Testosterone Replacement and General Urology

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Objectives

Hypogonadism and Testosterone Replacement Therapy

Hematuria Guidelines

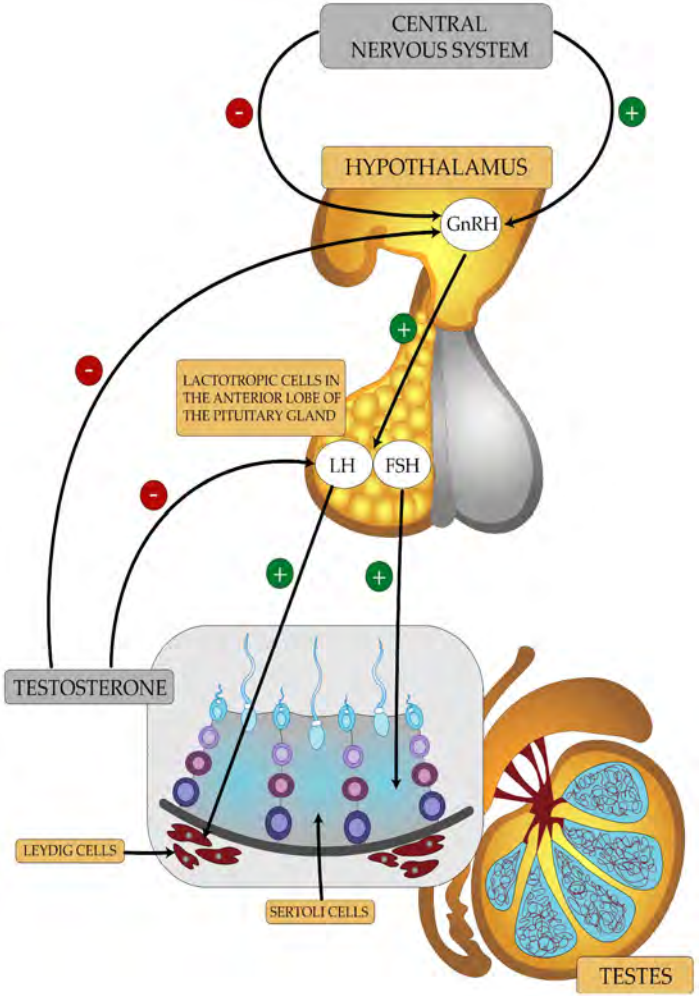
Overactive Bladder

BPH

Hypogonadism

Hypogonadism is a clinical syndrome characterized by the failure of the testes to produce physiological concentrations of testosterone.

- **Primary (testicular origin)** - gonadal (testicular) failure, where the testes are unable to produce adequate testosterone and/or sperm despite normal or elevated stimulation by pituitary gonadotropins.
  - Low testosterone levels with elevated LH and FSH due to loss of negative feedback.
  - Common causes: Klinefelter syndrome, testicular trauma, chemotherapy, radiation, and infections such as mumps orchitis.
- **Secondary (hypothalamic or pituitary origin)**
  - Results from dysfunction of the hypothalamus or pituitary, leading to low or inappropriately normal gonadotropin levels and low testosterone.
  - Etiologies include pituitary tumors, severe obesity, opioid or glucocorticoid use, and systemic illness.



Hypogonadism: Epidemiology

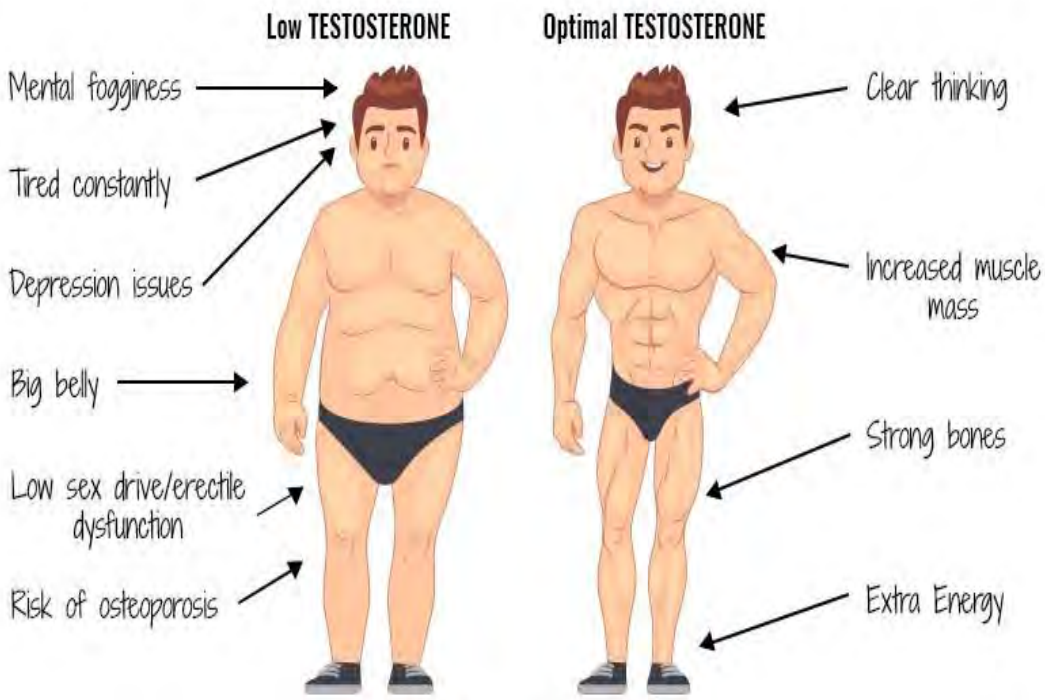
- Biochemical hypogonadism is observed in approximately 20% of men over 60, 30% over 70, and 50% over 80 years
- Serum total testosterone begins to decline gradually from the mid-30s at an average rate of 1.6% per year.
- Contributing factors: **Obesity**, diabetes, chronic illness, and medications (e.g., opioids, corticosteroids) further increase the risk of low testosterone in older men.
- In the US, TRT prescriptions have tripled in recent years, often in men with age-related or functional hypogonadism, not just those with classic (organic) hypogonadism.

Hypogonadism: Clinical Presentation

Signs & Symptoms

- Decreased libido
- Erectile dysfunction
- Reduced frequency of spontaneous erections
- Fatigue
- Decreased muscle mass and strength
- Increased body fat
- Impaired spermatogenesis

Physical findings are often limited, but may include decreased testicular volume, decreased body and facial hair, and gynecomastia.



Hypogonadism: Diagnosis

Lab Tests:

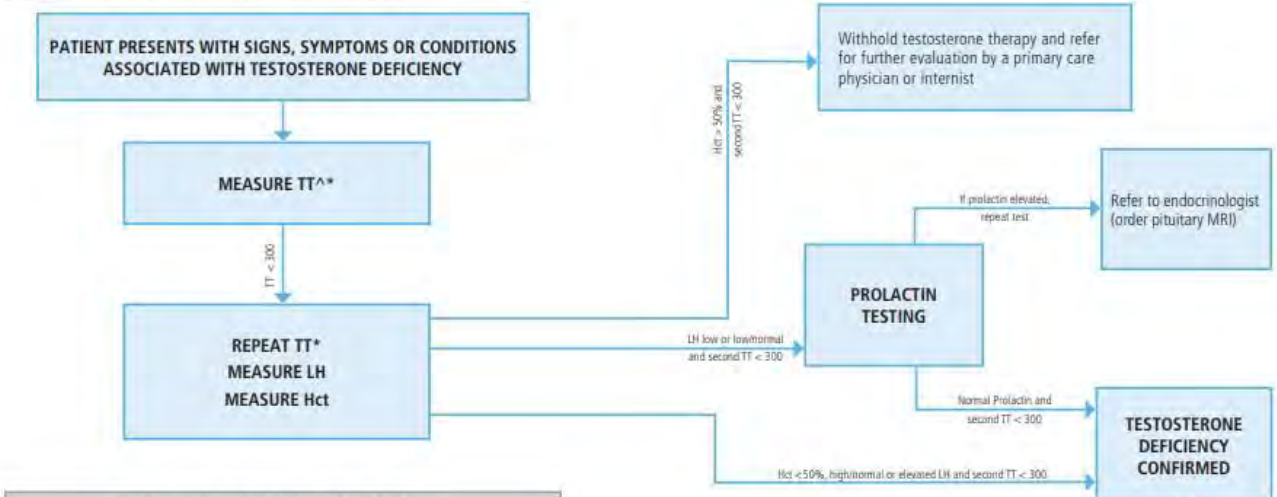
- Total testosterone level ***below 300 ng/dL***
- **Two low total testosterone measurements** are taken on separate occasions between 8am and 10am (No fasting required)

The clinical diagnosis of testosterone deficiency is only made when patients have low total testosterone levels **combined** with symptoms and/or signs.

Hypogonadism Workup:

- H&P
- Labs
  - Two AM TT
  - CBC (HCT)
  - LH
  - PSA in > 40yo
- Additional testing
  - Prolactin, Estradiol, FSH, A1c

EVALUATION AND MANAGEMENT OF TESTOSTERONE DEFICIENCY: DIAGNOSTIC ALGORITHM



ADDITIONAL TESTS FOR SPECIAL CASES **		
Estradiol	**FSH**	**HbA1c**
Patients who present with gynecomastia or breast symptoms	Patients who are interested in preserving their fertility	Patients who may be at risk for diabetes
DEXA	**Karyotype**	**PSA**
Patients who have a history of low trauma bone fracture	Patients with unexplained hyper-gonadatropic hypogonadism	If first PSA is elevated, repeat test before initiating testosterone therapy

^Testosterone values are measured as ng/dL
*All TT measurements ≥ 300 ng/dL are considered normal
**After testosterone deficiency is confirmed additional tests may be considered for special cases

FSH = Follicle Stimulating Hormone
Hct = Hematocrit
LH = Luteinizing Hormone
TD = Testosterone Deficiency
TT = Total Testosterone

Hypogonadism: Treatment

Lifestyle changes

- Weight loss
- Physical activity
- Diet changes
- Improving sleep quality
- Effective management of comorbidities
    - Sleep apnea, type 2 diabetes
- Discontinuation of medications that suppress the HPG axis (e.g., opioids, glucocorticoids

Testosterone Replacement Therapy Options

Injections
Cypionate, enanthate, or undecanoate

Topical
Gels and patches

Oral
Capsules and troches

Pellets
BioT and testopel

Intranasal Gel
Natesto

Testosterone Replacement Therapy

Importance of Testosterone Replacement Therapy (TRT):

- Restores physiological testosterone levels in symptomatic men with confirmed deficiency
- Improves sexual function, mood, bone density, muscle mass
- Recommended by the American Urological Association and Endocrine Society for men with organic hypogonadism
- Requires careful patient selection and monitoring

TRT Treatment Options

Injections

- Cypionate - IM Q 1-2 weeks
- Xyosted - enthanate - Subcutaneously weekly
- Long-acting testosterone undecanoate - IM Q 10–14 weeks (not sure this is available in the US

Topical - Gels and patches

- Transdermal gels - Risk of transference
  - Important to know if they are around a young female child often

Oral medications

- Jatenzo, Tlando, and Kyzatrex
- May have variable absorption

Pellets

- BioT or testopel - implanted every 3 - 6 months.

Nasal

- Intranasal gel - Natesto
- One pump (5.5 mg) in each nostril 3 times daily, for a total daily dose of 33 mg

TRT Monitoring

AUA recommends using the minimal dosing necessary to drive testosterone levels to the normal physiologic range of **450-600 ng/dL**, which is the **middle tertile of the normal range** for most laboratories.

450-600 ng/dL represents a viable range for all age-groups. Achieving testosterone levels in this window should ameliorate any symptoms that are genuinely associated with testosterone deficiency.

For men with on-treatment testosterone levels that fall below the suggested target range *but who experience complete resolution of symptoms, there is no need to titrate dosing.*

Age-specific Middle Tertile Levels

409-558 ng/dL (20-24 years old)

413-575 ng/dL (25-29 years old)

359-498 ng/dL (30-34 years old)

352-478 ng/dL (35-39 years old)

350-473 ng/dL (40-44 years old)

TRT Monitoring

Clinicians should measure an initial follow-up total testosterone level after an appropriate interval to ensure that target testosterone levels have been achieved.

- Typically around 4 weeks after initiating treatment

Every 6-12 months check **Total Testosterone and CBC (HCT)**

Clinicians should discuss the *cessation of testosterone therapy* three to six months after commencement of treatment in patients who experience normalization of total testosterone levels but *fail to achieve symptom or sign improvement*.

Dr. Hickson’s Workup and Management

Two AM total testosterones <300mg/dL

Labs every 3 months for the first year, then every 6 months thereafter.

If the PSA rises by 1.5 ng/ml or more in a year, or 0.75 ng/ml per year over two years, or an abnormal DRE is noted, stop TRT and discuss biopsy.

TRT Risks and Contraindications

Risks:

- Long-term impact of exogenous testosterone on spermatogenesis - important to discuss in pts who desire future fertility
- Testosterone deficiency and a history of prostate cancer should be informed that there is inadequate evidence to quantify the risk-benefit ratio of testosterone therapy
- No definitive evidence linking testosterone therapy to a higher incidence of venothrombolic events

Contraindications:

- Men who are trying to conceive
- Prostate cancer
- Breast cancer
- Within 3-6 months of a Cardiovascular event

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Hypogonadism and Testosterone Replacement Therapy

Hematuria Guidelines

Overactive Bladder

BPH

Hematuria

Gross hematuria: visibly seeing blood in the urine

Microhematuria: Clinicians should define microhematuria as **≥3 red blood cells per high-power field** on microscopic evaluation of a single, properly collected urine specimen.

Clinicians *should not define microhematuria by positive dipstick testing alone*.

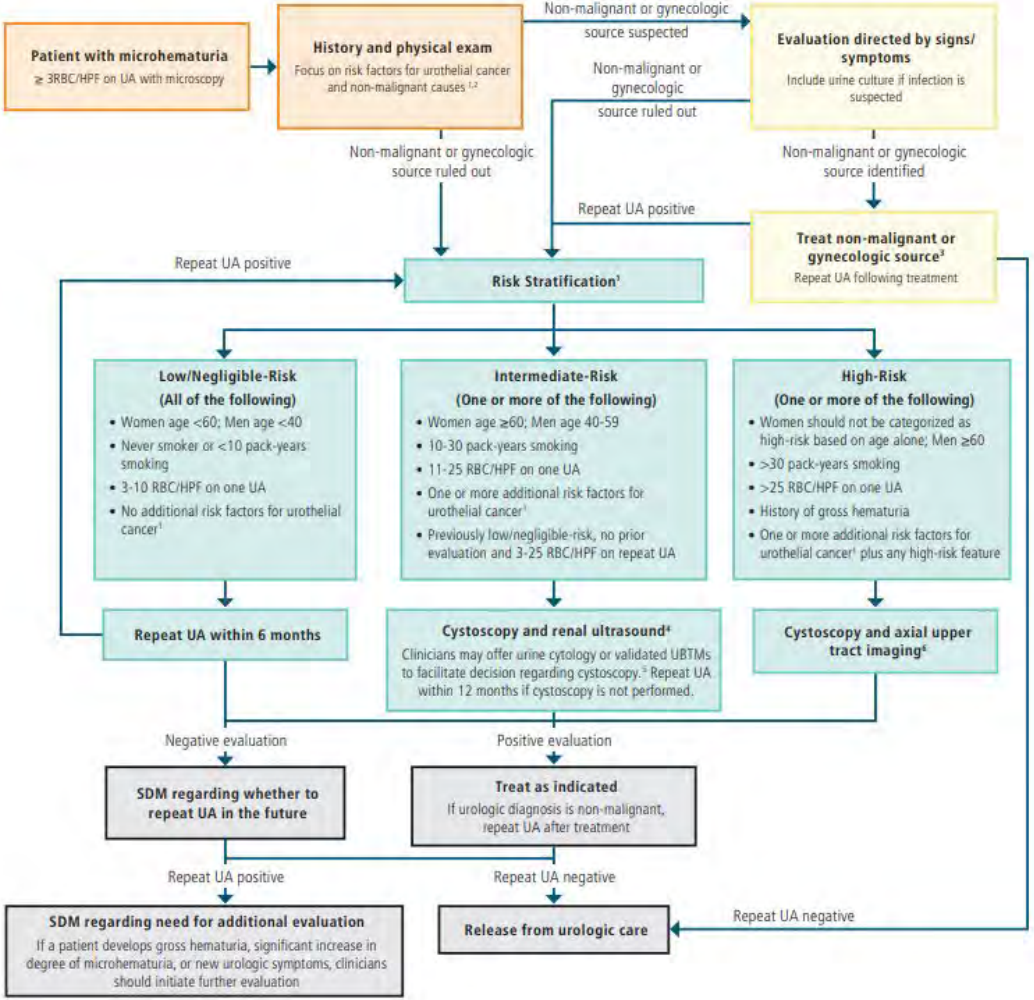
- A positive urine dipstick test (trace blood or greater) should prompt formal microscopic evaluation of the urine.

Hematuria: Workup

Evaluation

- H&P, BMP/CMP, UA
  - Urinalysis w/ microscopy, possibly urine culture
- Check for benign causes: UTI, menstruation, vigorous exercise/trauma, recent GU procedure or instrumentation, kidney stone.
- Smoking history
- If a non-malignant or gynecologic source is ruled out then will use risk stratification or refer to urology.

AUA/SUFU Microhematuria Diagnostic Algorithm



1. Additional risk factors include but are not limited to the following:
   - irritative lower urinary tract symptoms
   - prior pelvic radiation therapy
   - history of cyclophosphamide/ifosfamide chemotherapy
   - family history of urothelial carcinoma or Lynch syndrome
   - occupational exposure to benzene chemicals or aromatic amines
   - chronic indwelling foreign body in the urinary tract.

   Note, risk stratification and risk-based evaluation are the same for those on anti-platelet and anti-coagulation therapy as for those who are not.
2. If medical renal disease is suspected, consider nephrological evaluation, but pursue concurrent risk-based urologic evaluation.
3. There are non-malignant and gynecologic sources of hematuria that do not require treatment and/or may confound the diagnosis of microhematuria. Use careful judgment and patient engagement to decide whether to pursue microhematuria evaluation in the setting of such conditions.
4. Clinicians may perform cross-sectional imaging with urography or retrograde pyelograms if hematuria persists after negative renal ultrasound.
5. Intermediate-risk patients who decline cystoscopy following UBTMs should still undergo renal and bladder ultrasound.
6. MR urogram or non-contrast imaging plus retrograde pyelograms if contraindications to CT urogram.

HPF: high-power field
RBC: red blood cell
SDM: shared decision-making
UA: urinalysis
UBTM: urine-based tumor marker

Hematuria: Evaluation

- Upper Tract Imaging
  - Renal Ultrasound or CT Urogram : CT abdomen and pelvis without contrast, with contrast and with delayed contrast.
- Cystoscopy

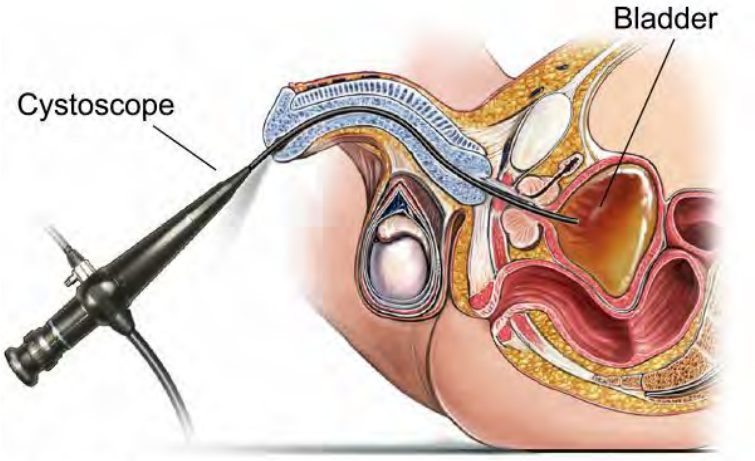


Figure 1
A flexible cystoscopy

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Hematuria Guidelines

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Overactive Bladder

Refers to urinary urgency, +/- frequency, nocturia, urge incontinence, absence of UTI or other pathology

Definitions

- Urgency = sudden desire to urinate, difficult to defer
- Urge incontinence = above + involuntary leakage

Epidemiology

- OAB is highly prevalent, affecting approximately 11–19% of adults in both men and women, with prevalence increasing with age

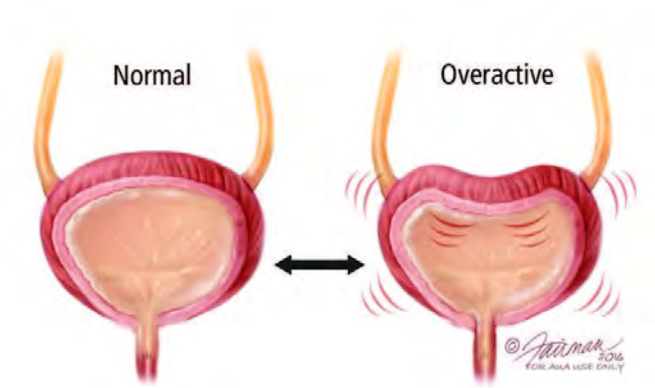
Risk Factors

- Age, postmenopausal, bladder inflammation, BOO, CNS dz – any brain or upper motor neuron lesion (MS, stroke, parkinsons, any SCI)

Overactive Bladder: Evaluation

Evaluation

- H&P, UA, PVR for uncomplicated pts
- Add voiding diary, urodynamics, etc if complicated (e.g. DM, CNS lesion, poor response to meds, young, hematuria, recurrent UTI, h/o pelvic CA or surgery)



Overactive Bladder: Treatment

Treatment

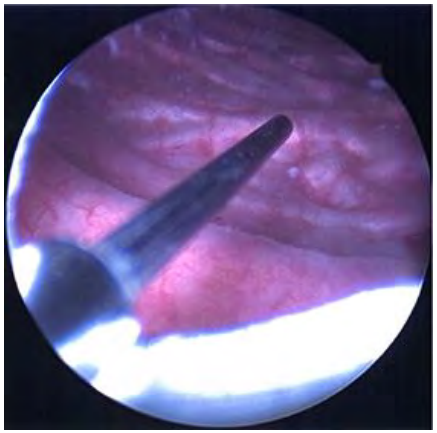
- Behavioral changes:
  - Timed voiding, double voiding
  - Pelvic floor Physical Therapy

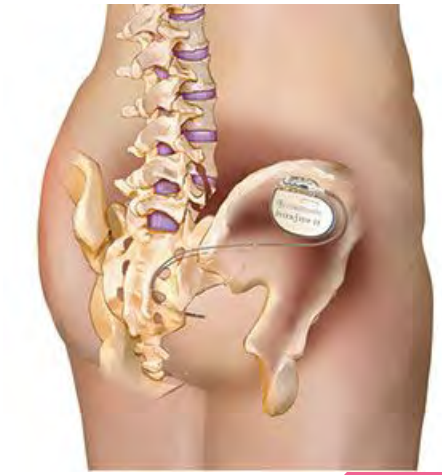
- Medication Therapy
  - Anticholinergics (Ditropan, Vesicare, Detrol…)
    - Cheap, but many SEs (drymouth, constipation)
  - B-agonist (Myrbetriq, Gemtesa)
    - Expensive, fewer SEs

Overactive Bladder: Treatment

Procedures

- Botox injections – fast, decent results, not durable
- Percutaneous tibial nerve stimulation
- Sacral nerve stimulation (Interstim/Axonics), decent results, more durable





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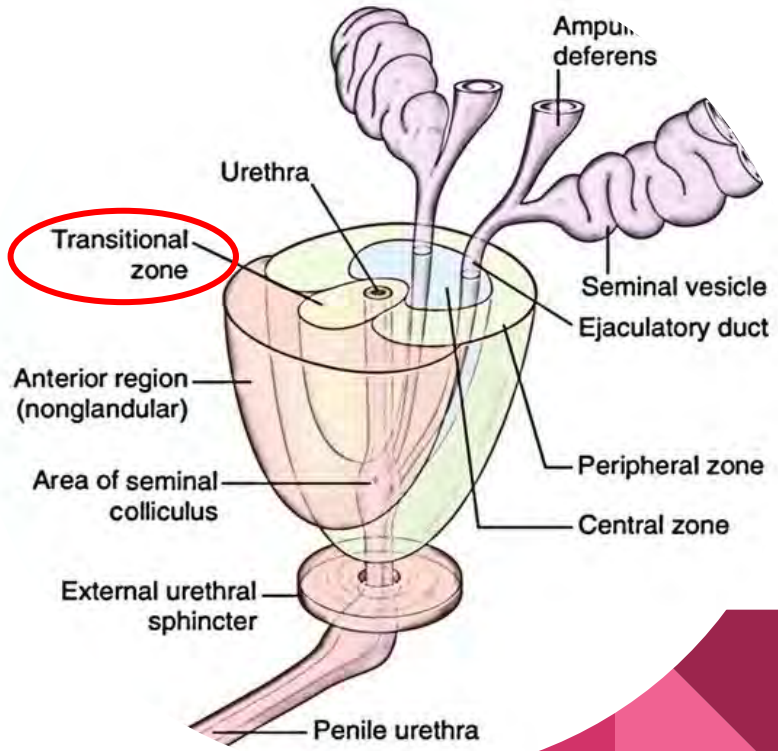
BPH: Benign Prostatic Hyperplasia

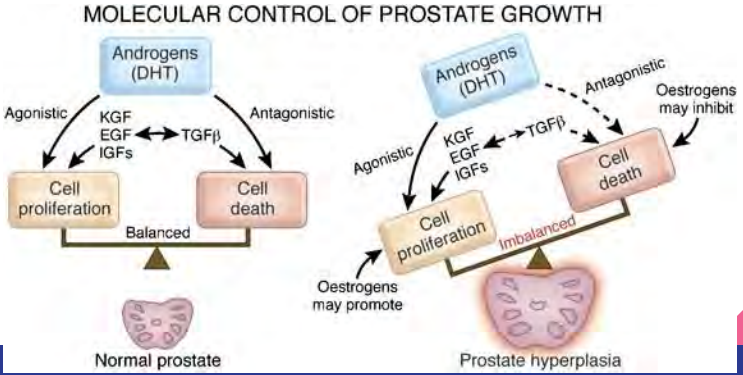
BPH: nonmalignant proliferation of both stromal and epithelial cells within the transition zone of the prostate, resulting in enlargement of the gland.

Transitional zone – located centrally and surrounds the urethra, comprising approximately 5-10% of normal prostate volume.



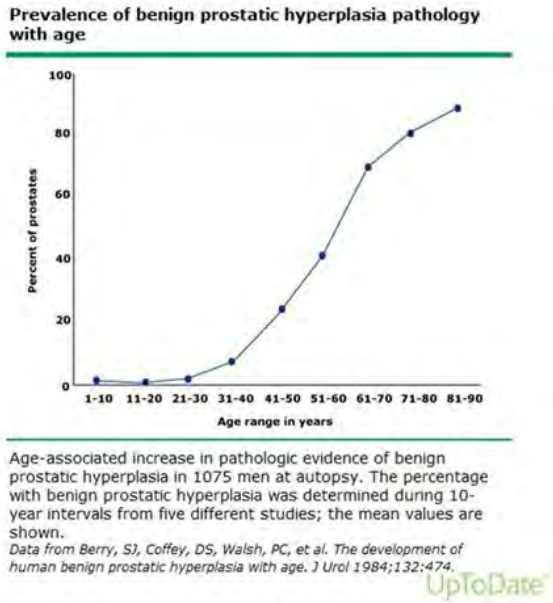
BPH : Pathophysiology

- This process characterized by the nonmalignant proliferation of both stromal and epithelial cells, predominantly **within the transition zone of the prostate.**
- The primary drivers are **androgen signaling**, particularly the action of dihydrotestosterone (DHT) via the androgen receptor, which promotes cellular proliferation and inhibits apoptosis in prostatic tissue.
- The enzyme 5α-reductase converts testosterone to DHT, and this pathway is central to BPH development and the rationale for 5α-reductase inhibitor therapy. (Finasteride)



BPH: Epidemiology

Age (years)	Histologic Evidence of BPH
31- 40	8%
41 - 50	20%
51 - 60	50%
61 - 70	75%
71 - 80	80%
> 80	90%



- Age 55: ~ 25% of men report obstructive LUTS
- Age 75: ~ 50% of men c/o obstructive LUTS

BPH: Presentation

<u>Obstructive Symptoms</u>
Prostate associated
Hesitancy
Weak stream
Sensation of incomplete emptying
Double voiding
Post void dribble

<u>Irritative symptoms</u>
Bladder associated
Frequency
Urgency
Nocturia

BPH

Medical History

- AUA symptom index / International Prostate Symptom Score
- Effect on QOL

Physical Exam

- Digital Rectal Exam (DRE) - guidelines now suggest DRE only at initial eval of patient suspected to have BPH. size, consistency, nodule
- Approximate prostate size - normal is 20-25cc (walnut)
- Labs – UA and PSA
- Post-void residual (PVR)

Office procedures:

- **Transrectal US for prostate sizing and cystoscopy**
  - **preferred for treatment guidance**

BPH: Prostate Size

Prostate Size/ Volume

- Small: < 30 g (walnut)
- Average: 30 – 80 g (ping pong ball, golf ball, clementine)
- Large: 81 – 150 g
- Very large: > 150 g (tennis ball)

BPH: Treatment

Treatment Goals

- Depends on how bothersome it is
- However important to rule out “silent” obstruction - Highly elevated PVR’s can lead to bladder dysfunction, hydronephrosis and ultimately declined kidney function.

Noninvasive/Behavior modifications

- Avoid α-agonists (pseudoephedrine, ephedra-containing diet supp)
- Dietary change – caffeine, EtOH, spicy foods
- Fluid restriction for nocturia, diuretics, ? sleep study
- Supplements/herbal: no data showing efficacy

BPH: Treatment

Medication management

- Alpha blockers (tamsulosin, doxazosin, alfuzosin)
  - Improved symptoms within days, prevent BPH progression
  - SEs: dizziness, nasal congestion, retrograde ejaculation
  - relaxes the smooth muscle in the prostate and bladder neck

- 5 α reductase inhibitors (finasteride, dutasteride)
  - Reduces prostate volume, ~6 mos, reduce BPH progression and risk of AUR; reduces PSA, need to double PSA for CAP screening
  - Simultaneous admin w/ α blockers improves voiding symptoms and PVR more than monotherapy

- PDE 5 inhibitors (tadalafil)
  - 5mg daily dose approved for BPH sxs

BPH: Treatment

Surgical Intervention

- Minimally invasive: Urolift, Rezum, PAE
  - For smaller sized prostates, <80g
  - Preserves sexual function
- More invasive
  - Transurethral resection of the prostate (TURP)
  - Transurethral laser surgery
    - Thulium or Green laser
    - Holmium Laser Enucleation of the Prostate (HoLEP)
  - Simple Prostatectomy - Open, Laparoscopic, or Robotic - usually for larger prostates

Contact information

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