7:45 – 8:45 am

Tackling Common GU Issues in Men

SPEAKER
Mohit Khera, MD, MBA, MPH

Presenter Disclosure Information

The following relationships exist related to this presentation:

► Mohit Khera MD, MBA, MPH: Advisory Boards for AbbVie Inc.; American Medical Systems, LLC; Coloplast; Endo Pharmaceuticals Inc.; and Lipocine Inc. Ownership Interest (eg stocks, stock options, etc.) Sprout Pharmaceuticals, Inc.

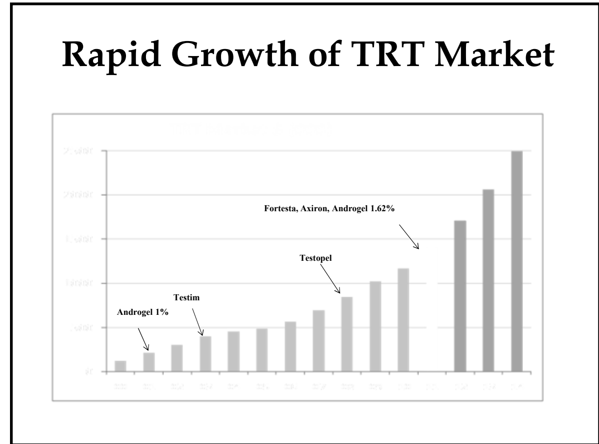
Off-Label/Investigational Discussion

► In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Diagnose and treat men with low testosterone
- Diagnose and treat men with BPH
- Review the new AUA updated BPH guidelines
- Diagnose and treat men with ED

Rapid Growth of TRT Market

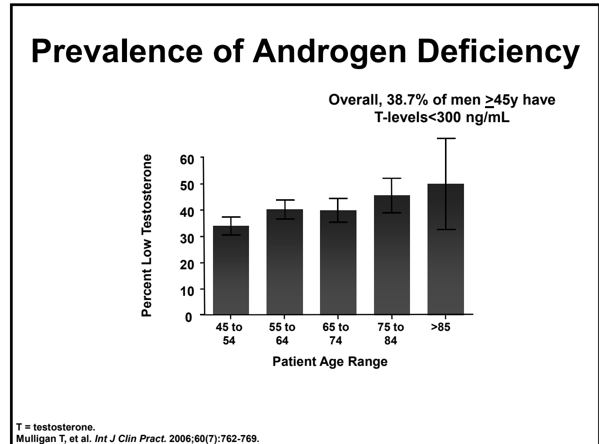


Diagnosis of Androgen Deficiency and Late Onset Hypogonadism (LOH)

Biochemical

Signs and Symptoms

Prevalence of Androgen Deficiency

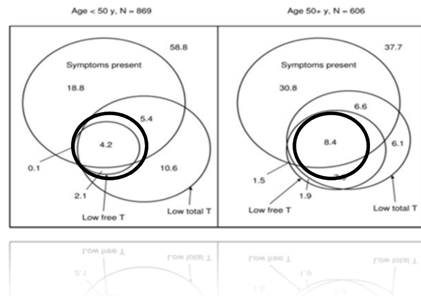


T = testosterone.
Mulligan T, et al. *Int J Clin Pract.* 2006;60(7):762-769.

Prevalence of Symptomatic Androgen Deficiency in Men

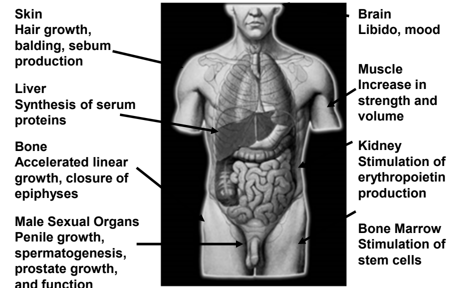
Andre B. Araujo, Gretchen R. Esche, Varant Kupelian, Amy B. O'Donnell, Thomas G. Travison, Rachel E. Williams, Richard V. Clark, and John B. McKinlay

New England Research Institutes, Inc. (A.B.A., G.R.E., V.K., A.B.O., T.G.T., J.B.M.), Watertown, Massachusetts 02472; and GlaxoSmithKline Research and Development (R.E.W., R.V.C.), Research Triangle Park, North Carolina 27709



Araujo et al., J Clin Endocrinol Metab 2007 Nov;92(11):4241-7

The Impact of Testosterone



AACE Hypogonadism Task Force. *Endocrinol Pract.* 2002;8:439-456; Morley JE, et al. *Metabolism.* 2000;49:1239-1242.

Physical Signs of Low Testosterone

Physical Signs

- Increased body fat, BMI
- Reduced muscle bulk and strength
- Low bone mineral density
- Loss of body hair (axillary and pubic)

Adapted from The Endocrine Society Guidelines, 2006.

Symptoms of Low Testosterone

Symptoms

- Decreased energy or motivation
- Diminished libido, erectile and ejaculatory dysfunction
- Diminished work performance
- Poor concentration and memory
- Sleep disturbance
- Depression

ORIGINAL ARTICLE

The effect of testosterone supplementation on depression symptoms in hypogonadal men from the Testim Registry in the US (TRiUS)

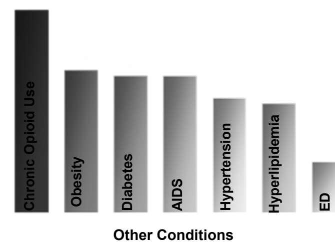
Mohit Khera[1], Rajib K. Bhattacharya[2], Gary Blick[3], Harvey Kushner[4], Dat Nguyen[4] & Martin M. Miner[5]

[1]Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA, [2]University of Kansas Medical Center, Kansas City, KS, USA, [3]Circle Medical LLC, Norwalk, CT, USA, [4]Auxilium Pharmaceuticals, Malvern, PA, USA, and [5]Miriam Hospital Men's Health Center, Warren Alpert School of Medicine, Brown University, Providence, RI, USA

- Multicenter, 12-month observational registry (*N = 849)* of hypogonadal men prescribed testosterone gel
- Depression symptoms were measured using PHQ-9
- Before treatment with TRT, 92.4% demonstrated some level of depressive symptoms, with 17.3% having severe depressive symptoms
- After 12 months of TRT, patients with severe depressive symptoms decreased from 17.3% to 2.1%
- Patients already on anti-depressants also experienced a significant improvement in PHQ-9 at 12 months

Khera et al. *Aging Male* 2011

Prevalence of Low Testosterone in Other Conditions

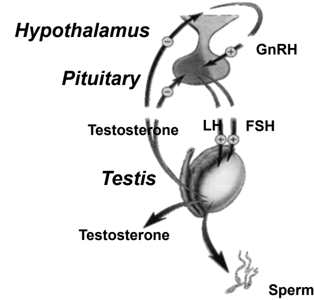


Other Conditions

HIV = 30%.
ED = erectile dysfunction.
Bodie J, et al. *J Urol.* 2003;169:2262–2264; Daniell HW. *J Pain.* 2002;3:377-384; Dobs AS. *Baillière's Clin Endocrinol Metab.* 1998;12:379-390; Grinspoon S, et al. *Ann Intern Med. 1998;129:18-26;* Mulligan T, et al. *Int J Clin Pract.* 2006;60:762–769.

Diagnosis of Low Testosterone

Production of Testosterone



Adapted from Bagatell CJ, Bremner WJ. *N Engl J Med*. 1996;334:707-714.

Classification of Hypogonadism

Primary	Secondary		Mixed
Testicular Causes	**Hypothalamic Causes**	**Pituitary Causes**	**Dual HPG Axis Defects**
▪Klinefelter syndrome ▪Orchitis ▪Congenital or acquired anorchia ▪Testicular tumors	▪Kallman syndrome ▪Constitutional delay in growth and development ▪Chronic illness	▪Hypopituitarism ▪Pituitary tumors	▪Hemochromatosis ▪Sickle cell disease ▪Glucocorticoid treatment ▪Alcoholism ▪Aging

AACE Hypogonadism Task Force. *Endocr Pract.* 2002;8:439-456.
Bhasin S, et al. *J Clin Endocrinol Metab.* 2006;91:1995-2010.

Indications for Testosterone Therapy

1 INDICATIONS AND USAGE

AndroGel 1% is an androgen indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations, but have gonadotropins in the normal or low range.

U.S. Food and Drug Administration
Protecting and Promoting Your Health

Drug Safety Communications

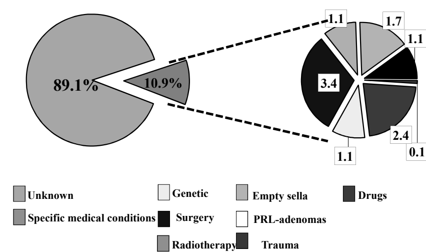
FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use

This information is an update to the FDA Drug Safety Communication: FDA Evaluating Risk of Stroke, Heart Attack, and Death with FDA-Approved Testosterone Products issued on January 31, 2014.

Safety Announcement

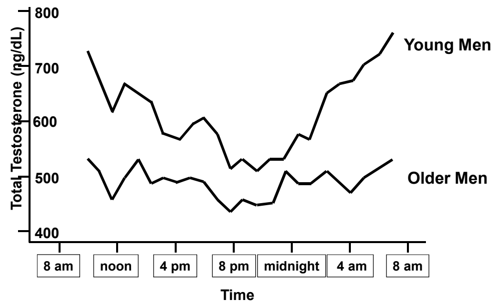
[03-03-2015] The U.S. Food and Drug Administration (FDA) cautions that prescription testosterone products are approved only for men who have low testosterone levels caused by certain medical conditions. The benefit and safety of these medications have not been established for the treatment of low testosterone levels due to aging, even if a man's symptoms seem related to low testosterone. We are requiring that the manufacturers of all approved prescription testosterone products change their labeling to clarify the approved uses of these medications. We are also requiring these manufacturers to add information to the labeling about a possible increased risk of heart attacks and strokes in patients taking testosterone. Health care professionals should prescribe testosterone therapy only for men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests.

Specific Medical Conditions Associated with Hypogonadism



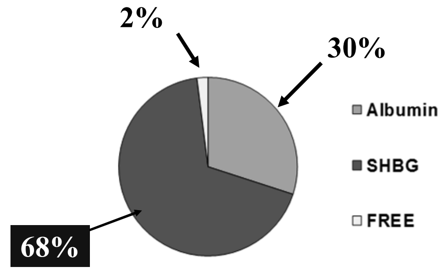
aseroli et al J Sex Med 2015 Apr;12(4):956-65.

Diurnal Variation in Serum Total Testosterone Levels



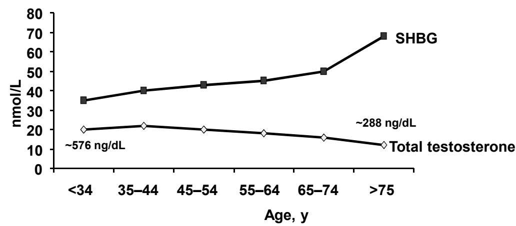
Bremner WJ et al. *J Clin Endocrinol Metab.* 1983;56:1278-1281.

Testosterone Distribution



AACE Hypogonadism Task Force "Medical Guidelines for the Evaluation and Rx of Hypogonadism in Adult Male Patients-2002 Update" Endocrine Practice 2002;8(6):440-456

Male Hormonal Status Changes With Age as SHBG Increases



- Low testosterone is increasingly common as men age
- Levels of free testosterone *decrease* and levels of SHBG *increase* with age

Gray A, et al. *J Clin Endocrinol Metab.* 1991;73(5):1016-1025.

Free & Bioavailable Testosterone calculator

These calculated parameters more accurately reflect the level of bioactive testosterone than does the sole measurement of total serum testosterone. Testosterone and dihydrotestosterone (DHT) circulate in plasma unbound (free approximately 2 - 3%) ,bound to specific plasma proteins (sex hormone-binding globulin SHBG) and weakly bound to nonspecific proteins such as albumin. The SHBG-bound fraction is biologically inactive because of the high binding affinity of SHBG for testosterone. Free testosterone measures the free fraction, bioavailable testosterone includes free plus weakly bound to albumin.

Albumin	4.3	g/dL
SHBG	50	nmol/L
Testosterone	13.1	nmol/L

Calculate   Explanation and examples

Free Testosterone	0.202 nmol/L = 1.54 %
Bioavailable Testosterone	4.74 nmol/L = 36.2 %

Disclaimer: Results from this calculator should NOT be solely relied upon in making (or refraining from making) any decision in any case/ circumstances without the prior consultation of experts or professional persons. No responsability whatsoever is assumed for its correctness or suitability for any given purpose.

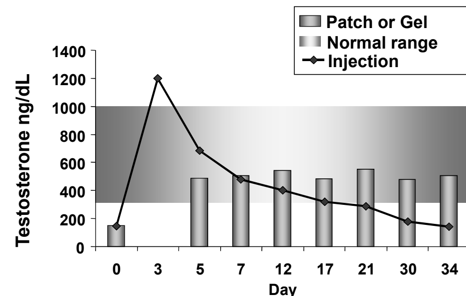
WARNING! The calculated free and bioavailable testosterone are reliable in most clinical situations, but should not be relied upon in situations with potential massive interference by steroids binding to SHBG; e.g. in women during pregnancy, in men during treatment inducing high levels of DHT (e.g. transdermal DHT, oral testosterone) or mesterolon

This calculator was developed at the Hormonology department, University Hospital of Ghent, Belgium. If you have suggestions to improve this calculator, or for further questions or help contact us Dr. Tom Fiers or Prof. Dr. J.M. Kaufman

www.issam.ch

Treatment of Low Testosterone

Different Testosterone Levels After Replacement Therapy



Adapted from Bhasin and Bremner. *J Clin Endocrinol Metab.* 1997;82:3-8
Testosterone gel (AndroGel ®1%) Unimed Pharmaceuticals and Solvay Pharmaceuticals,

Testosterone: Recommended Rx Formats

Testosterone enanthate or cypionate IM	100 mg q week 200 mg q2 weeks
Testosterone patch	2-4 grams (1-2 patches) qhs
Testosterone gel (topical/nasal)	variable
Bioadhesive buccal testosterone	30 mg q12h
Testosterone pellets	75g x 10 q4-6m*
Testosterone undecanoate	Inject q 10 weeks

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

Testosterone and Cardiovascular Disease

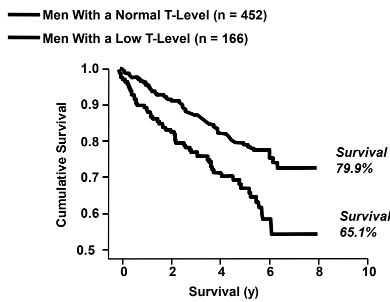
Millions of Men at Potential Risk for Fatal Harm Due to Unnecessary 'Low T' Therapy

If you, or a loved one, have been prescribed any of the following low testosterone drugs, you may be entitled to compensation, and should speak to an attorney about your legal rights.

McLaughlin & Lauricella P.C.
Low-T Testosterone Lawsuit Lawyers

Aging Males and Mortality

Low Serum T and Mortality in Male Veterans



Shores M, et al. *Arch Intern Med.* 2006;166:1660-1665.

Low Testosterone and Increased Mortality (N >500)

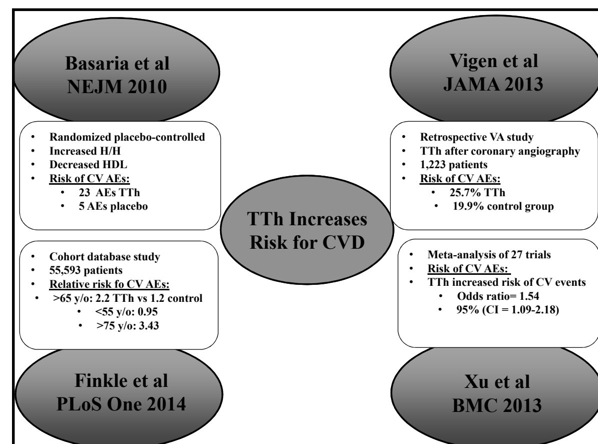
Recent Studies	HR (95% CI)	Nature	Men, n	Follow-Up, y	Mortality
Shores, 2006	1.88 (1.34–2.63)	Retrospective	858	8	All-cause
Laughlin, 2008	1.38 (1.02–1.85)	Prospective	794	20	CVD
Khaw, 2007	2.29 (1.60–3.26)	Prospective	2314 of 11,606	10	All-cause and CVD
Haring, 2010	2.32 (1.38–3.89)	Prospective	1954	7.2	All-cause
	2.56 (1.15-6.52)				CVD
Malkin, 2010	2.27 (1.45–3.60)	Prospective	930	6.9	All-cause in men with coronary disease
Tivesten, 2009	1.65 (1.29–2.12)	Prospective	3014	4.5	All-cause
Menke, 2010	1.43 (1.09–1.87)	Prospective	1114	9	All-cause
Vikan, 2009	1.24 (1.01–1.54)	Prospective	1568	11.2	All-cause
Corona, 2010	7.1 (1.8–28.6)	Prospective	1687	4.3	CVD

HR=hazard ratio; CI=confidence interval.

Prior Articles Demonstrating Beneficial Effects of T Against CVD

Type of Article	Number of Articles
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

Total studies= 49



FDA Warning

U.S. Department of Health and Human Services

U.S. Food and Drug Administration
Protecting and Promoting Your Health

Drugs

FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use

The testosterone product labels have been updated. The revised labels clarify the approved uses of these medications and include information about a possible increased risk of heart attacks and strokes in patients taking testosterone.

This information is an update to the FDA Drug Safety Communication: FDA Evaluating Risk of Stroke, Heart Attack, and Death with FDA-Approved Testosterone Products issued on **January 31, 2014**.

SPECIAL ARTICLE

MAYO CLINIC

Testosterone Therapy and Cardiovascular Risk: Advances and Controversies

Abraham Morgentaler, MD; Martin M. Miner, MD; Monica Caliber, MSc; Andre T. Guay, MD[†]; Mohit Khera, MD; and Abdulmaged M. Traish, PhD

- Low levels of Total T, bioavailable T and free T are associated with increased risk of mortality from all causes and CVD (LOE IIa)
- Severity of CAD is inversely correlated with serum concentrations of total T, bioavailable T or free T (LOE IIa)
- Testosterone therapy is associated with a significant reduction in obesity and fat mass (LOE Ib)
- Testosterone therapy improves time to onset of symptomatic angina (LOE 1b)
- Exercise capacity and peak oxygen consumption in men with symptomatic CHF as defined by New York Heart Association functional class II (LOE Ia)

Morgentaler et al. Mayo Clin Proc. 2014 Nov 1

Summary of 2010 Endocrine Guidelines

Do Not Treat

- Patients with breast or prostate cancer
- A palpable prostate nodule or induration
- Abnormal PSA
- Consider consultation in high risk patients
- Patients with erythrocytosis
- Untreated severe sleep apnea
- Severe lower urinary tract symptoms with Internation Prostate Symptom Score > 19
- Uncontrolled or poorly controlled heart failure

Bhasin S, Cunningham GR, Hayes FJ, et al. *J Clin Endocrinol Metab* . 2010, 96(6): 2536-2559.

Hypogonadism Conclusions

- Our current diagnosis and management of hypogonadism needs further evidence based support
- Androgen deficiency affects approximately 20-40% of men while symptomatic androgen deficiency, or LOH, is seen in 4-8% of men
- Low testosterone can be diagnosed by a simple blood test and a questionnaire
- There are now safe and effective ways to increase a man's testosterone

Case #1

- Mike is 54 y/o male with a 9 month history of hesitancy, urgency, frequency and nocturia x 6
- AUA symptom score 25
- PMH: DM, HTN
- Sx: appendectomy
- Social: no tob, occ ETOH
- PE: DRE 50 grams
- Labs: PSA 3.0
- Next step?

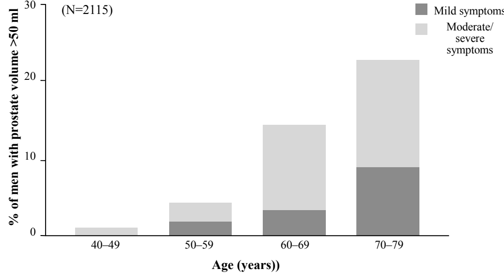
AUA = American Urologic Association

Prevalence of BPH

Age (years)	Prevalence
31-40	8%
51-60	40-50%
80+	80%

Guess HA et al. Prostate 1990; 17:241.

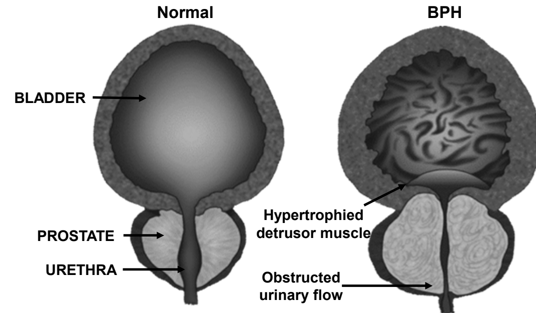
Natural History of BPH: Relationship Between Symptoms and Prostate Volume



Adapted from Girman CJ et al *J Urol* 1995;153:1510-1515.

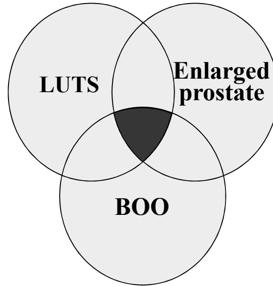
Slide I.5

Anatomy of Benign Prostatic Hyperplasia



Kirby RS et al. *Benign prostatic hyperplasia.* Health Press, 1995.

Pathophysiology of Clinical BPH: Overlapping but Independent Features



Adapted from Nordling J et al. In *Benign Prostatic Hyperplasia.* Plymouth, United Kingdom: Health Publication, 2001:107-166.

LUTS= lower urinary tract symptoms

BOO= bladder outlet obstruction

Slide I.2

LUTS – Bladder or Prostate?

LUTS = Lower Urinary Tract Symptoms

- Voiding (Obstructive)
  - Incomplete urination
  - Stopping / starting
  - Weak stream
  - Pushing / straining
- Irritative (Storage)
  - Frequency
  - Urgency
  - Nocturia

1. AUA Guidelines on Management of Benign Prostatic Hyperplasia *J Urol.* 2003 170(2):530-547.
2. Nordling J et al. In: Chatelain C et al, eds. *Benign Prostatic Hyperplasia.* Plymouth, UK: Health Publication Ltd; 2001:107166.

AUA Symptom Score

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time time	Almost always
1. Over the past month, how often have you had the sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
3. Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	1 time	2 times	3 times	4 times	5 or more times
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5
Total Symptom Score						

LUTS: History

- How long?
- Most bothersome symptom? **Degree of bother?**
- Voiding (Obstructive)
  - Incomplete urination
  - Stopping/starting
  - Weak stream
  - Pushing/straining
- Irritative (Storage - OAB)
  - Frequency
  - Urgency
  - Nocturia
- Other: fluid intake, UTI, pain, hematuria, LE swelling
- IPSS/AUA Symptom Score

1. AUA Guidelines on Management of Benign Prostatic Hyperplasia *J Urol.* 2003 170(2):530-547.
2. Nordling J et al. In: Chatelain C et al, eds. *Benign Prostatic Hyperplasia.* Plymouth, UK: Health Publication Ltd; 2001:107166.

LUTS: Exam

- Digital rectal exam
  - Estimate prostate size, asymmetry, induration, nodule or bogginess (exclude carcinoma or chronic prostatitis)
  - Check for rectal sphincter tone
- Bladder percussion/palpation for distention
- Focused neurologic examination
  - Rule out neurologic conditions that might contribute to voiding dysfunction

Adapted from Anderson RJ. *Hospital Practice.* 1998;March:11-21.

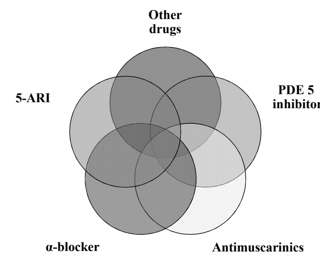
LUTS: Labs/Studies

- Urinalysis – rule out other urinary tract pathology
- PSA – appropriately aged male to screen for prostate cancer
- Upper tract imaging – only if recurrent UTI, hematuria, renal insufficiency, urolithiasis or prior urinary tract surgery
- Urodynamics/cystoscopy NOT required for initial evaluation or prior to starting therapy in standard patient
- Urolflow

Adapted from Anderson RJ. *Hospital Practice.* 1998;March:11-21.

BPH: Treatment Options

Evolution of Medical Therapy for LUTS/BPH/BOO/BPE



Alpha-blockers Adverse Events

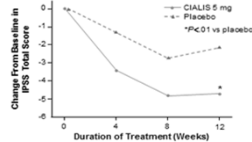
- Asthenia
- Postural hypotension
- Dizziness
- Somnolence
- Nasal congestion
- Retrograde ejaculation

5-alpha Reductase Inhibitors
Finasteride/Dutasteride

- Blocks conversion of testosterone to DHT
- Reduces volume of enlarged prostate as DHT primary androgen responsible for prostate growth
- Reduces risk of AUR/surgery by 50% (prostates $\geq$ 40 gm)
- Reduces PSA by 50%
- Takes 3-6 months to show maximal effects
- Common side effects: erectile dysfunction, decreased libido, decreased ejaculate volume

Cialis for Once Daily Dose

- FDA Indications
  - ED
  - BPH
  - ED + BPH
- Side effects
  - Headache (4.1%)
  - Dyspepsia (2.4%)
  - Back pain (2.4%)
  - Nasopharyngitis (2.1%)



Tadalafil full prescribing information 2011

Surgical Options

- Transurethral resection of the prostate (TURP)
- Simple prostatectomy
- Minimally invasive options
  - Transurethral microwave therapy (TUMT)
  - Greenlight laser
  - Transurethral needle ablation (TUNA)
  - Urolift™

When to Refer to a Urologist

- DRE reveals palpable nodules or irregularities
- PSA level of >4 ng/dL or PSA doubles in 1 year
- Inadequate response to medication
- Refractory LUTS
- Refractory cases, medical complications such as
  - Refractory AUR
  - Gross hematuria
  - Bladder stones
  - UTIs
  - Renal insufficiency

1. Moul. Postgrad Med. 1993;94:141-146,151-152.
2. Dull. Fam Pract Recert. 1998;20:43-45,51-52,59-60,68-70.
3. Murphy et al. The American Cancer Society's Informed Decisions. 1997:605-609.
4. Quick Reference for Clinicians Number 8: Benign Prostatic Hyperplasia. Rockville, Md: AHCPR; 1994
5. AUA Guidelines on Management of Benign Prostatic Hyperplasia (2003) AUA Practice Guidelines Committee. *J Urol.* 2003 170(2):530-547.

Updated 2014 AUA BPH Guidelines

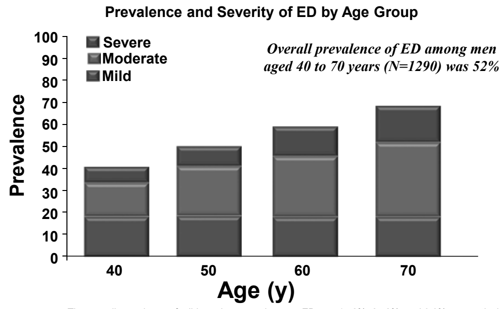
- **Laboratory tests should include PSA and urinalysis to exclude infection or other causes for LUTS**
- **Serum creatinine levels is not indicated in the initial evaluation of men with LUTS secondary to BPH**
- **For coexisting BOO and overactive bladder symptoms, the patient can be treated with combination alpha-blocker and anticholinergic therapy**
- **For LUTS resulting from BPH with predominant BOO symptoms, alpha-blockers are the first treatment of choice**

BPH Conclusions

- BPH is a common condition that impacts patients' quality of life
- Complications of untreated BPH include acute urinary retention, urinary tract infections, bladder calculi, bladder damage, renal impairment and hematuria
- Alpha blockers - first line therapy for men with bothersome LUTS
- Combination therapy with anticholinergics can be considered for certain patients
- 5-alpha reductase inhibitors may be appropriate second line therapy

Erectile Dysfunction: Diagnosis and Treatment

Massachusetts Male Aging Study (MMAS)



- The overall prevalence of mild, moderate, and severe ED was 17.2%, 25.2%, and 9.6%, respectively

Feldman HA, et al. *J Urol*. 1994;151(1):54-61.

Etiologies of ED[1-3]

Vasculogenic	Cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia, smoking, major surgery (radical prostatectomy) or radiotherapy (pelvis or retroperitoneum)
Neurogenic	Spinal cord and brain injuries, Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke
Local penile (cavernous) factors	Peyronie's disease, cavernous fibrosis, penile fracture
Hormonal	Hypogonadism, hyperprolactinemia, hyper- and hypothyroidism, hyper- and hypocortisolism
Drug-induced	Antihypertensives, antidepressants, antipsychotics, antiandrogens, recreational drugs
Psychogenic	Performance-related issues, traumatic past experiences, relationship problems, anxiety, depression, stress

1. Wespes E, et al. European Association of Urology Guidelines on Male Sexual Dysfunction: erectile dysfunction and premature ejaculation. 2013. http://www.uroweb.org/gls/pdf/14_Male%20Sexual%20Dysfunction_LR.pdf. Accessed November 24, 2013; 2. Shamloul R, Ghanem H. *Lancet*. 2013;381(9861):153-165; 3. Grant P, et al. *Clin Med*. 2013;13(2):136-140.

Efficacy Measures: IIEF-EF

International Index of Erectile Function (IIEF) Erectile Function (EF) Domain

Measured on a 30-point scale

No ED
25–30

Mild ED
17–25

Moderate ED
11–16

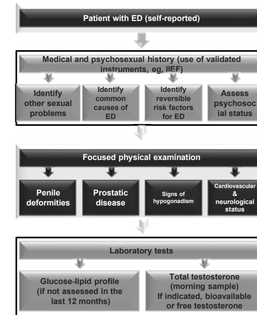
Severe ED
≤10

Over the past 4 weeks:

1. How often were you able to get an erection during sexual activity?
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
3. When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?
4. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
5. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
6. How do you rate your confidence that you can get and keep your erection?

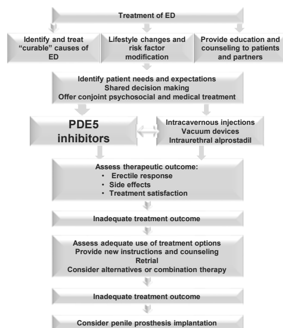
Rosen RC, et al. *Urology*. 1997;49(6):822-830.

Diagnostic Evaluation of Men with ED



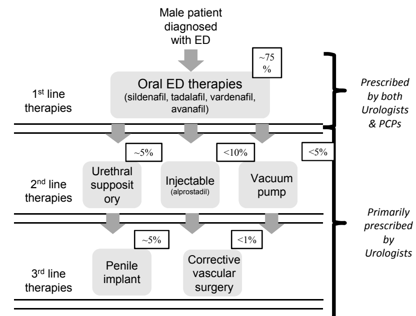
Adapted from Wespes E, et al. European Association of Urology Guidelines on Male Sexual Dysfunction:

Treatment Algorithm for ED



Adapted from Wespes E, et al. European Association of Urology Guidelines on Male Sexual Dysfunction: \2013.

Current ED Treatment Approaches



Source: Adapted from American Urologic Association Treatment of ED Guidelines,
emedicine.com, L.E.K. Consulting Interviews and analysis.

Medical Therapy of ED

- Sildenafil April 1998
- Vardenafil August 2003
- Tadalafil: November 2003
- Avanafil: January 2014

IMPORTANT SAFETY INFORMATION

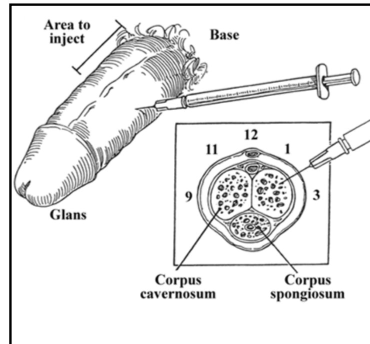
- Administration of PDE5is with any form of organic nitrates is contraindicated. PDE5is have been shown to potentiate the hypotensive effects of nitrates
- Patients with the following characteristics (recent serious cardiovascular events, resting hypotension or uncontrolled hypertension, unstable angina, angina with sexual intercourse, New York Heart Association Class 2 or greater congestive heart failure, or hereditary degenerative retinal disorders, including retinitis pigmentosa) were not included in the clinical safety and efficacy trials. PDE5is are therefore not recommended for those patients
- Caution is advised when PDE5 inhibitors are coadministered with alpha-blockers. Patients who demonstrate hemodynamic instability on alpha-blocker therapy alone are at increased risk of symptomatic hypotension with concomitant use of PDE5 inhibitors. Patients should be stable on alpha-blocker therapy prior to initiating treatment with a PDE5 inhibitor. In those patients who are stable on alpha-blocker therapy, PDE5 inhibitors should be initiated at the lowest dose

Androgens Enhance PDE5i Efficacy

- Shabsigh et al.[1]
  - 75 hypogonadal men (T<400 ng/dl) failed sildenafil 100mg
  - Randomize to testosterone gel or placebo
  - All men received sildenafil 100 mg as needed for 12 weeks
  - IIEF significantly improved in TRT vs placebo (4.4 vs 2.1, p=0.029)
- Rosenthal et al.[2]
  - 24 hypogonadal men failed 3 trials of sildenafil 100mg within 3 months
  - Started on 4 weeks of testosterone gel and then restarted on silendafil
  - After 16 weeks, 92% of men who initially failed sildenafil therapy reported improvements in potency
- Khera et al. [3]
  - Multicenter registry of hypogonadal men (n=849) treated with TRT and followed for 12 months
  - Patients already on PDE5i therapy also had a significant increase in BMSFI scores after starting TRT

[1]Shabsigh et al. *J Urol.* 2004 Aug;172(2):658-63.
[2]Rosenthal et al. Urology 2006 Mar; 67(3):571-4
[3] Khera et al JSM 2011 Nov;8(11):3204-13

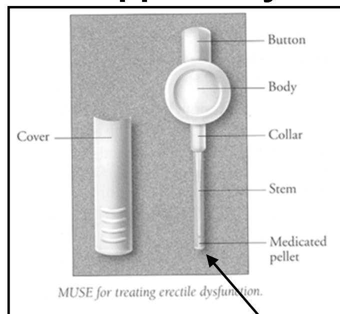
Intracavernosal Injection Therapy (ICI)



Caverject
EDEX
(Alprostadil)

Trimix
(PGE, Phentolamine, Papaverine)

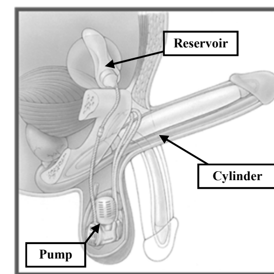
MUSE Intraurethral Suppository



MUSE for treating erectile dysfunction.

*

Inflatable 3-Piece Penile Implant



ED Summary

- ED is a progressive condition with prevalence increasing with age
- Patients with ED should have a cardiovascular assessment as ED and CVD often present simultaneously
- PDE5is are an effective first-line therapy for ED
- Patients not responding to PDE5i can either be referred to a Urologist or second-line therapies can be utilized
  - Vacuum erection device
  - Intra-urethral suppositories
  - Intercavernosal injection therapy