An Update on Men's Health and Sexual Function

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Outline

- **Testosterone Deficiency**
  - **Definition**
  - **Pathophysiology**
  - **Prevalence**
  - **Disease modification**
  - **Diagnosis**
  - **Treatment options**
  - **Risks**
  - **Treatment alternatives**
- **Men's Sexual Health**
  - **Premature ejaculation**
  - **Delayed orgasm**
  - **Erectile dysfunction**

SPECIAL ARTICLE

MAYO CLINIC

CrossMark

Adult-Onset Hypogonadism

Mohit Khera, MD, MBA, MPH; Gregory A. Broderick, MD; Culley C. Carson III, MD; Adrian S. Dobs, MD, MHS; Martha M. Faraday, PhD; Irwin Goldstein, MD; Lawrence S. Hakim, MD; Wayne J.G. Hellstrom, MD; Ravi Kacker, MD; Tobias S. Köhler, MD, MPH; Jesse N. Mills, MD; Martin Miner, MD; Hossein Sadeghi-Nejad, MD; Allen D. Seftel, MD; Ira D. Sharlip, MD; Stephen J. Winters, MD; and Arthur L. Burnett, MD, MBA

- **AOH is a clinical and biochemical syndrome characterized by a deficiency of testosterone with signs and symptoms that can be caused by testicular and/or hypothalamic-pituitary dysfunction**
- **AOH is clinically distinct from classical primary and secondary hypogonadism**
- **AOH more often occurs in men who have chronic medical conditions**

Khera et al Mayo Clin Proc. 2016 Jul, 91(8): 908-26

Pathophysiology

- **GnRH levels decrease with age**
- **Sex hormone binding globulin (SHBG) levels increase with age**
- **Testosterone levels begin to decline by 0.3% - 1.4% per year beginning at 20 – 30 years of age**
- **Many chronic illnesses are associated with low T levels**

Araujo et al. 2011; Feldman et al. 2002; Wu et al. 2008

- **AOH is often overlooked because patients ignore their symptoms.**
  - **Hypoactive sexual desire**
  - **Reduced nocturnal/morning erections**
  - **Delayed ejaculation**
  - **Reduced semen volume**
- **The Endocrine Society suggests measuring T levels in men with any symptoms or conditions in the table.**

Conditions in which serum T measurement is suggested
Infertility
Osteoporosis, low trauma fracture
Type 2 diabetes
Glucocorticoids, ketoconazole, opioid medications that affect T metabolism/production
Moderate to severe COPD
Sellar mass, radiation to the sellar region
End-stage renal disease
HIV-associated weight loss

Dandona et al 2010; Bhasin et al 2010

Prevalence

- **European Male Aging Study (EMAS)**
  - **3369 participants**
  - **Aged 40 – 79**
  - **Total testosterone cutoff 300 ng/dL**
  - **LH cutoff 9.8 U/L**
  - **13.8% Hypogonadism**
    - **2% Primary hypogonadism**
    - **11.8% Secondary hypogonadism**
  - **9.5% Compensated hypogonadism**
    - **Meaning elevated LH with normal T**
- **Hypogonadism in Males (HIM) study**
  - **Overall prevalence 39% in males >45**
    - **34% – 45-54**
    - **50% – >80**
- **Massachusetts Male Aging Study (MMAS)**
  - **Symptomatic prevalence increased somewhat with age**
    - **4.1% - 40 – 49 years**
    - **4.5% - 50 – 59 years**
    - **9.4% - 60 – 69 years**

Tajar et al 2010; Mulligan et al. 2006; Araujo 2004

Prevalence in Other Conditions

- **74 % - Chronic opioid use**
- **52 % - Obesity**
- **50% - Diabetes**
- **50% - AIDS**
- **42% - Hypertension**
- **40% - Hyperlipidemia**
- **30% - HIV**
- **19% - ED**

Odds ratio for hypogonadism for various comorbidities from HIM study	
Obesity	2.38
Diabetes	2.09
Hypertension	1.84
Hyperlipidemia	1.47
Osteoporosis	1.41
Asthma/COPD	1.40

High BMI, central adiposity and metabolic syndrome are associated with low serum total T and free T levels

Bodie et al. 2003; Daniel et al. 2002; Wang et al. 2011; Mulligan et al 2006; McLachlan et al 2010

Disease Modification

- **Treatment can be started with disease modification**
  - **Obesity**
  - **Diabetes**
  - **Hypertension**
  - **Hyperlipidemia**

- **Diet and exercise**
- **Improved glycemic control**
- **Weight loss**
- **Improved sleep**
- **Stress reduction**
- **Varicocele repair**

Journal of Andrology, Vol. 30, No. 6, November/December 2009

Fifty-two–Week Treatment With Diet and Exercise Plus Transdermal Testosterone Reverses the Metabolic Syndrome and Improves Glycemic Control in Men With Newly Diagnosed Type 2 Diabetes and Subnormal Plasma Testosterone

ARMIN E. HEUFELDER,* FARID SAAD,†‡ MATHIJS C. BUNCK,§ AND LOUIS GOOREN§

*From †Business Unit Primary Care, Men's Healthcare, Scientific Affairs, Bayer Schering Pharma AG, Berlin, Germany; ‡Gulf Medical University, Ajman, United Arab Emirates; and the §Department of Endocrinology, Vrije University Medical Center, Amsterdam, the Netherlands. *Dr Heufelder is in private practice in Munich, Germany.*

32 men with metabolic syndrome
- **16 diet + exercise**
- **16 diet + exercise + testosterone**

- **81% diet + exercise + testosterone no longer with metabolic syndrome**
- **31% diet + exercise alone no longer with metabolic syndrome**

European Journal of Endocrinology (2013) **168** 445–455 ISSN 0804-4643

CLINICAL STUDY

Age-associated changes in hypothalamic–pituitary–testicular function in middle-aged and older men are modified by weight change and lifestyle factors: longitudinal results from the European Male Ageing Study

E M Camacho, I T Huhtaniemi[1], T W O'Neill[2], J D Finn, S R Pye[2], D M Lee[2], A Tajar[2,*], G Bartfai[3], S Boonen[4], F F Casanueva[5,6], G Forti[7], A Giwercman[8], T S Han[9], K Kula[10], B Keevil[11], M E Lean[12], N Pendleton[13], M Punab[14], D Vanderschueren[15], F C W Wu and the EMAS Group[†]

- **Longitudinal survey – 2,736 men**
- **Assessed changes in weight and T levels**
- **>10% decrease weight = 85 ng/dL increase in T**

European Journal of Endocrinology (2013) **168** 829–843 ISSN 0804-4643

CLINICAL STUDY

Body weight loss reverts obesity-associated hypogonadotropic hypogonadism: a systematic review and meta-analysis

Giovanni Corona[1,2], Giulia Rastrelli[1], Matteo Monami[3], Farid Saad[4], Michaela Luconi[5], Marcello Lucchese[6], Enrico Facchiano[6], Alessandra Sforza[2], Gianni Forti[5], Edoardo Mannucci[7] and Mario Maggi[1]

- **Meta-analysis of 24 articles**
- **Mean percent weight loss:**
  - **32% with surgery**
  - **9.8% with diet**
- **Bariatric surgery being more effective in comparison with the low-calorie diet**
  - **TT increase:**
    - **252 ng/dL for bariatric surgery**
    - **83 ng/dL for the low-calorie diet**
    - **both p<0.0001 vs baseline**

Steroids

Volume 57, Issue 2, February 1992, Pages 86–89

Subnormal serum testosterone levels in male internal medicine residents

Frank Singer, Barnett Zumoff

- **The consequences of sleep deprivation and stress in residency training**
- **Unexpectedly observed a significant (P < 0.005) and marked depression of serum testosterone levels in healthy male internal medicine residents(340 ng/dL) compared with other hospital personnel (594 ng/dL)**
  - **254 ng/dL difference**
- **Testosterone concentrations in the two groups were entirely nonoverlapping, while luteinizing hormone levels were not significantly different.**

Varicocele Repair Impact on Testosterone

- Retrospective, 53 men underwent varicocele repair
  - Mean testosterone values increased from 319 +/- 12 to 409 +/- 23 ng/dL ($p<0.0004$)
- Prospective, 200 men
  - Varicocele vs observation
  - Mean improvement 80 ng/dL
- Meta-analysis of 9 studies
  - 814 patients
  - Mean improvement 100 ng/dL

Su LM et al.1995; Sathya et al. 2011; Li et al. 2012

Diagnosis Recommendations

- The International Society of Andrology (ISA), International Society for the Study of Ageing Male (ISSAM), European Association of Urology (EAU), European Academy of Andrology (EAA), American Society of Andrology (ASA) recommendations:
  - Total testosterone - 230 ng/dl is a limit below which patients will usually benefit from testosterone replacement treatment
- Endocrine Society
  - Total testosterone - approximately 280–300 ng/dl
  - Free testosterone - approximately 5–9 ng/dl
  - An evaluation of androgen deficiency should not be made during an acute or subacute illness.

Wide Variability in Laboratory Reference Values for Serum Testosterone

Stephen Lazarou, MD, Luis Reyes-Vallejo, MD, and Abraham Morgentaler, MD
Harvard Medical School, Division of Urology, Beth Israel Deaconess Medical Center, Boston, MA, USA

DOI: 10.1111/j.1743-6109.2006.00334.x

- **A telephone survey of 12 academic, 12 community medical laboratories, and one national laboratory**
- **Eight different assays were used to measure TT and four for FT**
- **Of the 25 labs, there were 17 and 13 different sets of reference values for total and free testosterone, respectively.**

	Reference value	Range	Variation
Total Testosterone	Lower Value	130 – 450 ng/dL	350%
Total Testosterone	Upper Value	486 – 1593 ng/dL	325%
Free Testosterone	Lower Value	5.0 – 13.5 pg/mL	270%
Free Testosterone	Upper Value	19.0 – 54.7 pg/mL	290%

- **All reference values were based on a standard statistical model without regard for clinical aspects of hypogonadism.**

J Sex Med. 2006 Nov;3(6):1085-9.

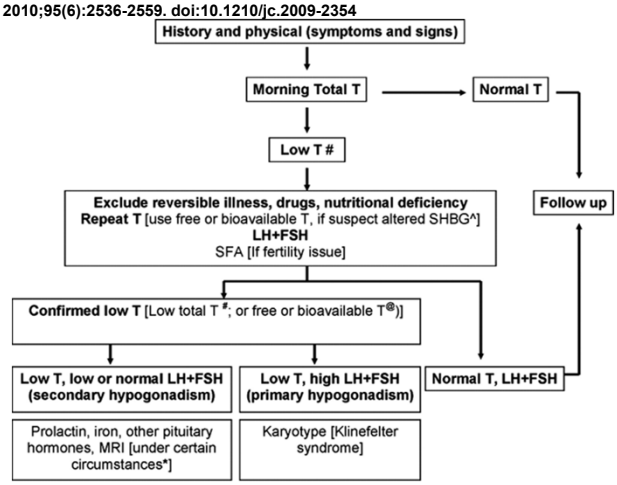
Free vs Total Testosterone and Sex Hormone Binding Globulin

- **Approximately 40% to 50% of the circulating T in men is SHBG-bound.**
- **Because SHBG binds T with high affinity, the level of SHBG is a major determinant of the circulating total T level, and the level of SHBG and its affinity for T are used to calculate the free or "bioavailable" T concentration.**

Increased SHBG concentrations	Decreased SHBG concentration
Aging	Hypothyroidism
Hepatic cirrhosis	Obesity; metabolic syndrome
Use of anticonvulsants	Type 2 diabetes
Use of estrogens	Nephrotic syndrome
Hyperthyroidism	Use of steroids (glucocorticoids, progestin, anabolic)
HIV infection	
Malnutrition; malabsorption	

From: Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline

J Clin Endocrinol Metab. 2010;95(6):2536-2559. doi:10.1210/jc.2009-2354



In men with secondary hypogonadism, we suggest further evaluation to identify the etiology of hypothalamic and/or pituitary dysfunction. This evaluation may include measurements of serum prolactin and iron saturation, pituitary function testing, and magnetic resonance imaging of the sella turcica.

Symptoms of Low Testosterone

Sexual	Constitutional	Cognitive
Low sexual desire	Anemia	Insomnia
Delayed orgasm	Decreased muscle	Irritability
Erectile dysfunction	Decreased bone density	Depression
Decreased nocturnal erection	Hot flashes	Lethargy
		Short-term memory loss
		Decreased motivation
		Decreased sense of overall well-being

- **Total Testosterone (ng/dL)**
- **577**
- **433**
  - **Loss of libido**
  - **Loss of vigor**
- **346**
  - **Obesity**
- **288**
  - **Feeling depressed**
  - **Disturbed sleep**
  - **Lacking concentration**
  - **Diabetes mellitus type 2**
- **231**
  - **Hot flashes**
  - **Erectile dysfunction**

- **Increasing prevalence of symptoms with decreasing testosterone levels**

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doi: 10.1210/jc.2006-0401

Association of Specific Symptoms and Metabolic Risks with Serum Testosterone in Older Men

Michael Zitzmann, Stephanie Faber, and Eberhard Nieschlag
Institute of Reproductive Medicine of the University, D-48129 Münster, Germany

Treatment options

Formulation	Dose	Precautions
Intramuscular injections	75–100 mg weekly or 150–200 mg every 2 weeks	
Transdermal gels	5–10 g applied daily to upper arms/ shoulders, or abdomen (5–10 mg testosterone systemically absorbed)	Gel transference to partner or children
Transdermal patches (non-scrotal)	2.5–7.5 mg applied nightly for 24 h	Skin reaction
Subcutaneous pellets	6–16, 75 mg pellets implanted subcutaneously every 4–6 months	
Long-lasting intramuscular injection	750 mg every 10 weeks	Pulmonary oil microembolization
Buccal tablets	30 mg tablet applied to the buccal mucosa every 12 h	Inflammation of the gums

Monitoring – Endocrine Society recommendations

- Follow-up at 3 and 6 mo, then annually; signs/symptoms, weight, TT, Hct, PSA; at 6 mo; if total T<400 ng/dL and no improvement, then consider dose increase with reassessment in another 3-6 mo;
- If hematocrit >54%, then stop TRT until Hct decreases to safe level; evaluate for hypoxia and sleep apnea; reinitiate TRT at reduced dose
- Measure BMD of lumbar spine and/or femoral neck after 1-2 y of TRT in men w/ osteoporosis or low trauma fracture
- In men aged ≥40 years w/ baseline PSA >0.6 ng/mL, perform DRE and check PSA before TRT, at 3 to 6 mo, and then based on prostate cancer screening guidelines
- Evaluate formulation-specific adverse events at each follow-up visit

Risks and Safety of Testosterone

- Challenges:
  - Lack definitive evidence derived from properly-designed studies
  - Mixed evidence that is not definitive from literature that is available
- Patients must be monitored for adverse events
- Cardiovascular risks
- Prostate cancer risks
- Erythrocytosis
- Benign Prostatic Hypertrophy (BPH)/Lower Urinary Tract Symptoms (LUTS)
- Rises in estrogen levels

Cardiovascular risks

- **"There are multiple published meta-analyses that evaluated possible CVD risks associated with T treatment. Challenges to interpreting findings across meta-analyses include that these publications varied in study inclusion criteria, outcomes evaluated, and data analytic strategies. In addition, most authors report that the methodological quality of the included trials was poor to moderate."**

Khera et al Mayo Clin Proc. 2016 Jul, 91(8): 908-26


Research

Original Investigation

Association of Testosterone Therapy With Mortality Myocardial Infarction, and Stroke in Men With Low Testosterone Levels

Rebecca Vigen, MD, MSCS; Colin I. O'Donnell, MS; Anna E. Barón, PhD; Gary K. Grunwald, PhD; Thomas M. Maddox, MD, MSc; Steven M. Bradley, MD, MPH; Al Barqawi, MD; Glenn Wening, MD; Margaret E. Wierman, MD; Mary E. Plomondon, PhD; John S. Rumsfeld, MD, PhD; P. Michael Ho, MD, PhD

- **"7486 patients not receiving testosterone therapy, 681 died, 420 had MIs, and 486 had strokes. Of the 1223 patients receiving testosterone therapy, 67 died, 23 had MIs, and 33 had strokes. The Kaplan-Meier estimated cumulative percentages with events among the no testosterone therapy group vs the testosterone therapy group at 1 year after coronary angiography were 10.1% vs 11.3%; at 2 years, 15.4% vs 18.5%; and at 3 years, 19.9% vs 25.7%."**

	No T (n=7486)	**T (n=1223)**
Died	681	67
MI	420	23
Stroke	486	33
Total	1587	123
Absolute rate	1587/7486=**21.2%**	123/1223=**10.1%**

World Experts and Androgen Study Group Petition JAMA to Retract Misleading Article on Testosterone Therapy

"Gross data mismanagement" led to unreliable results that contradicted 30+ years of medical literature, producing a media frenzy that misled consumers and compromised public health

Mar 25, 2014, 08:00 ET from The Androgen Study Group

This article has already undergone two published corrections. The first was published January 15, 2014, due to misreporting of primary results. A second correction published just a few weeks ago, on March 4, 2014, now reveals major errors presented in the article's text and figure. Specifically, in response to a letter questioning a group of 1,132 men, the authors re-examined their data and discovered the correct number should have been only 128, an 89% error rate, involving more than 1,000 individuals. The value for a second group has now been increased by more than 900 individuals. Finally, the authors discovered this dataset included 100 women, meaning nearly 10% were the wrong gender for the study.

The protest was signed by three medical societies and more than 125 scientists and physicians from 24 countries, including 59 full professors (8 emeritus), 6 journal editors, and 12 medical society presidents. Signers include U.S. faculty from Harvard, Johns Hopkins, Brown, Cornell, Cleveland Clinic, Mayo Clinic, Baylor Medical College, Tufts, and Boston University, among others. The professional societies are The International Society for Sexual Medicine (ISSM), The Sexual Medicine Society of North America (SMSNA), and The International Society for the Study of the Aging Male.

Original Investigation ONLINE FIRST

February 21, 2017

Association of Testosterone Replacement With Cardiovascular Outcomes Among Men With Androgen Deficiency

T. Craig Cheetham, PharmD, MS[1]; JaeJin An, BPharm, PhD[2]; Steven J. Jacobsen, MD, PhD[1]; et al

» Author Affiliations

JAMA Intern Med. Published online February 21, 2017. doi:10.1001/jamainternmed.2016.9546

- **A retrospective cohort study was conducted within an integrated health care delivery system.**
- **The cohorts consisted of 8808 men (19.8%) ever dispensed testosterone (ever-TRT) (mean age, 58.4 years; 1.4% with prior cardiovascular events) and 35 527 men (80.2%) never dispensed testosterone (never-TRT) (mean age, 59.8 years; 2.0% with prior cardiovascular events).**
- **Among men with androgen deficiency, dispensed testosterone prescriptions were associated with a lower risk of cardiovascular outcomes over a median follow-up of 3.4 years.**

Prostate Cancer risks

- **Although no appropriately designed and powered study has been conducted to assess prostate cancer related risks of TT, the available evidence suggests that T treatment does not increase prostate cancer risk.**
- **Low T levels are associated with higher rates of prostate cancer as well as more advanced prostate cancer tumor grade, stage, and volume compared with men who are not hypogonadal**
- **Observational studies also suggest that men taking T do not have an increased risk of developing prostate cancer. A large longitudinal study evaluating roughly 10,000 men found no association between androgen levels and prostate cancer risk**

Roddam et al 2008; Bhasin et al 2010; Isom-Batz et al 2005

Studies on Prostatic Cancer

I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate*

Charles Huggins, M.D., and Clarence V. Hodges, M.D.

(From the Department of Surgery, the University of Chicago, Chicago, Illinois)

(Received for publication March 22, 1941)

Carcinoma of the prostate gland is peculiarly favorable for endocrine investigation since frequent serial observations of the activity of phosphatases in serum were found to provide objective indices of activity of the neoplasm when the enzymes were increased in amount above normal. In the present paper data are given for the values of serum phosphatases in carcinoma of the prostate and in normal men. We shall demonstrate that the acid phosphatase of serum is reduced in metastatic carcinoma of the prostate by decreasing the activity of androgens through castration or estrogenic injections and that this enzyme is increased by injecting androgens. We have been unable to find previous observations indicating any relationship of hormones to carcinoma of the prostate gland.

Methods and Materials

The phosphatase activity of serum was determined by the method of King and Armstrong (10) using 0.005 M disodium monophenylphosphate as substrate. The buffers used were 0.05 M barbital-sodium at pH 9.3, and 0.1 M Sörensen's citrate-HCl or Walpole's 0.2 N sodium acetate-acetic acid buffers at pH 5. All serums were tested in duplicate and were added directly to buffer-substrate solutions without dilution; they were incubated at 37.5° C. for 30 minutes. Precautions were observed that all solutions were at this temperature before testing. Blanks were run by adding the protein precipitant to the buffer-substrate solution before adding serum. Colorimetric procedures were carried out with the Evelyn photoelectric color-

Androgen Hypothesis 1941 - 2006

- High T causes Prostate cancer
- Low T protects against Prostate cancer
- T administration in men with known Prostate cancer is like “pouring gasoline on a fire” or “feeding a hungry tumor”

Morgentaler slide

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

Risks of Testosterone-Replacement Therapy and Recommendations for Monitoring

Ernani Luis Rhoden, M.D., and Abraham Morgentaler, M.D.

- No evidence of increased risk for Prostate cancer with testosterone therapy

Review – Prostate Cancer

Shifting the Paradigm of Testosterone and Prostate Cancer: The Saturation Model and the Limits of Androgen-Dependent Growth

Abraham Morgentaler [a,*], *Abdulmaged M. Traish* [b]

- The Saturation Model describes a steep T-dependent curve at T concentrations at or below the near-castrate range, with a plateau representing little or no further growth above this concentration.

Testosterone Replacement Therapy in Patients with Prostate Cancer After Radical Prostatectomy

Alexander W. Pastuszak,* Amy M. Pearlman,* Win Shun Lai,* Guilherme Godoy,* Kumaran Sathyamoorthy,* Joceline S. Liu,* Brian J. Miles,* Larry I. Lipshultz† and Mohit Khera‡,§

- **Post prostatectomy**
  - **103 hypogonadal men**
    - **26 (25%) high risk**
  - **49 eugonadal controls**
    - **15 (31%) high risk**
  - **Mean follow-up – 27 mo**
  - **Biochemical recurrence**
    - **4 (4%) T group**
    - **8 (16%) control group**

Asian Journal of Andrology (2016) 18, 16–20

www.asiaandro.com; www.ajandrology.com

Open Access

INVITED ORIGINAL ARTICLE

Male Endocrinology

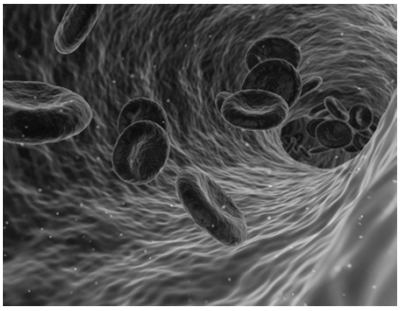
Can testosterone therapy be offered to men on active surveillance for prostate cancer? Preliminary results

Ravi Kacker[1], Mariam Hult[1], Ignacio F San Francisco[2], William P Conners[1], Pablo A Rojas[2], William C Dewolf[3], Abraham Morgentaler[1]

- **All men on active surveillance for prostate cancer**
- **28 hypogonadal men with Testosterone therapy**
- **96 hypogonadal men no Testosterone therapy**
- **3 yr median f/u**
- **No difference in progression between groups**

Erythrocytosis

- Testosterone is a known stimulant of erythropoiesis, so a rise in hematocrit is not unusual and it needs to be monitored.
- During TT, levels of Hb and Hct rise for the first 5 to 6 months, then tend to plateau; levels decline to baseline within 3 to 12 months after TT discontinuation.
- Intramuscular formulations are most commonly associated greatest increases



Swerdloff & Wang 2003; Dobs et al 1999; Rhoden & Morgentaler 2004; Schreijer et al 2010; Braekkan et al 2010.

BPH…

- Several studies demonstrate either no change or improvement in BPH/lower urinary tract symptoms with T administration.
- Placebo-controlled trials of exogenous administration of dihydrotestosterone (DHT) and T resulted in no changes in prostate DHT or T in blood sampling or prostate biopsy specimens.
- Bone mineral density measurement should also be tested at baseline because hypogonadism is an important cause of male osteoporosis.

Amano et al 2010; Francomano et al 2014; Haider et al 2009; Kalin chenko et al 2008

Contraindications

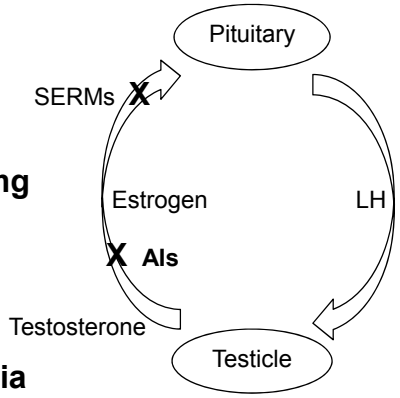
- Infertility
  - various alternative options
- Male breast cancer
- Controversial
  - Stroke
  - Spontaneous Venous Thromboembolism

Testosterone Alternatives

- To preserve fertility
- Preserve testicular volume
- Concern for safety of testosterone products
- Medical therapies
  - Selective Estrogen Receptor Modulators (SERMs)
  - Aromatase Inhibitors (AIs)
  - Human Chorionic Gonadotropin (HCG)

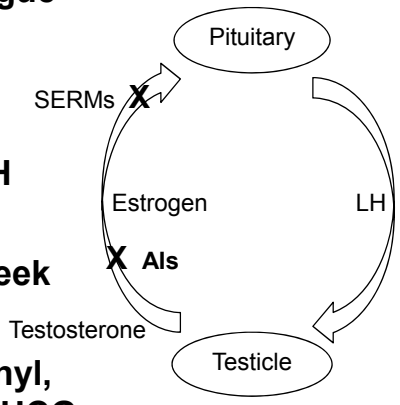
Medical therapies

- **SERMs**
  - **Act as estrogen receptor agonists and antagonists depending on location**
  - **In the brain, acts as an antagonist**
  - **Clomiphene (Clomid) 50 mg every other day**
    - **OFF LABEL**
- **AIs**
  - **Block conversion of testosterone to estrogen via aromatase**
  - **Anastrozole (Arimidex) daily, Letrozole**



HCG

- **Placental glycoprotein homologue of LH**
- **Able to stimulate testicular testosterone production like LH**
- **Needs to be injected 3 times/week**
- **Brands: Novarel, Ovidrel, Pregnyl, A.P.L., Profasi, Chorex, Gonic, HCG, Chorigon, Choron-10**



Future Options

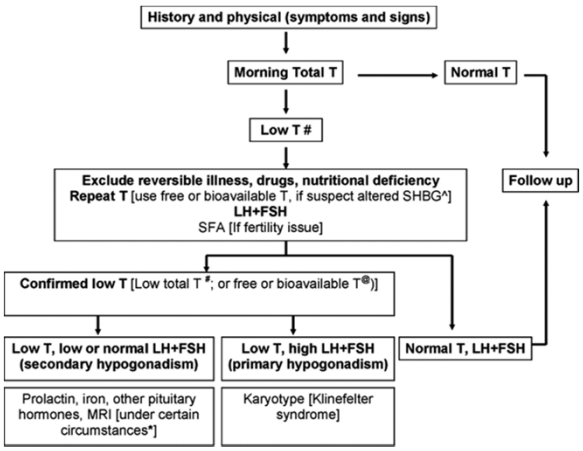
- Stem cell therapies
- New formulations of testosterone
  - Oral
  - Preloaded injections
- Updates on testosterone alternatives
  - More selective SERMs
  - Long acting HCG

Conclusion

- Disease modification should be considered in patients with reversible co-morbidities
  - Diet, exercise, weight loss, improved glycemic control, sleep, stress reduction, and varicocele repair
- Obtain 2 early morning levels to make diagnosis
- Treat symptomatic patients who meet criteria
- Monitor all patients on therapy
- Do not use testosterone when trying to preserve fertility
  - Risk should be discussed with patients prior to initiation of testosterone
- Trial of therapy is an option

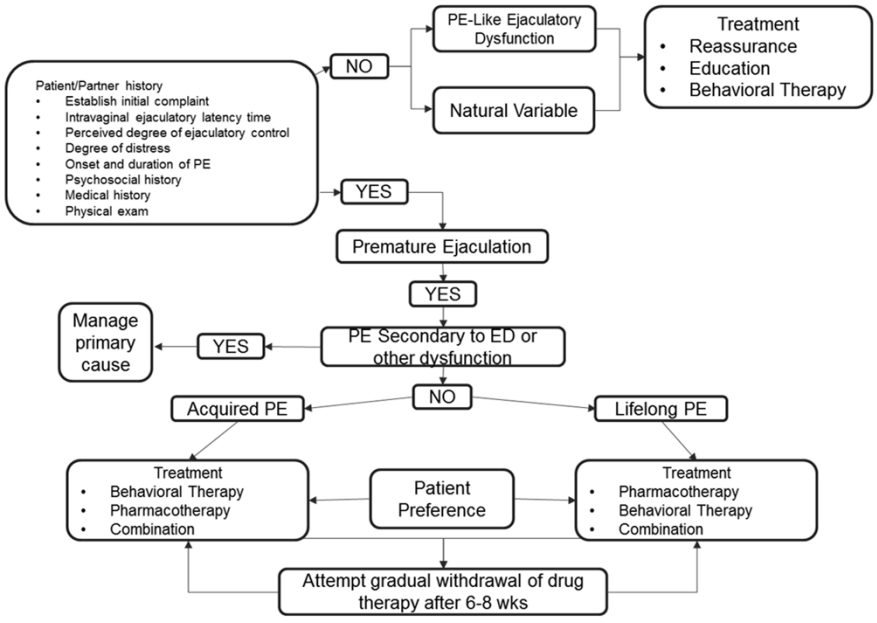
From: Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline

J Clin Endocrinol Metab. 2010;95(6):2536-2559. doi:10.1210/jc.2009-2354



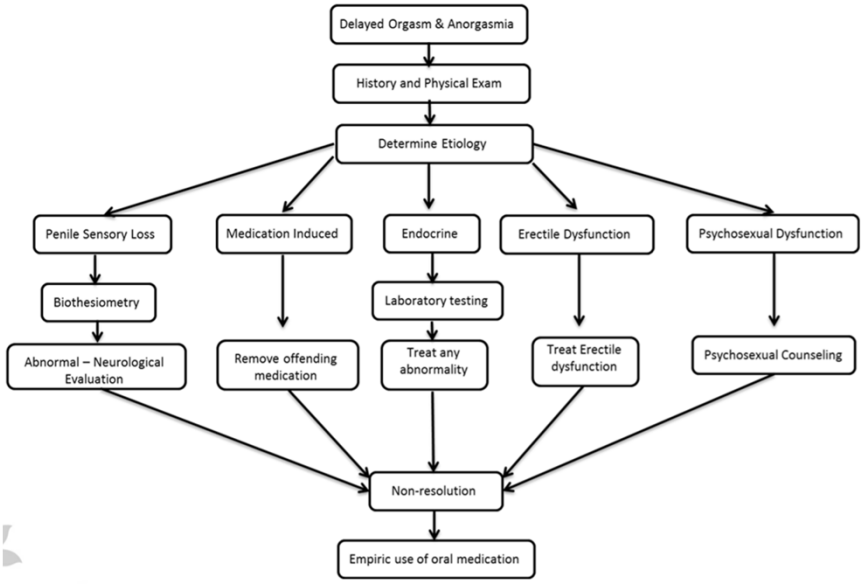
In men with secondary hypogonadism, we suggest further evaluation to identify the etiology of hypothalamic and/or pituitary dysfunction. This evaluation may include measurements of serum prolactin and iron saturation, pituitary function testing, and magnetic resonance imaging of the sella turcica.

Premature Ejaculation



Rowland et al 2010

Delayed Orgasm and Anejaculation



Jenkins & Mulhall 2015

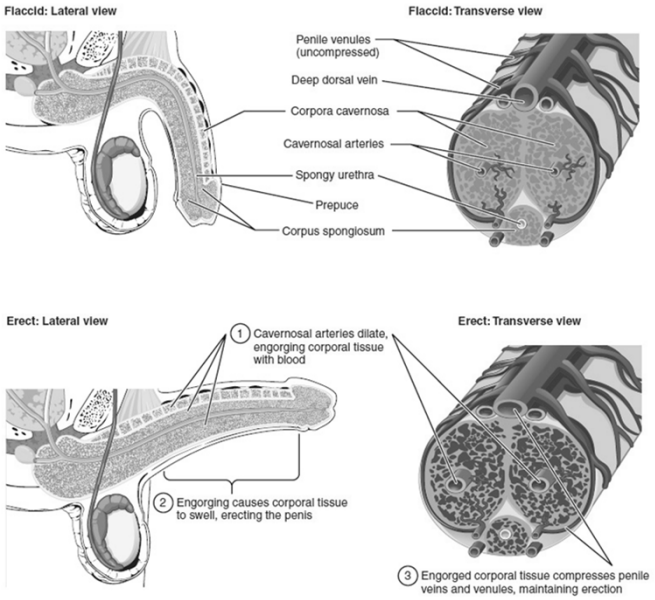
Hormones: Testosterone, Prolactin, TSH

Erectile dysfunction

- 3rd International Consultation on Sexual Medicine:
  - ED is the consistent or recurrent inability to attain and/or maintain a penile erection sufficient for sexual performance
- Intercourse or masturbation
- Rigidity, presence of spontaneous morning/night erections
- Psychological factors
- Questionnaires
  - IIEF, IIEF-5, EPIC, EDITS, Hardness scale, Fullness score…..

Incrocci L. Transl Androl Urol. 2015 Apr;4(2):124-30.

Mechanics of an erection



OpenStax, Anatomy and Physiology of the Male Reproductive System. OpenStax CNX. Feb 6, 2017 http://cnx.org/contents/370d6d11-8e11-4b2b-8fa4-a70c14b0554b@9

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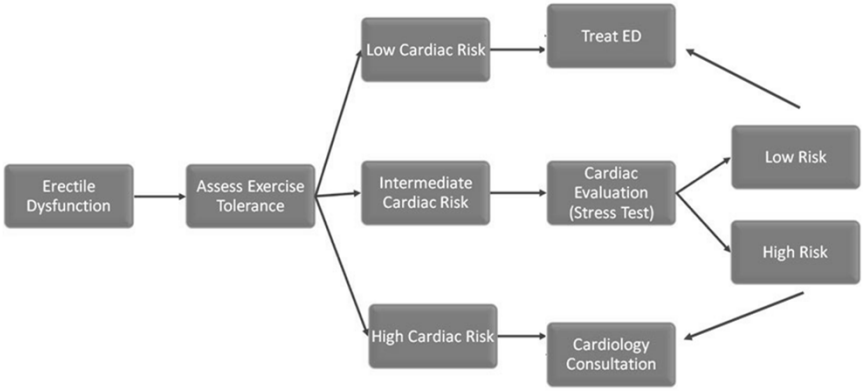
Effects of Castration and Androgen Replacement on Erectile Function in a Rabbit Model*

ABDULMAGED M. TRAISH, KWANGSUNG PARK, VINITA DHIR, NOEL N. KIM, ROBERT B. MORELAND, AND IRWIN GOLDSTEIN

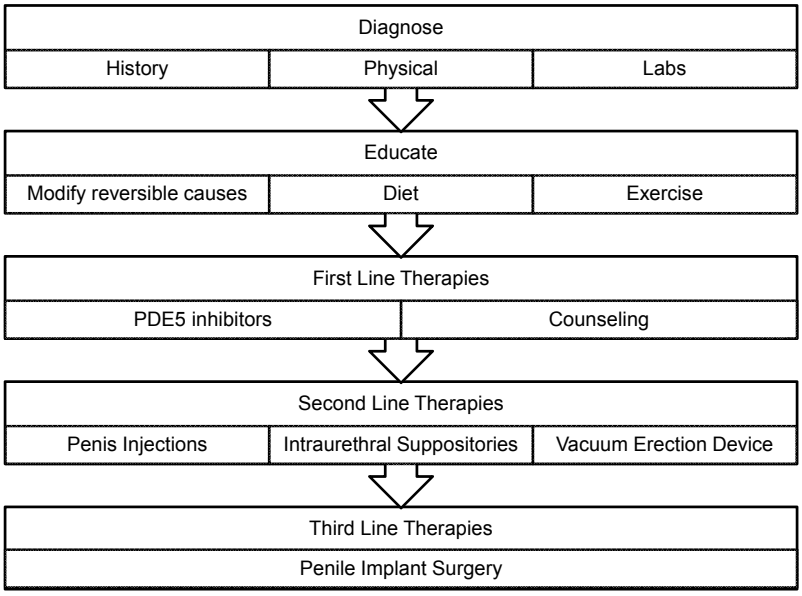
- Castration resulted in a statistically significant loss of trabecular smooth muscle ($P < 0.02$)
- Testosterone treatment prevented the loss of smooth muscle induced by castration
- Estradiol treatment did not prevent the loss of trabecular smooth muscle ($P < 0.02$).

Princeton III Consensus Conference Guidelines on Cardiac Evaluation for the ED Patient

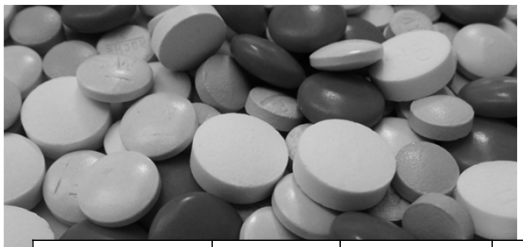


Nehra et al. 2012

Process of care model for ED

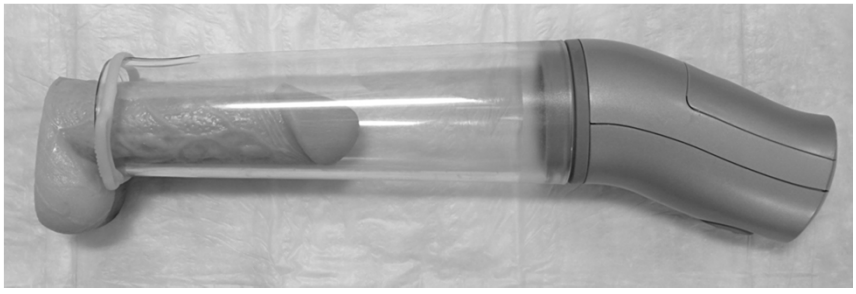


Oral Medications

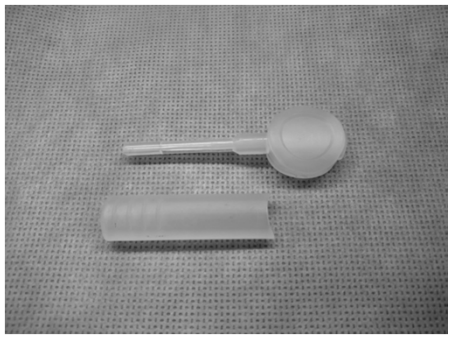


Drug name	Highest doasage	Trade name	Peak absorption (hours)	Serum half-life (hours)	Take on empty stomach
Sildenafil	100 mg	Viagra®	1-2	3-5	Yes
Vardenafil	20 mg	Levitra®	1-2	3-5	Yes
Tadalafil	20 mg	Cialis®	2-4	18	No
Avanafil	200 mg	Stendra®	0.3 - 0.5	3	No

Vacuum Erection Device



Intraurethral Suppository



Penile Injection Therapy

Penile Implant Surgery

- 92% Patients reported sexual activity with the implant to be excellent or satisfactory
- 96% Partners reported sexual activity with the implant to be excellent or satisfactory
- 95% Patients reported no change or better orgasm following the surgery
- 98% Patients reported satisfactory or excellent erections following the surgery

Image courtesy of Coloplast A/S, Humlebæk, Denmark

Montorsi et al 2000

Men's Sexual Health

- Identify patients who need further cardiovascular evaluations
- Educate patients that there are more options beyond pills
- Focus patients on long-term goals to help minimize anxiety
- Identify barriers to treatment
- Make sure pills are maximized and taken appropriately before considering failure
- Penile implant surgery provides a safe-effective option for the right patient