Hormone Pellet Therapy In Men

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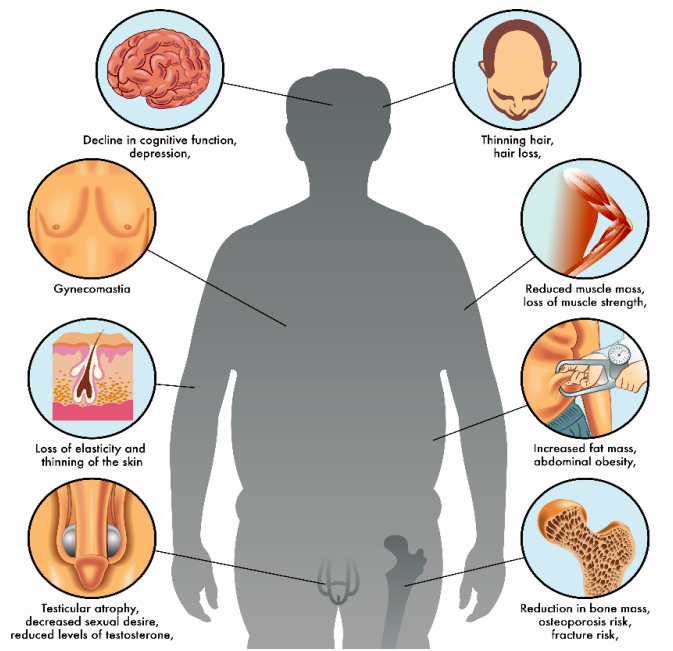
Testosterone deficiency

- Sexual Dysfunction
- Decreased bone density
- Decreased lean body mass
- Increased metabolic syndrome and insulin resistance
- Atherosclerosis with increased angina, ischemia, and various CVD
- Alzheimer's disease
- Hypercholesterolemia, hypertension
- Increases Mortality



Golan, R., Scovell, J., & Ramasamy, R., (2016) Age Related testosterone decline due to waning of testicular and hypothalamic pituitary function. *Aging Male 18(3)m 201-204.;* Shabsigh R, et al. Am J Cardiol. 2005;96(12B):67M-72M; Nettleship JE, et al. Front Horm Res. 2009;37:91-107; Page ST, et al. Asian J Androl. 2008;10(2):193-200; Stanworth, R. & Jones, T., (2008) Testosterone for the aging male: current evidence and recommended practice. *Clinical Interventions in Aging 3*(1), 25-44.

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TD Therapy is Effective, Rational and Evidence Based

- High level evidence showed TD therapy
  - Increases sexual desire, erectile and orgasmic function
  - Increases lean body mass
  - Decreases fat mass
  - Improves bone density
- Strongly suggested improvement in mood and energy

Morgentaler, A, Zitsman, M., et al. (2016) Fundamental concepts regarding testosterone deficiency and treatment: International Expert Consensus Resolutions. Mayo Clin Proc, July:91(7):881-896

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Contraindications

- Male breast cancer
- Prostate cancer
- Palpable prostate nodule or induration
- Abnormal PSA
- Erythrocytosis (Secondary Polycythemia)
- Untreated severe sleep apnea
- Severe lower urinary tract symptoms with International Prostate Symptom Score >19
- Uncontrolled or poorly controlled heart failure

Bhasin S, et al. J Clin Endocrinol Metab. 2006;91(6):1995-2010.

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No Basis to Deny TD Therapy Based on Age

- Age related hypogonadism of questionable validity- more attributable to comorbidities
- Older men do as well as younger on T therapy
- Increased risk erythrocytosis requires monitoring not withholding
- Illogical not to treat because TD more prevalent with age

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Primary Hypogonadism

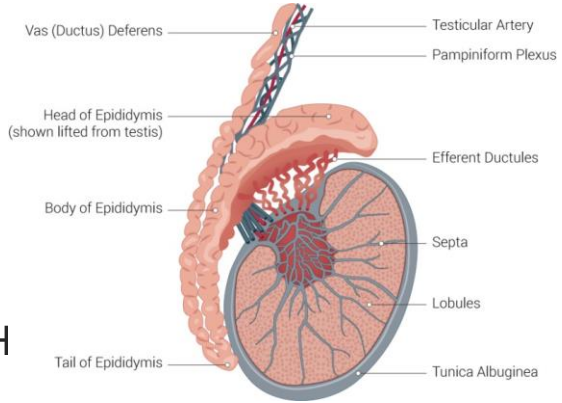
Hypergonadotropic Hypogonadism

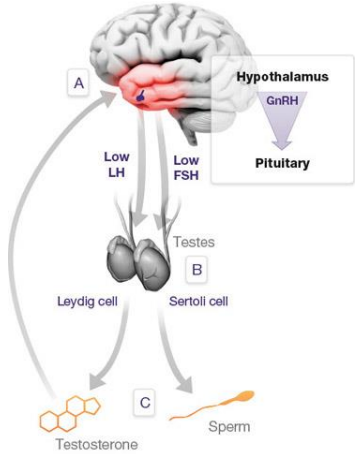
What occurs?

- **Testicular dysfunction**
- Normal hypothalamic/pituitary function

What results are seen?

- Low testosterone levels
- Impairment of spermatogenesis
- Elevated gonadotropin levels, LH and FSH





Seftel A. Int J Impot Res. 2006;18(3):223-228.
Bhasin S, et al. J Clin Endocrinol Metab. 2010;96(6):2536-2559

Secondary Hypogonadism

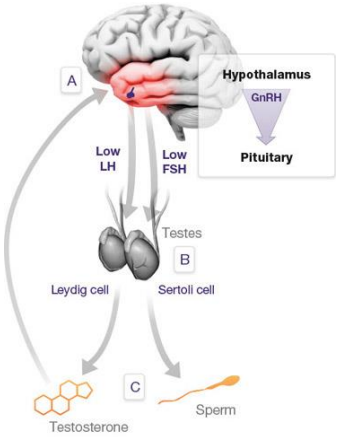
Hypogonadotropic Hypogonadism

What occurs?

- Normal testicular function
- **Hypothalamic/pituitary dysfunction**

What results are seen?

- Low testosterone levels
- Impairment of spermatogenesis
- Low or low-normal gonadotropin levels, LH and FSH
- R/O Pituitary Adenoma measure Prolactin levels



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Pre-insertion Labs

- Testosterone (total, free)
- Estradiol
- CBC (Hgb & Hct.)
- Comprehensive Metabolic panel
- Lipid profile
- PSA and percentage of free PSA
- DHEA
- TSH and free T3 and total T4
- Homocysteine
- C-reactive protein

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Single Testosterone Threshold Unreliable

- No study identified serum level that experience symptoms from those who do not
- T concentration confounded by
  - Individual variation
  - Serum SHBG variation due to how it binds to T
  - Genetic variation in androgen sensitivity (polymorphisms)
- Free T can be useful

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What is a Low Serum Testosterone Level?

- Total Testosterone <300 ng/dL
- Free Testosterone <50 pg/mL .005 ng/dl
- Bioavailable Testosterone <70 ng/dL

- Total testosterone is the most frequently used laboratory test for the diagnosis of hypogonadism in the medical literature

Brawer MK. Rev Urol. 2004;6 suppl 6:S9-S15.
AACE Hypogonadism Task Force. Endocr Pract. 2002;8:439-456.

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Dosing Men

Experience and Anecdotal

- 900-1200 mg testosterone pellets
- 1400-1600 mg larger men
- Most studies look at 600-1200 mg doses

On Line Calculator

- Based on daily Testosterone production
- Normal 3-9 mg/ day
- Daily Testosterone Pellet release
  - 100 mg: 0.65 mg/day
  - 200 mg: 1.35 mg/day 9mg= 6 12mg=9 15 mg =11 pellets
  - 300mg: 2mg/ day
- Normal Levels 300-900 ng/dl

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Testosterone Side effects

- alterations in liver function tests
- enlarged breasts in men
- water retention
- skin rash
- headache
- anxiety
- depression
- numbness and tingling
- allergic reactions

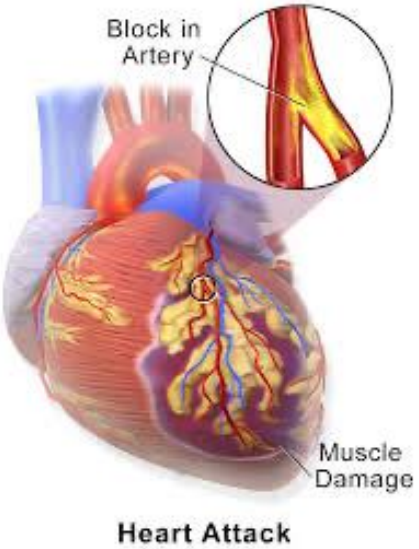
Varying effect on hematocrit with different testosterone formulations

Testosterone formulation	Dosing regimen	Rate of hematocrit elevation >50%
Testosterone cypionate or enanthate (short-acting injectable)	100-200 mg IM every week	67%
Testosterone undecanoate (long-acting injectable)	1000 mg, first interval 6 weeks, followed by intervals of 12 weeks	7%
Transdermal gel	Testosterone 50-100 mg every day(sachets) Testosterone 20-80 mg every day (dosing pump)	13%
Pellets	Crystalline testosterone 75 mg/pellet implanted, 10-14 pellets every 3-6 month	35%

Ohlander SJ, Varghese B, Pastuszak AW. Erythrocytosis Following Testosterone Therapy. *Sex Med Rev*. 2017 [May 16, Epub ahead of print]

T Therapy and Risks of CV Events

- No evidence to support increased risk
  - Two studies reported risk, but major flaws and misreported
  - Low T associated with increased atherosclerosis, CAD, diabetes, obesity and mortality
  - RCTs with heart disease showed benefits (time to ischemia and exercise capacity)
  - Largest meta-study no increased risk, and reduced risk with metabolic conditions
  - No increased risk VTE with Testosterone therapy



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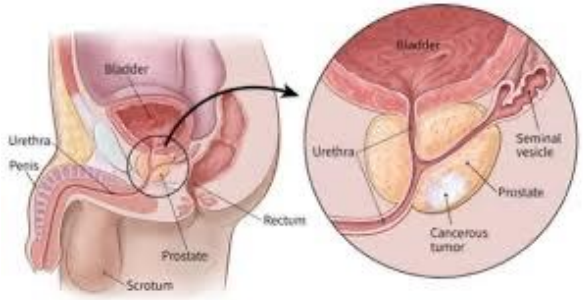
T Therapy and Risk of Prostate Cancer (PCa)

- Androgen concentration not associated with risk of PCa or aggressive disease
- Aggressive disease associated with low T level
- No increased risk of recurrent/progression with T therapy in previously treated
- T therapy no greater risk PCa than placebo



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Post-Insertion Labs

- **Testosterone, DHEA**
- Sensitive **estradiol** if Elevated
  - Re-check before aromatase inhibitor (AI)
  - Arimidex (anastrozole) 0.5 mg twice weekly
  - Femara (letrozole) 1.25 mg once weekly or every other wk.
- **Hgb & Hct**.
  - If Hematocrit is close to 50 repeat before next insertion.
  - If hematocrit s greater than 53 suggest donation of 2 units of blood.
- **If Testosterone levels > 1500, repeat levels prior to next insertion**.

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Monitoring Pellet Testosterone Therapy

Symptoms: Evaluate response after each treatment

Goal :Restore testosterone to upper limits of normal for young men

- 900-1100 ng/dL if levels are checked at 4 or 6 weeks
- Maintain testosterone over 600 ng/dL

Measuring Testosterone:

- Check 6 weeks after insertion.
- Continue adjusting and checking as required
- End point patient feels great

Hematocrit :

- Check at 3-6 months, then annually.
- If level is greater than 53. Donate blood.

Osteoporosis : Measure BMD after 2 years

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Monitoring Testosterone Therapy

Prostate

- Baseline PSA on men older than, 40 . If normal annually.

Urology Consultation

- If PSA increase >1.4 ng/mL in any 12-month period
- PSA velocity of >0.4 ng/mL-yr after 6 months of therapy
- AUA/IPSS score of >19

If measuring Percentage free PSA : Prostate biopsy if level is 4-10% . Normal >25%
A lower percentage of free PSA means that your chance of having prostate cancer is higher.

AUA=American Urological Association; IPSS=International Prostatic Symptom Score.

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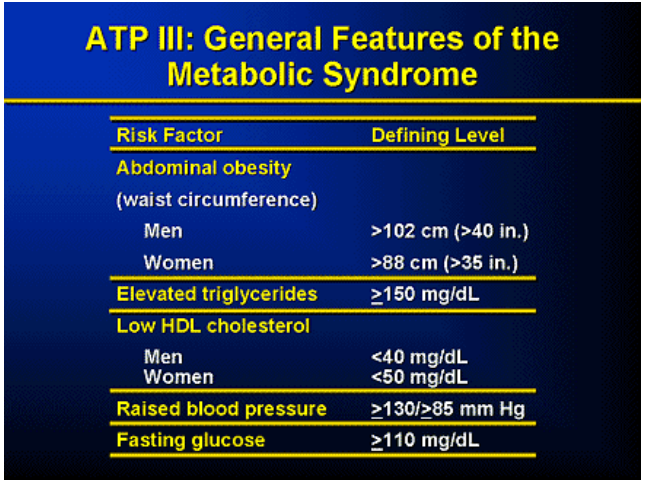
T Therapy and Cardiometabolic Disease

- Evidence suggests low T associated with CV risk - high T levels protective
- T increases lean mass, decreases fat mass and improves glycemic control
- Mortality reduced by ½ in treated men
- Treated normalized T levels reduced rates CV events /mortality vs persistently low



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Optimal Testosterone Level

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THANK YOU FOR YOUR ATTENTION

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