid profile
- Reduces lipoprotein (a)
- Reduces blood pressure
- Improves endothelial function
- Reduces plaque formation
- Improves insulin sensitivity

FDA approved Estradiol-Progesterone Pill
DOES NOT ALTER COAGULATION FACTORS

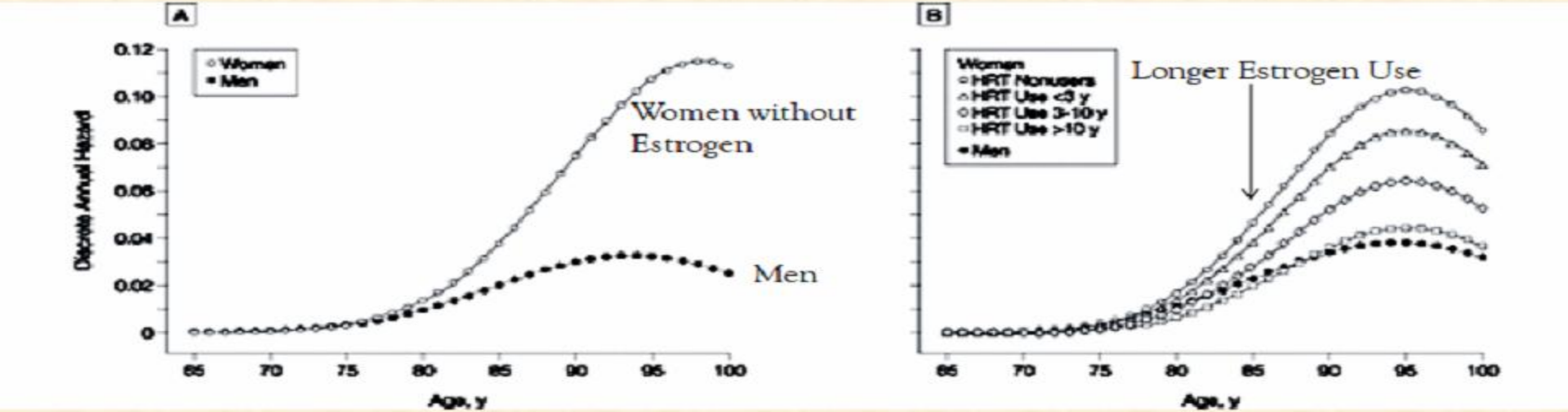
ACTIVATED PARTIAL THROMBOPLASTIN LEVELS WITH [redacted] COMPARED WITH PLACEBO[5]



FIBRINOGEN LEVELS WITH [redacted] COMPARED WITH PLACEBO[5]



Estrogen Replacement Prevents Alzheimer's Disease



72% used Premarin® only

Zandi PP, et al., Cache County Study. JAMA. 2002 Nov 6;288(17):2123-9.
RR 0.46 in Kawas C, The Baltimore Longitudinal Study of Aging. Neurology 1997;48:1517-1521
RR 0.65 Paganini-Hill A, Arch Intern Med 1996;156:2213-2217.
RR 0.4, Tang M-X, Lancet 1996;348:429-432.

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)

• Mueck AO. Et al. Postmenopausal hormone replacement therapy and cardiovascular disease: the value of transdermal estradiol and micronized progesterone. Climacteric. 2012 Apr;15 Suppl 1:11-7

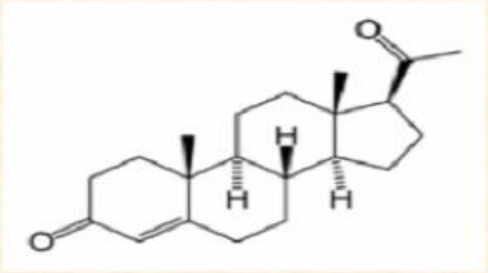
Estrogen Dominance

- 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



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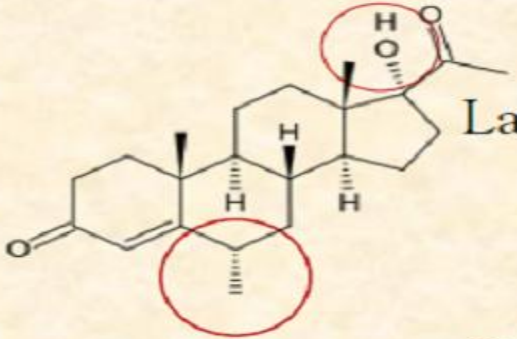
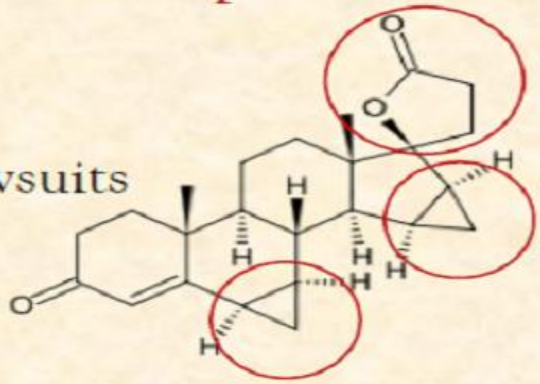


Provera® Prempro®

Lawsuits



Yasmin®

Confusion:

Progestins are often called "progesterone", in the media and in scientific papers!

Scientific studies show that:

Provera®	≠	Progesterone
• Causes birth defects		• Maintains pregnancy
• Can cause depression		• Improves mood
• Insomnia, irritability		• Improves sleep
• Fluid retention		• Diuretic
• Raises blood sugar		• No effect on blood sugar
• Counteracts estrogen-induced arterial dilation		• Maintains estrogen-induced arterial dilation
• Worsens lipid profile		• Improves lipid profile
• Causes heart attacks		• No evidence of ↑ CVD
• Increases estrogenic stimulation of breasts		• Reduces estrogenic stimulation of breasts
• **Causes breast cancer**		• **Prevents breast cancer**

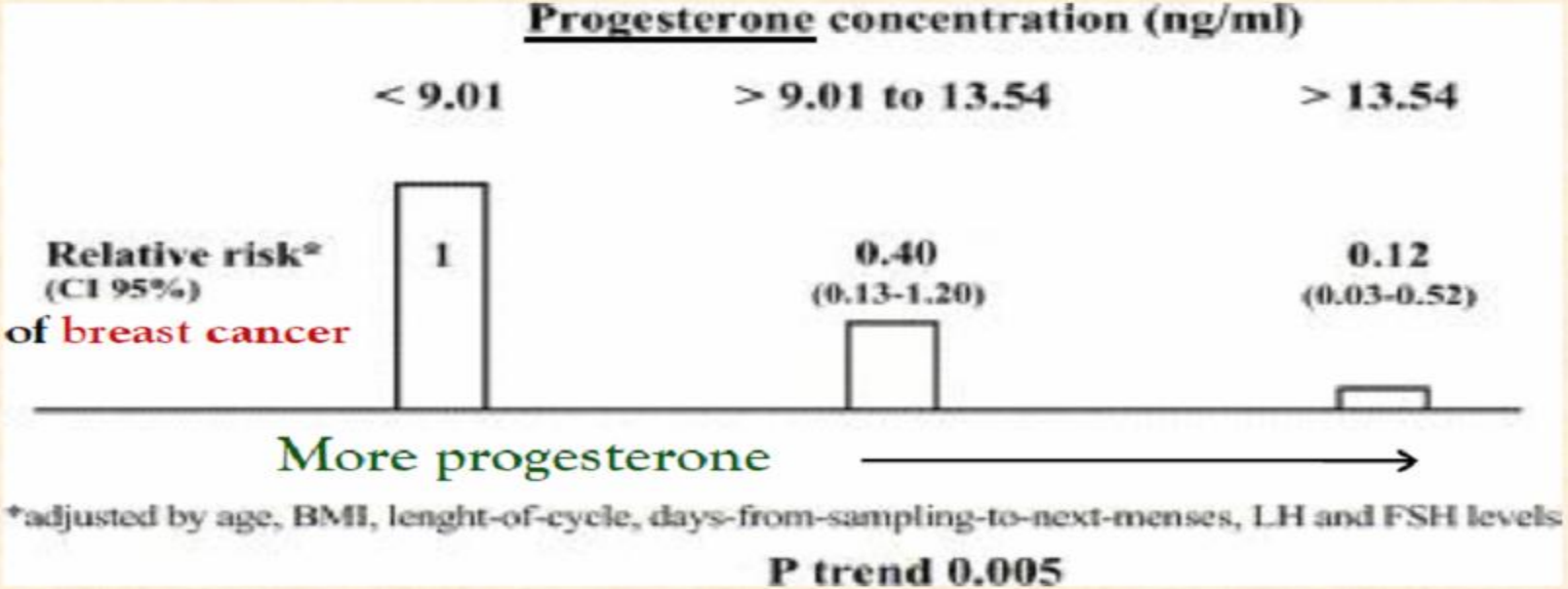
Who Needs Progesterone Supplementation?

- Irregular menstrual cycles
- No periods—amenorrhea
- Heavy bleeding
- Fibrocystic breast disease
- Endometriosis/adenomyosis
- Every woman in menopause

Ordet Study: Int. J. Cancer **112** (2004) (2), pp. 312–318.

Progesterone vs. Breast Cancer in menstruating women

6,000 women
5 yr. F/U



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**

• Sayeed I et al. Progesterone inhibits ischemic brain injury in a rat model of permanent middle cerebral artery occlusion. Restor Neurol Neurosci. 2007;25(2):151-9

• 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

Yousuf S et al. Progesterone in transient ischemic stroke: a dose response study. Psychopharmacology (Berl). 2014 Sep;231(17):3313-23

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

http://www.menopause.org/docs/default-document-library/bioidenticalht_endosoc7FEEC6FE637F.pdf?sfvrsn=3799660e_2

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

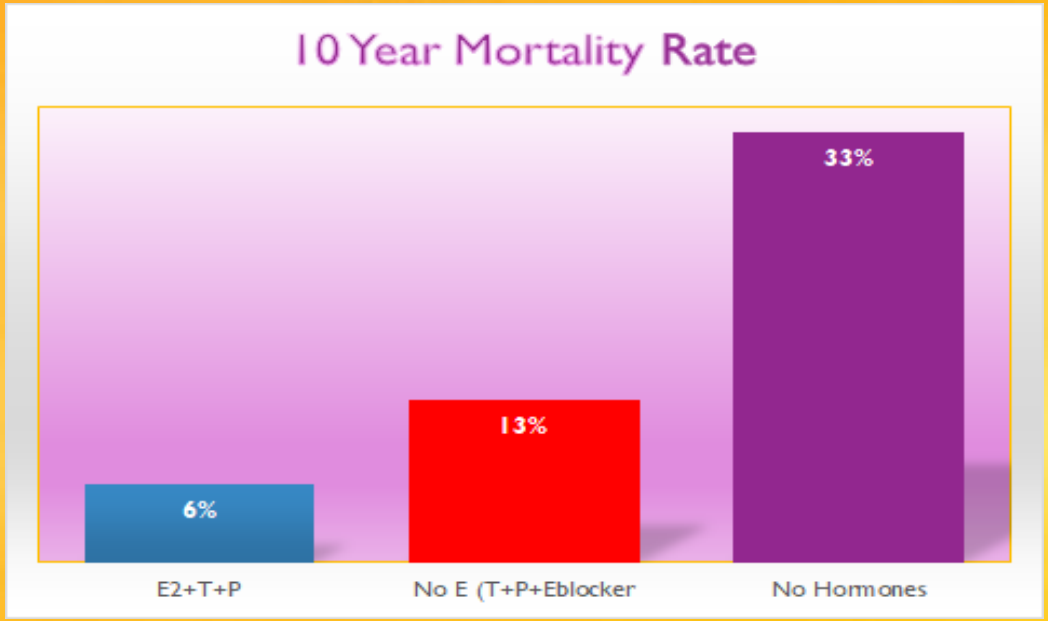
- Significantly reduced risk of mortality, heart failure, myocardial infarction

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.

Natrajan, PK, Soumakis, K., Gambrell, RD Jr. Estrogen replacement in women with previous breast cancer. Am J. Obstet Gynecol. 1999 Aug;181(2):288-95. Atlanta, GA.

Estrogen, Progesterone and Breast Cancer

Never, Ever, Never, Ever Use Estrogen without Progesterone

•

Never, Ever

You All Have to Pinky Swear


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."

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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

Durna, Wren, et al. Hormone replacement therapy after a diagnosis of breast cancer: cancer recurrence and mortality. MJA 2002; 177: 347–351

Peters, Fodera, et al. Estrogen replacement therapy after breast cancer: a 12-year follow-up. Ann Surg Oncol. 2001 Dec;8(10):828-32.

O'Meara, Rossing, et al. Hormone Replacement Therapy After a Diagnosis of Breast Cancer in Relation to Recurrence and Mortality. Journal of the National Cancer Institute, Vol. 93, No. 10, May 16, 2001

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

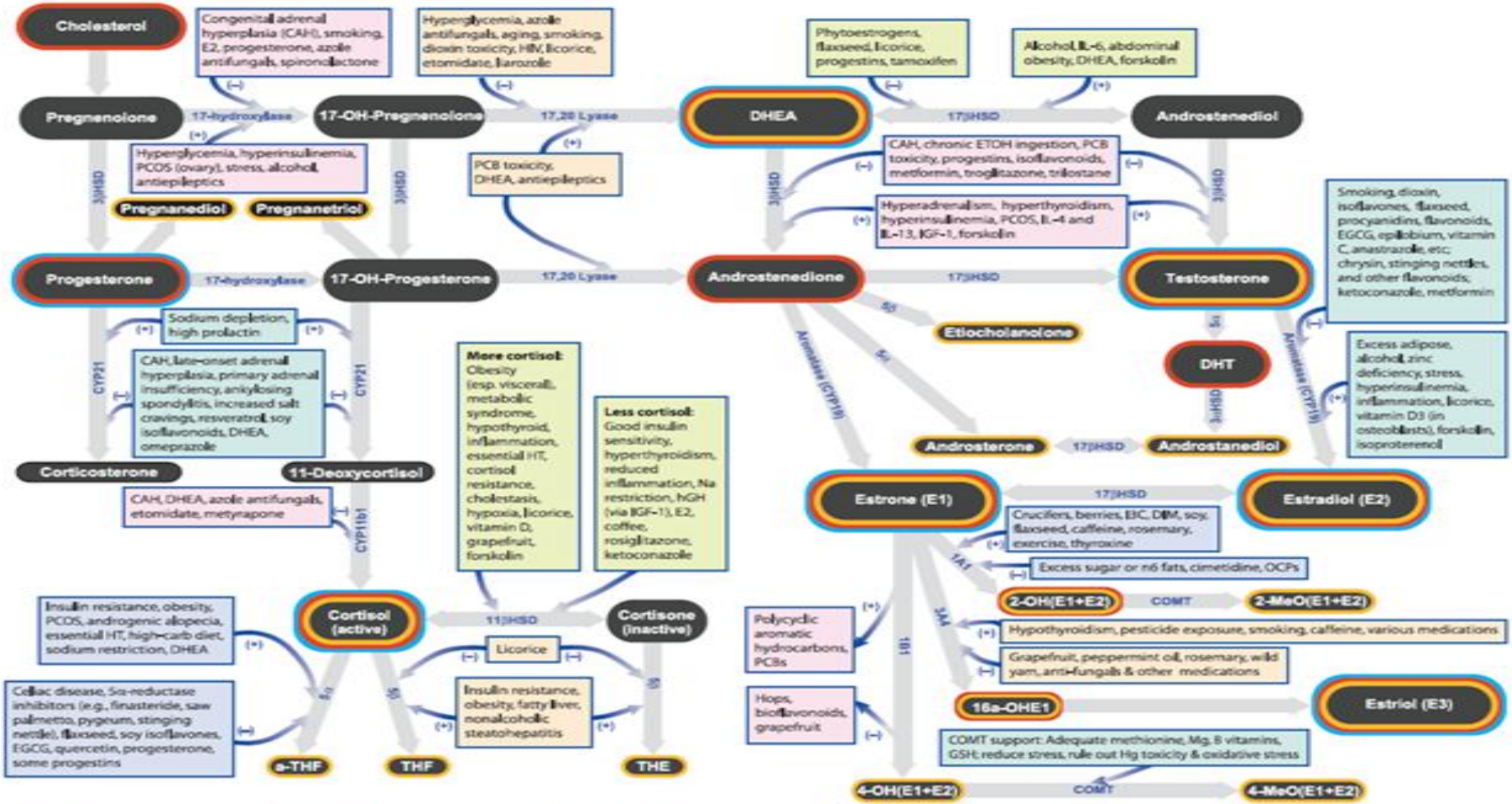
- BONE HEALTH
- HOT FLASHES
- SEDATING EFFECTS
- MOOD & DEPRESSION

- Seifert-Klauss, V., & Prior, J. C. (2010). Progesterone and bone: Actions promoting bone health in women. Journal of Osteoporosis, 2010. doi:10.4061/2010/845180
- Leonetti, H. B., Longo, S., & Anasti, J. N. (1999). Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss. Obstetrics and Gynecology, 94(2), 225-228.
- Brinton, R. D., Thompson, R. F., Foy, M. R., Baudry, M., Wang, J., Finch, C. E., . . . Nilsen, J. (2008). Progesterone receptors: Form and function in brain. Frontiers in Neuroendocrinology, 29(2), 313-339. doi:10.1016/j.yfrne.2008.02.001
- Bronson, P. J. (2001). Mood biochemistry of women at mid-life. Journal of Orthomolecular Medicine, 16(3), 141-154. Retrieved from http://www. orthomolecular.org/library/jom/2001/pdf/2001-v16n03-p141.pdf

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

- **DHEA-**regulates estrogen and testosterone, plays a role in bone health and mood disorders. Enhances immune function. Helps prevent diabetes. Facilitates weight loss.
- **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.

Steroidogenic Pathways



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

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

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for “anti aging”: A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

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

Nestler JE, Barlascini CO, Clore JN, Blackard WG. Dehydroepiandrosterone reduces serum low density lipoprotein levels and body fat but does not alter insulin sensitivity in normal men. J Clin Endocrinol Metab. 1988;66(1):57-61

Jankowski CM, Gozansky WS, Kittelson JM, Van Pelt RE, Schwartz RS, Kohrt WM. Increases in bone mineral density in response to oral dehydroepiandrosterone replacement in older adults appear to be mediated by serum estrogens. J Clin Endocrinol Metab. 2008 Dec;93(12):4767-73

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

Gordon GB, Bush DE, Weisman HF. Reduction of atherosclerosis by administration of dehydroepiandrosterone. A study in the hypercholesterolemic New Zealand white rabbit with aortic intimal injury. J Clin Invest. 1988 Aug;82(2):712-20

Jesse RL, Eoesser K, Eich DM, Zhen Y, Hess M, Nestleer JE. Dehydroepiandrosterone Inhibits Human Platelet Aggregation in vitro and in vivo. Ann NY Acad Sci. 1995:774:281-90

Iwasaki Y, Asai M, Yoshida M, Nigawara T, Kambayashi M, Nakashima N. Dehydroepiandrosteronesulfate inhibits nuclear factor-kappaB-dependent transcription in hepatocytes, possibly through antioxidant effect. J Clin Endocrinol Metab. 2004 Jul;89(7):3449-54

Labrie, et al. Menopause, Sept-Oct 2009

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**

Ohlsson C et al. Low Serum Levels of Dehydroepiandrosterone Sulfate Predict All-Cause and Cardiovascular Mortality in Elderly Swedish Men. J Clin Endocrinol Metab. 2010 Jul 7.

• Kritz-Silverstein, D et al. Effects of DHEA supplementation on cognitive Function and Quality of Life: The DHEA and Well- Ness (DAWN) Study. J Am Geriatric Soc. 2008 July; 56(7):

FDA Approved DHEA Vaginal Insert

Only DHEA converts to androgens and estrogens in a woman's body with no restrictions on duration of use[1*]

- First and only FDA-approved, vaginal non–estrogen-based therapy[1,2*]
- Demonstrated efficacy[1-3]
- Once-daily treatment at bedtime[1]

*Prasterone, a synthetic version of endogenous dehydroepiandrosterone (DHEA), is an inactive precursor that is converted into active androgens and estrogens. The mechanism of action of s not fully established.

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**

Ihler G et al. 7-oxo-DHEA and Raynaud's phenomenon. Med Hypotheses. 2003 Mar;60(3):391-7.

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”**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for “anti aging”: A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

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

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- Holick, MF. High Prevalence of Vitamin D Inadequacy and Implications for Health. Mayo Clinic Proc. 2006;81(3):353-373
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- Giovannucci E al. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. Arch Intern Med. 2008 Jun 9;168(11):1174-80.

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  - Pierpaoli W, Regelson W. Pineal control of aging: effect of melatonin and pineal grafting on aging mice. Proc Natl Acad.
  - Carrillo-Vico A et al. Melatonin: buffering the immune system. Int J Mol Sci. 2013 Apr 22;14(4):8638-83.
  - 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
  - Carretero, M et al. Long-term melatonin administration protects brain mitochondria from aging. Journal of Pineal Research. 47(2):192-200, September 2009.
  - Wilhelmsen M et al. Analgesic effects of melatonin: a review of current evidence from experimental and clinical studies. J Pineal Res. 2011 Apr 18
  - 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

References

Telomeres

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- Jaskelioff M et al. Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice. Nature. 2011 Jan 6;469(7328):102-6.
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- Johansson, S et al. Telomere length predicts survival independent of genetic influences (2007) Aging Cell, 2007. 130
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- Liu J Epid, 2013, Liu Hum Reprod 2013
- Marta Crous-Bou et al. Mediterranean diet and telomere length in Nurses' Health Study: population based cohort study BMJ 2014; 349
- • Østhus IB et al. Telomere length and long-term endurance exercise: does exercise training affect biological age? A pilot study. PLoS One. 2012Oct;19(10):1109-15.

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
  - Halonen J, Hinton AS, Frisina RD, Ding B, Zhu X, Walton JP. Long-term treatment with aldosterone slows the progression of age-related hearing loss. *Hear Res*. 2016;336:63-71. doi:10.1016/j.heares.2016.05.001

Is it... HORMONES?

Ask Your Doctor

Symptom Chart

Caused by: ↑ Dominate Levels ↓ Submissive Levels

↑↓ Fluctuating Levels ↑ + ↓ High & Low Levels

	Adrenals	Estrogen	Progesterone	Testosterone	Thyroid
Anxiety		↑+↓	↓		
Arthritis			↓	↓	
Bladder Symptoms		↓		↓	
Breakthrough Bleeding		↑	↓		
Breast Tenderness		↑	↓+↑	↑	
Cramps		↑	↓		
Decreased Sex Drive	↓	↑		↓	↓
Depression	↑	↓	↓	↓	↓
Dry Skin/Hair	↓	↓			↓
Fatigue	↓		↑	↓	↓
Fibrocystic Breast		↑	↓		
Fluid Retention		↑	↓		
Hair Loss		↓ ↑	↓ ↑	↑	↓ ↑
Harder to Reach Climax		↓	↓	↓	↓
Headaches		↓ ↑	↓ ↑	↓+↑	↓+↑
Heavy / Irregular Menses		↑	↓		
Hot Flashes	↓ ↑	↓	↓		↓
Irritability		↑	↓ ↑		
Loss of Memory		↓	↓	↓	
Mood Swings		↑	↓		
Night Sweats	↓ ↑	↓	↓		↓
Insomnia		↓	↓	↑	
Vaginal Dryness		↓		↓	
Weight Gain		↑	↓	↓	

Do You Agree?

- **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.**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for “anti aging”: A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

Do You Agree?

- **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”**

Executive Summary of the AMA House of Delegates 2009 Annual Meeting: Council on Science and Public Health Report. The use of hormones for “anti aging”: A review of efficacy and safety. *Report 5 of council on science and public health (A-09).* 2009:1-17.

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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