Testosterone Replacement in Adults

John A. Seibel, MD, MACE
History of Testosterone Rx

• Ancient Europe and Asia
  – Castrated males had no secondary sex characteristics
  – Used as eunuchs to guard Women

• 1765 Hunter Transplanted Tissue in Animals

• 1849 Berthold “Results of Castration Caused by a substance secreted from testicles.”
...a radical change took place in me....I fully regained my old powers....My limbs...showed a decided gain of strength. With regard to the facility of intellectual labour,...a return to my previous ordinary condition became quite manifest during and after the first two or three days of my experiments.”

• Called Testosterone “the Elixir of Life”.
Brown-Sequard 1889

• Immediately 12,000 Physicians began injecting “testosterone extract”

• Unfortunately it had little testosterone and the effects were placebo.
Sergio Veronoff  1920

• Began transplanting animal testes into men.
• Others used goat and sheep testicles.
• Uniformly rejected by the body and the only effects were placebo
Synthetic Testosterone

• 1935 David isolated testosterone
• 1939 Kock used 40 pounds of bull testes to get 20 mg of testosterone
• 1939 Butenandt and Ruzika received Nobel Prize in Medicine for synthesizing Testosterone
• Testosterone injections began
• 1990 patch is introduced.
Role of Testosterone in Male Health
The Impact of Testosterone

Skin
Hair growth, balding, sebum production

Liver
Synthesis of serum proteins

Brain
Libido, mood

Muscle
Increase in strength and volume

Male Sexual Organs
Penile growth, spermatogenesis, prostate growth, and function

Kidney
Stimulation of erythropoietin production

Bone
Accelerated linear growth, closure of epiphyses

Bone Marrow
Stimulation of stem cells

TESTOSTERONE SECRETION
Testosterone Production

Production and Regulation of Testosterone

FSH = follicle-stimulating hormone; GnRH = gonadotropin-releasing hormone; LH = luteinizing hormone; T = testosterone.

Definition of Male Hypogonadism

“... clinical syndrome that results from failure of the testes to produce physiological levels of testosterone ... due to disruption of one or more levels of the hypothalamic-pituitary-gonadal (HPG) axis.”

_endocrine society guideline (2006)_

“... inadequate gonadal function, as manifested by deficiencies in ...the secretion of gonadal hormones.”

_American Association of Clinical Endocrinologists Guidelines (2002)_

Definition of Hypogonadism

• Male gonadal dysfunction
• Low levels of testosterone
• May be congenital or acquired

Signs And Symptoms of Low T

- Loss of muscle mass and strength
- Loss of libido and erectile function
- Depression
- Fatigue
- Osteoporosis
- Hot Flashes, Sweats
- Some regression of secondary sexual characteristics
- Oligospermia or azoospermia

Incidence of Hypogonadism
Prevalence of Low Testosterone

13.8 Million Men in the US

Overall, 38.7% of men ≥45 years had testosterone levels <300 ng/dL


Prevalence and Treatment of Hypogonadism

10-14 Million Men with Hypogonadism

Low Testosterone Is Increasingly Common as Men Age

- 1 in 10
  - Men in their 40s and 50s
- 1 in 5
  - Men in their 60s
- 1 in 4
  - Men in their 70s

However, less than 10% are being treated for low testosterone

Conditions Associated with Hypogonadism
Prevalence of Low Testosterone in Other Conditions

- Chronic opioid use for pain: 74%
- Obesity: 52%
- Diabetes: 50%
- AIDS (HIV 30%): 50%
- Hypertension: 42%
- Hyperlipidemia: 40%
- ED: 19%

ED = erectile dysfunction

Chronic Opioid Use

• Direct Effect on Hypothalamus
  – Decreases GhRH Production & Release
• Direct Effect on Testes
  – Decreases Production of Testosterone and Androgenic Binding Proteins
• Effect begins almost immediately
Prevalence of Low Testosterone in HIV and AIDS

- 30% of men with HIV and 50% of men with AIDS are hypogonadal\(^1,2\)
- Mechanisms of hypogonadism in men with HIV and AIDS are complex and not fully understood\(^2\)

Acquired Causes or Conditions

- Pituitary adenoma
- Inflammatory diseases (rheumatoid arthritis, Crohn’s disease, ulcerative colitis)
- Respiratory disorders (asthma, COPD, sleep apnea)
- Iatrogenic (ketoconazole, glucocorticoids, spironolactone, cimetidine, phenytoin, flutamide, opioids)
- Other endocrine disorders (hyperprolactinemia, hypothyroidism)
- Alcohol or anabolic steroid abuse

Primary Hypogonadism (Primary Testicular Disorder): Acquired Causes

- Medications
- Obesity
- Severe systemic illness
- Castration
- Hemochromatosis
- Mumps orchitis

- Idiopathic
- Neurodegenerative illnesses
- Malnutrition
- Respiratory disorders
- Trauma

Winters SJ. Arch Fam Med. 1999;8:257-263.
Diabetes/Metabolic Syndrome and Low Testosterone Levels

• Men with metabolic syndrome or type 2 diabetes may have concurrent low testosterone

• In three major studies with >2800 patients, patients with metabolic syndrome or type 2 diabetes were more likely to be in the lowest testosterone quartile\textsuperscript{1-3}

• Serum testosterone should be measured in men with type 2 diabetes with symptoms suggestive of testosterone deficiency\textsuperscript{4}

Association Between Hypogonadism, Obesity, and Insulin Resistance

Adipose tissue
- Increased number of adipocytes in obese and type-2 diabetic men
- Greater aromatase activity
- Increased metabolism of testosterone to estradiol

Low testosterone

Pituitary and hypothalamus
- Estradiol inhibits LH/FSH secretion

Leydig cells
- Increased insulin resistance affects cells

FSH = follicle stimulating hormone; LH = luteinizing hormone
Role of Testosterone in Erectile Function

• Screening
  – 19% of men with ED are known to have low testosterone\(^1\)
  – 23-50% of patients are non-responsive to PDE5 inhibitors\(^2\)
  – Patients failing PDE5 inhibitors may warrant screening for low testosterone

• Causes of ED include several factors\(^3\)
  – Psychogenic
  – Neurogenic
  – Endogenic
  – Vasculogenic

• Animal models suggest that the erectile pathway is testosterone dependent\(^4\)
  – Nitric oxide is necessary for penile erection

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Number Treated

• 2009  1.2 million
• 2013  2.3 million

Endocrine Today : April 2016
Source FDA
FDA Concerns Prompt New Warning

- FDA Concerns Have Decreased
- Use of TRT
  - Risk of CVD, VTE and stroke – FDA requires boxed warning on all TRT products since 6/14, 3/15.
  - Decision made based on 4 trials (Vigen, Finkle, Basaria, Xu).
  - All with methodological flaws or misleading results.
  - Concern with inappropriate use and use in aging men
Increased Use of TRT

- Increased opioid use
- Increased incidence of co-morbidities
  - Obesity
  - DM
  - HIV/AIDS
  - Increased steroid abuse
  - Stress
Heart and Testosterone
Testosterone & the Heart

• 4 Studies Concluded Increased CV Risk
• Vigen et al
  – Concluded that there was a doubling of risk
  – 29 different Medical groups demanded it be retracted for faulty design & Calculation
  – The group admitted errors and came out with correct conclusions
  – Results the opposite of original conclusions
Basaria et al showed increased CV Events

- Mean age was 74
- Subjects had Serious Chronic Diseases
  - High Percentage of Subjects
  - Diabetes, Abn. Lipids, HTN, Obesity and Pre-existing Heart Disease
- Selected Patients with Mobility Problems
The Studies that prompted FDA

• Finkle Study:
  – Too small to be significant

• Xu Study
  – Meta analysis that was flawed
Hypogonadal Males Treated with Testosterone

- Shores et al studied 1031 Males at VA
  - Showed increased mortality in the untreated group compared to treated group
    - 20.75 compared to 10.3%
- Glueck et al. showed that males with undiagnosed hypercoaguable states had more DVTs and PE in the treated group
Morganthaler Analysis
Mayo Clinic

• Reviewed over 100 studies.
  – Found the same 4 suggesting Increased CV Risk
• The rest had no evidence of increased CV risk.
  – Showed improved CV Function.
  – Increased Benefit for older men.

Medical Letter

- Adverse reactions to TRT include:
  - Gynecomastia
  - Acne
  - Edema
  - Polycythemia
  - No Convincing evidence of increased Prostate Cancer
  - Needs further study for CVD

JAMA Vol: 315#14; pp12-14
QTc interval

• Felt to be measure of Cardiac Repolarization
  – Short QTc goes with fewer cardiac problems
• Shortens in Men age 9-50
• Starts to prolong at age 60 or with low T
• Studies show Men with Low T have long QTc
• Charbit, van Noord & Picori Giraldi have shown hypogonadal males treated with Testosterone have short QTc intervals
Hypogonadal Males Treated with Testosterone

• Shores et al studied 1031 Males at VA
  – Showed increased mortality in the untreated group compared to treated group
    • 20.75 compared to 10.3%
• Glueck et al. showed that males with undiagnosed hypercoaguable states had more DVTs and PE in the treated group
• No increase in major CV events including MI or CVAs in healthy men > age 50.
  – 1472 men age 52 – 63 followed for 3 years
• Decrease in MI, CVA and death was seen.

• European Heart Journal 2015
Mayo Clinic Study
30 day Re Hospitalization Rate

- 6372 non-surgical Pts. age 66+ with Low T
  Re hospitalization rate
- 9.8% re hospitalization for pts on TRT
- 13% for those not treated with TRT
Wallis Study

- 10,311 men aged 66+ on TRT for 5 years
- Men on TRT had lower death rate and CV events.
- Short term Rx increased Mortality & CV
- Long Term Associated with lower Death rate and CV events

Wallis CJ et al. Lancet Diabetes Endocrinol
http://dx.doi.org/10.1016/s2213-8587(16)00112-1
Multiple Articles Show Benefit of TRT

- Low levels of endogenous testosterone and increased mortality 8
- Low testosterone levels and increased incidence of coronary artery disease 6
- Low testosterone level correlates with increased severity of coronary artery disease 4
- Low endogenous testosterone level and increased carotid intima-media thickness 8
- TRT decreases obesity 6
- TRT improved cholesterol levels (meta-analysis) 3
- TRT improves glycemic control 6
- TRT decreases markers of inflammation 8
Corona Meta-analysis of TRT and CV events (MACE)

- Available evidence “does not support a causal role between testosterone supplemental and adverse CV events when hypogonadism is properly diagnosed and replacement therapy correctly preformed”.

American Association of Clinical Endocrinologists and American college of Endocrinology

• There is no compelling evidence that testosterone therapy either increases or decreases cardiovascular risk.
• Large-scale prospective randomized controlled trials on testosterone therapy, focusing on cardiovascular benefits and risks, are clearly needed.
• As with therapeutics in general, common sense, experience, and an individualized approach are recommended.

Endocr Pract. 2015;21:1066-1073
50 + Years of Testosterone Rx

- Why After 50 years do we need more studies?
- 2 very Large VA Studies had shown:
  1. Decreased Mortality in Men Using T
  2. No Increase in CVD Incidents
- Could it be the Advent of the more Expensive Patch and Gel?
• Steven Nissen?
  – This story should not be about the use of testosterone therapy, it should be about the abuse of testosterone therapy“
  – “I think until proven otherwise, we should consider these supplements to be unsafe for men”.
  – “More studies are needed”
Have you or a loved one suffered a Heart attack, Stroke or DEATH from Testosterone replacement?

Injured by Testosterone Supplements? Call now for money you deserve.

Litigation Opportunity For Testosterone Patients Call 1-800 Sue Them

What's Next For The Thousands Of Angry Men Suing Over Testosterone?
Renowned Cleveland Clinic cardiologist Steven Nissen, MD is advising men to stop taking medication to treat low testosterone (low-T) caused by aging.

In his recent article, “Why Your Low-T Medications May Not Be Safe,” Nissen warns men looking to counteract the effects of aging not to start taking low-T medications, and he suggests current users discontinue use.

A U.S. Food and Drug Administration (FDA) advisory panel recently recommended that doctors limit the use of testosterone drugs to men diagnosed with low-T as a result of a medical condition, such as pituitary or testicular disease.

The panel’s recommendations would exclude millions of men who are taking low-T drugs to treat low testosterone levels caused by aging.

The FDA panel also recommends that low-T drug makers explore possible testosterone-related heart attack and stroke risks. A 2014 Journal of the American Medical Association (JAMA) study suggested that men taking testosterone had an increased risk of suffering a heart attack or stroke.

Nissen recommends that men taking testosterone drugs talk to their doctor to determine whether it is medically necessary. He discourages men from relying on it to feel or look younger, as they may be putting their health at risk.

A number of men who suffered a heart attack or stroke while taking low-T drugs have filed testosterone lawsuits. Men who want to take legal action after suffering a testosterone heart attack or stroke are urged to contact a testosterone lawyer to discuss their legal rights.

Tags: testosterone heart attack, testosterone lawyer, testosterone stroke
Signs of Low Testosterone

- Incomplete sexual development
- Breast discomfort, gynecomastia
- Increased body fat
- Reduced muscle bulk and strength
- Lack of effect of PDE5 inhibitors for erectile dysfunction
- Low BMD
- Loss of body hair (auxiliary and pubic), reduced shaving
- Low or zero sperm count

Screening for Low T

Androgen Deficiency in Aging Males (ADAM) Questionnaire

1. Do you have a decrease in libido (sex drive)?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased enjoyment of life?
6. Are you sad and/or grumpy?
7. Are your erections less strong?
8. Have you noticed a recent deterioration in your ability to play sports?
9. Are you falling asleep after dinner?
10. Has there been a recent deterioration in your work performance?

If the answer is yes to question 1 or 7, or at least three of the other questions, low testosterone may be present.

Symptoms of Low Testosterone

Sexual symptoms

- Low sexual desire (low libido)
- Erectile dysfunction (ED)
- Weaker and fewer erections
- Reduced sexual activity

Nonsexual symptoms

- Low energy or fatigue
- Bad mood or poor concentration
- Reduced muscle mass/strength
- Increased body fat

Male Hormonal Status
Changes With Age as SHBG Increases

As SHBG increases with age, levels of free testosterone decrease

Diurnal Variation in Serum Total Testosterone Levels

Circulating Testosterone

Bioavailable testosterone

Free  Albumin bound  SHBG bound

2%  38%  60%

Total testosterone

SHBG = sex-hormone binding globulin.
Adapted from Braunstein GD. In: Basic & Clinical Endocrinology. 5th ed. Stamford, Conn: Appleton & Lange; 1997:422-452.
Diagnosing Hypogonadism

• Signs and symptoms

• Clinical laboratory diagnostic tests
  – Total testosterone levels (<300 ng/dL)*
  – Bioavailable testosterone (<70 ng/dL)
  – Free testosterone (<50 pg/mL)

• Screening tools
  – ADAM (Androgen Deficiency in the Aging Male) Questionnaire
  – AMS (Aging Males' Symptoms) Scale
  – MMAS (Massachusetts Male Aging Study) Questionnaire

*Most frequently used lab test for the diagnosis of hypogonadism.
Additional Tests

• LH and FSH
  – To ascertain whether cause is primary or secondary

• Serum prolactin
  – High prolactin levels may suggest presence of pituitary tumor

Further Diagnostic Recommendations

Primary Hypogonadism
- Karyotype to rule out Klinefelter syndrome

Secondary Hypogonadism
- Measure serum prolactin, iron saturation, and other pituitary hormones
- Obtain MRI if
  - Severe secondary hypogonadism (TT <150 ng/dL)
  - Hyperprolactinemia
  - Other pituitary-hormone deficiency (panhypopituitarism)
  - Symptoms/signs of tumor-mass effect (headache, visual-field defect, or impairment)

TT = total testosterone
MRI = magnetic resonance imaging.
Testosterone Replacement Therapy
TRT
Testosterone-Replacement Therapy
Dosing and Administration

**Intramuscular Injection**
- Testosterone enanthate or cypionate
- 75-100 mg weekly or 150-200 mg every 2 weeks

**Transdermal Patches (Nonscrotal)**
- 2.5-7.5 mg applied nightly for 24 hours*

**Transdermal Gels 1%**
5-10 g applied daily (5-10 mg testosterone systemically absorbed)

**Buccal Tablets**
- 30 mg tablet applied to the buccal mucosa every 12 hours

**Pellets**
- 150-450 mg implanted subcutaneously every 3-6 months†
Transdermal Gels Are the Most Commonly Prescribed Form of TRT

IMS NPA; 2008.
Testosterone Levels After Replacement With Gel or Injection*

* Schematic representation; not an actual study.
TRT Replacement

• Injections
  – Mood swings
  – Polycythemia – Strokes or AMI

• Oral Tablets – Methyl Testosterone
  – Toxic Hepatitis

• Skin Patches
  – Skin Reactions

• Pellets
  – Infection

• Gels
  – Transference to partner
Monitoring After Initiation of Testosterone Replacement Therapy

<table>
<thead>
<tr>
<th>Monitoring of testosterone replacement therapy</th>
<th>Baseline</th>
<th>At month 1</th>
<th>At month 3</th>
<th>Annually</th>
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<tbody>
<tr>
<td>SYMPTOM ASSESSMENT</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>At baseline: Evaluate symptoms</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>During treatment: Evaluate symptom relief and adverse effects</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>TESTOSTERONE LEVELS</td>
<td></td>
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</tr>
<tr>
<td>Determine that serum testosterone levels are low:</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>- Total testosterone &lt; 300 ng/dL</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Free testosterone &lt; 50 pg/mL</td>
<td>✓</td>
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<tr>
<td>During treatment: Determine whether serum testosterone levels have risen into the mid-normal range</td>
<td>✓</td>
<td></td>
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<tr>
<td>PSA[^1]</td>
<td></td>
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<tr>
<td>Obtain urologic consultation if:</td>
<td></td>
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<tr>
<td>- PSA &gt; 4.0 ng/mL</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>- PSA increases &gt; 1.4 ng/mL within any 12-month period</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- PSA velocity &gt; 0.4 ng/mL/yr using PSA level after 6 months of treatment as reference (only if PSA available &gt; 2 years)</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- AUA[^1] or IPSS[^1] prostate symptom score &gt; 19</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>DRE[^1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obtain urologic consultation if prostatic abnormality is detected</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEMATOCRIT</td>
<td></td>
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<tr>
<td>If &gt; 54%, stop therapy until it decreases to a safe level</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What About Prostate Cancer?

- Geriatric patients may be at an increased risk for prostatic hyperplasia and prostatic carcinoma
- PSA levels in hypogonadal men are often abnormally low\textsuperscript{1,2}
  - TRT may increase PSA levels reflecting normalization and typically plateau within 12 months of initiating therapy
  - Increases in PSA levels beyond this warrant further screening

Testosterone and Prostate Cancer
Concerns and Current Views

Original Basis for Concern
- Castration caused prostate cancer regression, and T administration caused progression (Huggins C, et al., 1941)
- Case reports of conversion of occult cancer into clinically apparent lesions

Current View
- Prevalence rate of prostate cancer in TRT patients similar (1.1%) to that found in general population (over 6-36 months)
- Despite decades of work, there is no compelling evidence that testosterone has a causative role in prostate cancer
- Prostate cancer prevalence increases as T levels decline
- Studies show no significant differences in testosterone levels between those who develop prostate cancer and those who do not

Future Direction
- The Institute of Medicine and National Institute of Aging are embarking on studies to further evaluate causality

T = testosterone; TRT = testosterone-replacement therapy.
Reasons for Urological Consultation

- Serum PSA concentration >4 ng/mL
- An increase in serum PSA >1.4 ng/mL within any 12-month period of T replacement
- A PSA velocity of >0.4 ng/mL/yr using the PSA level at 6 months after initiation of T replacement as the reference
  - Only applicable if PSA data are available for a period >2 years
- Detection of prostatic abnormality on DRE

AUA = American Urological Association; DRE = digital rectal exam; IPSS = International Prostate Symptom Score; PSA = prostate specific antigen.
Benefits of TRT
Testosterone and Depression

An overview of older studies shows mixed results regarding the relationship between testosterone levels in men and depression1. However, several well-controlled studies indicate that endogenous testosterone levels are lower in depressed aging men than in healthy subjects *2,3. In particular, low bioavailable testosterone levels in aging men correlate strongly with depression *3.


Testosterone and Cognitive Function

Cognitive measures demonstrate significant correlation with plasma bioavailable testosterone levels in some, but not all studies. Plasma testosterone levels influence the performance of cognitive tasks with positive correlations with spatial tests and negative correlations with verbal tests. Plasma testosterone is lower in men with Alzheimer’s Disease than in healthy men.

Goals and Benefits of Testosterone Replacement Therapy

• Improve libido and improve erectile function
• Improve body mass and strength
• Improve bone mineral density
• Improve energy level
• Improve mood/sense of well-being

Improvement in Sexual Function Parameters

• 90-day study in 406 hypogonadal men
  – Randomized, multidose, multicenter, active, and placebo controlled
• Significant improvement from baseline vs placebo included
  – Motivation ($P<0.05$)
  – Performance ($P<0.05$)
  – Desire ($P<0.01$)
  – Spontaneous erections ($P<0.001$)
• An additional open-label extension study supported these data

Significant and Sustained Improvement in Sexual Performance* With TRT
(in 12-month extension study following 90-day pivotal trial)

*Based on average number of days with orgasm, ejaculation, intercourse, masturbation, or erection in response to sexual activity.

Significant Improvement in Body Composition With TRT
(in 12-month extension study following 90-day pivotal trial)

Lean Body Mass
-4.84 lb
\(P<0.0001\)

Fat Mass
\downarrow 3.96 lb
\(P<0.0001\)

Results after 36 Months of TRT Therapy: Sexual Function

Results after 36 Months TRT Therapy: Bone Mineral Density

Results after 36 Months of TRT Therapy: Effect on Mood

Contraindications and Relative Contraindications of Testosterone Replacement Therapy

- Known or suspected prostate cancer
- Known or suspected carcinoma of the breast
- Prostatic hyperplasia in geriatric patients
- Sleep apnea (may exacerbate condition; patients should be treated for sleep apnea first [CPAP])
- Edema with or without congestive heart failure
- Patients with polycythemia
- Is not indicated for women, has not been evaluated in women, and must not be used in women.
Testosterone-Replacement Therapy
Contraindications and Precautions

Contraindications
- Male breast cancer
- Prostate cancer (known or suspected)
- Use in pregnant or breast-feeding women
- Known or suspected sensitivity to ingredients used in T delivery systems

Precautions
- Benign prostatic hyperplasia (BPH)
  - Lower urinary tract symptoms (LUTS)
- Edema in patients with preexisting cardiac, renal, or hepatic disease
- Gynecomastia
- Precipitation or worsening of sleep apnea
- Azoospermia
  - Testicular atrophy

BMD = bone mineral density; DRE = digital rectal exam; PSA = prostate specific antigen; TRT = testosterone-replacement therapy.
Conclusions

• Hypogonadism in adult men is often unrecognized
• Known diseases of aging are associated with an *increased* decline in testosterone
• Low testosterone is characterized by changes in the body fat/lean muscle ratio; bone mineral density; cognition, memory, and mood; and sexual desire and function
• Before prescribing be sure that it is needed
• Check Levels to be sure that they do not go too high.
What about Women
Women - Symptoms

• Symptoms:
  – Decreased sexual desire
  – Decreased sexual thoughts & fantasies
  – Decreased strength
  – Decreased genital response & orgasm
  – Decreased lubrication
What about Women

- Can they have low testosterone levels?
- 43% age 18 – 59 suffer from sexual dysfunction
## Low Testosterone Levels in Women

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Free</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>&lt;25 ng/dl</td>
<td>&lt;1.5 pg/ml</td>
</tr>
<tr>
<td>&gt;50</td>
<td>&lt;20 ng/dl</td>
<td>&lt;1.0 pg/ml</td>
</tr>
</tbody>
</table>

Guay, A & Davis, S  
http://www.bumc.bu.edu/sexualmedicine/publications/testosterone-insufficiency-in-women-fact-or-fiction
Women and Testosterone

• All women make testosterone
  – ¼ from Ovaries
  – ¼ from Adrenals
  – ½ Peripheralally

• In US no testosterone product is indicated in women.
Women and Testosterone

- Precursors of testosterone
  - DHEA
  - DHEA Sulfate
- DHEA has been suggested as treatment for women
- Over the counter
Endocrine Society Guidelines

- Put together a task force to create Guidelines
- Unable to come up with guidelines
- Too many things were not standardized
# Guidelines – British Society for Sexual Medicine

<table>
<thead>
<tr>
<th>Condition</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual Distress + Psychosexual problems</td>
<td>Counseling</td>
<td>Counseling May consider Pharmacology</td>
</tr>
<tr>
<td>Sexual distress+ Medical Problems</td>
<td>Treat Medical problem</td>
<td>Pharmacology may be appropriate</td>
</tr>
<tr>
<td>Postmenopausal Psychosexual Sexual Distress</td>
<td>Counseling Pharmacology may be appropriate</td>
<td>Generalized therapy not recommended</td>
</tr>
<tr>
<td>SHBG &gt; 160</td>
<td>Testosterone not appropriate</td>
<td>Pharmacology may be appropriate</td>
</tr>
</tbody>
</table>
Thank You!