Hormones and Healthy Aging

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Manopause?! 

Aging, insecurity and the $2 billion testosterone industry 

BY DAVID VON DREHLE
HEALTH AND HORMONES

Learning about health and hormones has become my life's passion. While I don't feel comfortable telling you how to manage your health, I do want to expose you to the things I have learned about health and hormones, and the doctors I have worked with so you can gather research and make the best decision for yourself. Anti-aging medicine has helped me to fully learn how to practice "health" care instead of "disease" care through bioidentical hormones. This is life saving information!!
How do you tell the difference between aging and disease?
Examples of “normal” changes: the “Pauses”
Menopause/Estrogen
Andropause/Testosterone
Adrenopause/DHEA
Somatopause/GH
During aging:
- Menopause: $E_2$ ↓
- Andropause: $T$ ↓
- Adrenopause: DHEA ↓
- Somatopause: GH/IGF-I ↓
Women’s Health Initiative
ERT/HRT Program Design

Hysterectomy

YES
N=10,739

CEE* 0.625 mg/d

Placebo

NO
N=16,608

CEE 0.625 mg/d + MPA** 2.5 mg/d

Placebo

Adapted from: Writing Group for the Women’s Health Initiative. *Conjugated Equine Estrogen
JAMA. 2002;288:321-333. **Medroxyprogesterone Acetate
WHI HRT Study
Baseline Hypotheses

Risk
- Breast Cancer

Benefit
- Stroke
- Coronary Artery Disease

Plan to Study Until 2005

Threshold Level
Early STOP=Clear Harm

Threshold Level
Early STOP=Clear Benefit

Additional Risks:
- VTE

Additional Benefits:
- Osteoporosis Treatment
- Colon Cancer
- Overall Mortality

WHI HRT Study
Findings at Early Interruption

**Risk**
- 26% Increase Breast Cancer
- Early STOP = Clear Harm
- VTE
- Overall Mortality

**Benefit**
- Stroke
- Coronary Artery Disease
- Fracture Reduction
- Colon Cancer

Threshold Level

Women’s Health Initiative
Findings at Early Interruption

Risk

29% Increase
Coronary Artery Disease

41% Increase
Stroke

26% Increase
Breast Cancer

Benefit

Fracture Reduction
Colon Cancer

Early STOP=Clear Harm

VTE

Threshold Level

<table>
<thead>
<tr>
<th>Event</th>
<th>Number Needed To Harm</th>
<th>Number Needed To Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>237</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>225</td>
<td></td>
</tr>
<tr>
<td>CV- All (CHD or Stroke)</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>VTE</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>Invasive Breast Cancer</td>
<td>237</td>
<td></td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>336</td>
<td></td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>403</td>
<td></td>
</tr>
<tr>
<td>Vertebral Fracture</td>
<td>387</td>
<td></td>
</tr>
</tbody>
</table>

**Global Index**

Number Needed to Harm: 88

*Based on an average exposure of 5.2 years

Other Findings from WHI

• Estrogen-alone Study
  – 9% decrease in CHD events (not stat sig)
  – 23% decrease in breast CA (not stat sig)
  – Similar findings for stroke, VTE, hip fx
  – Global index: no risk or benefit

• WHI Memory Study
  – No difference in global cognitive function
  – No prevention of dementia
Bioidentical Hormones

- Defined as compounds that have exactly the same chemical and molecular structure as hormones that are produced in the human body
- Often used to describe formulations containing estrogens, progesterone, and androgens
- Promoted as safer and more effective alternatives to traditional hormone therapies
- What about dose, purity, safety, and efficacy?

The Endocrine Society Position Statement; ACOG Committee on Gynecologic Practice
Myths about Bioidenticals

1. "Bioidentical" hormones are safer and more effective than FDA-approved MHT drugs.
2. "Bioidentical" hormone products can prevent or cure heart disease, Alzheimer's disease, and breast cancer.
3. "Bioidentical" hormone products that contain estriol, a weak form of estrogen, are safer than FDA-approved estrogen products.
4. If "bioidentical" products were unsafe, there would be a lot of reports of bad side effects.
5. A pharmacy can make a "BHRT" drug just for you based on hormone levels in a saliva sample.
6. FDA wants all compounded hormone therapies off the market.
7. All women who take FDA-approved HT drugs are going to get blood clots, heart attacks, strokes, breast cancer, or gall bladder disease.

http://www.fda.gov/forconsumers/consumerupdates/ucm049311.htm
WHI Absolute Risks by Age

Risks and Benefits of HRT Aged 50-59 y

What have we learned from the estrogen therapy story?
T in Aging Men

Harmon SM et al, J Clin Endocrinol Metab. 2001; 86(2): 724-31
Diurnal Rhythm of T Secretion

IOM Recommendations for Clinical Trials of T in Older Men

1. Focus on the population most likely to benefit.
2. Use T as a therapeutic intervention, not as a preventive measure.
3. Establish a clear benefit before assessing long-term risks.
4. Focus on clinical outcomes in which there is a preliminary suggestion of efficacy and for which safe and effective therapeutic options are not currently available.
5. Ensure safety of the research participants.

Benefit vs. Risk

**BENEFIT**
- Body Composition
- Strength
- Bone Density
- Energy
- Mood
- Sexual Function
- Immunomodulation

**RISK**
- BPH
- Prostate Cancer
- Polycythemia
- Gynecomastia
- ? Sleep Apnea
- ?CVD
Deciding Whom to Treat for T Deficiency

- Consistent signs and symptoms and low T level (280-300 ng/dl)
- Morning (8-10 am) testosterone level by a reliable assay
- Repeat for confirmation if abnormal, possibly with free testosterone
- Not during acute or subacute illness
- If confirmed, check etiology (LH, FSH)

### Percentage of US Men Given Androgen Replacement Therapy by Age Group, 2011

<table>
<thead>
<tr>
<th>Age group</th>
<th>Percent of male population</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49 years</td>
<td>2.29%</td>
</tr>
<tr>
<td>50-59 years</td>
<td>3.26%</td>
</tr>
<tr>
<td>60-69 years</td>
<td>3.75%</td>
</tr>
<tr>
<td>70 years and older</td>
<td>2.22%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>2.91%</strong></td>
</tr>
</tbody>
</table>

Trends in Testosterone Laboratory Testing and Initiation in the US and UK

Trends in Testosterone Laboratory Testing Results in the US and UK in Non-T Users

Initiation Rates by Baseline T Level

A man on TV is selling me a miracle cure that will keep me young forever. It’s called Androgel…for treating something called Low T, a pharmaceutical company–recognized condition affecting millions of men with low testosterone, previously known as getting older.


Low “T” as in “Template”
How to Sell Disease

• Lower the bar for diagnosis (turning ordinary life experiences into conditions that require medical diagnoses)
• Raise the stakes so that people want to get tested
• Spin the evidence about drug benefits and harms

The Latest from the FDA: Sept 17, 2014

• Panel convened to consider changes to the labeling for testosterone products
• Committee voted 19 to 1 in favor of changing the labeling, wording to be determined by the FDA
• Also voted to require clinical trials for safety
What the Public Sees

Mother of all hormones

Superhormone

Fountain of youth hormone

Quite possibly the single greatest advancement made in the area of human biochemistry and health preventative medicine
What the US Public is Getting

What the Public Sees

Grow Young with HGH

The Amazing Medically Proven Plan To
- Reverse the Effects of Aging
- Strengthen the Immune System
- Improve Sexual Performance
- Lower Blood Pressure and Cholesterol

Based on Cutting-Edge Scientific Research

Dr. Ronald Klatz
President, American Academy of Anti-Aging Medicine

With Carol Kahn
Systematic Review: The Safety and Efficacy of Growth Hormone in the Healthy Elderly

*a review of 31 studies in*

*Annals of Internal Medicine*

2007

New Developments in the Illegal Provision of Growth Hormone for “Anti-Aging” and Body Building

*JAMA*

2008
Examples of increases in endocrine disease with age
% US Population with Diabetes, by Age

Centers for Disease Control and Prevention, National Center for Health Statistics
Defining a Threshold for Treatment
TSH Levels in a Reference Population in NHANES

Surks and Hollowell, J Clin Endocrinol Metab 2007;92:4575-4582
What is subclinical hypothyroidism?

TSH

- LOW <0.45mU/L
  - HYPERTHYROID
    - Free T<sub>4</sub>
      - HIGH OVERT
      - NORMAL SUBCLINICAL HYPERTHYROID

- “NORMAL” 0.45-4.5mU/L
  - EUTHYROID

- HIGH >4.5mU/L
  - HYPOTHYROID
    - Free T<sub>4</sub>
      - LOW OVERT
      - NORMAL SUBCLINICAL HYPOTHYROID
Defining a Threshold for Treatment
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Age and the Threshold for Treatment
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Age and the Threshold for Treatment

TSH Levels in a Reference Population in NHANES

Surks and Hollowell, J Clin Endocrinol Metab 2007;92:4575-4582
Defining the Threshold
Treatment is Reasonable When:

1. Overt hypothyroidism is prevented.
2. People feel better.
3. Adverse clinical outcomes are prevented.
The Geriatrician’s Approach

• How much of a difference will treating subclinical thyroid dysfunction make in my patient?
• Especially in the context of the other physical, mental, and social issues facing them.
• Right target group?
Coronary Heart Disease

CARDIOVASCULAR HEALTH STUDY

Cappola AR et al, JAMA. 2006;295:1033-41
CHD events: 1.18 (0.99-1.42)
CHD mortality: 1.14 (0.99-1.32)
Total mortality: 1.09 (0.96-1.24)
Risks According to Age Categories

Subclinical hypothyroidism

<table>
<thead>
<tr>
<th>Age</th>
<th>Subclinical hypothyroidism Events / Participants</th>
<th>Euthyroidism Events / Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18-49 years</td>
<td>12 / 221</td>
<td>272 / 5405</td>
</tr>
<tr>
<td>Age 50-64 years</td>
<td>54 / 517</td>
<td>997 / 7876</td>
</tr>
<tr>
<td>Age 65-79 years</td>
<td>322 / 1158</td>
<td>511 / 9668</td>
</tr>
<tr>
<td>Age ≥80 years</td>
<td>42 / 124</td>
<td>260 / 1008</td>
</tr>
</tbody>
</table>

CHD events

<table>
<thead>
<tr>
<th>Age</th>
<th>CHD events Events / Participants</th>
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<tr>
<td>Age 18-49 years</td>
<td>12 / 221</td>
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Total mortality

<table>
<thead>
<tr>
<th>Age</th>
<th>Total mortality Events / Participants</th>
<th>CHD mortality Events / Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18-49 years</td>
<td>14 / 465</td>
<td>340 / 13832</td>
</tr>
<tr>
<td>Age 50-64 years</td>
<td>108 / 1121</td>
<td>1492 / 18875</td>
</tr>
<tr>
<td>Age 65-79 years</td>
<td>623 / 1636</td>
<td>5316 / 16785</td>
</tr>
<tr>
<td>Age ≥80 years</td>
<td>170 / 228</td>
<td>1601 / 2345</td>
</tr>
</tbody>
</table>

* HR adjusted for gender and age as a continuous variable (to avoid residual confounding within age strata).

Rodondi et al, JAMA. 2010; 304:1365-74
**Risks according to TSH levels**

<table>
<thead>
<tr>
<th></th>
<th>Events / Participants</th>
<th>Hazard Ratio (95% CI) a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHD events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSH 0.5-4.49 mU/L</td>
<td>4040 / 23957</td>
<td>1.0</td>
</tr>
<tr>
<td>TSH 4.5-6.9 mU/L</td>
<td>264 / 1344</td>
<td>1.00 (0.86, 1.18)</td>
</tr>
<tr>
<td>TSH 7.0-9.9 mU/L</td>
<td>96 / 441</td>
<td>1.17 (0.96, 1.43)</td>
</tr>
<tr>
<td><strong>TSH 10-19.9 mU/L</strong></td>
<td>70 / 235</td>
<td><strong>1.89 (1.28, 2.80)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ptrend&lt;0.001</td>
</tr>
<tr>
<td><strong>CHD mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSH 0.5-4.49 mU/L</td>
<td>1958 / 50953</td>
<td>1.0</td>
</tr>
<tr>
<td>TSH 4.5-6.9 mU/L</td>
<td>132 / 2363</td>
<td>1.09 (0.91, 1.30)</td>
</tr>
<tr>
<td><strong>TSH 7.0-9.9 mU/L</strong></td>
<td>50 / 652</td>
<td><strong>1.42 (1.03, 1.95)</strong></td>
</tr>
<tr>
<td><strong>TSH 10-19.9 mU/L</strong></td>
<td>28 / 333</td>
<td><strong>1.58 (1.10, 2.27)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ptrend=0.005</td>
</tr>
<tr>
<td><strong>Total mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSH 0.5-4.49 mU/L</td>
<td>8749 / 51837</td>
<td>1.0</td>
</tr>
<tr>
<td>TSH 4.5-6.9 mU/L</td>
<td>640 / 2431</td>
<td>1.06 (0.96, 1.17)</td>
</tr>
<tr>
<td>TSH 7.0-9.9 mU/L</td>
<td>170 / 672</td>
<td>1.02 (0.84, 1.24)</td>
</tr>
<tr>
<td>TSH 10-19.9 mU/L</td>
<td>105 / 347</td>
<td>1.22 (0.80, 1.87)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ptrend=0.39</td>
</tr>
</tbody>
</table>

* HR adjusted for age and gender. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

Rodondi et al, JAMA. 2010; 304:1365-74
Prescription of Levothyroxine

Serum Free T4 and Atrial Fibrillation

“Aging seems to be the only available way to live a long life.”

Daniel Francois Esprit Auber
Replacement Therapy

• **Target population**
  – What age to start
  – What level of hormone deficiency
  – When to use: chronic weakness vs. acute recovery needs

• **How to administer**
  – Delivery method, dose, and target level
  – Duration of use
  – Duration of effects when stop therapy

• **Use in conjunction with other measures**
  – Hormone cocktail
  – Exercise
  – Improved nutrition