Men's Health

Late-onset Male Hypogonadism

What is it?

- Clinical and biochemical syndrome characterized by an unequivocally and consistent deficiency of testosterone (T) with symptoms and signs that can be caused by testicular and/or hypothalamic-pituitary (HP) dysfunction
- Male hypogonadism definition: clinical syndrome resulting from failure to produce testosterone, or normal amounts of sperm, or both
  - Primary hypogonadism: testes (testosterone ↓, LH/FSH ↑)
  - Secondary hypogonadism: hypothalamus/pituitary (testosterone ↓, LH/FSH ↓)

To diagnose:

- Clinical suspicion (testosterone deficiency syndrome) – check full list of TDS indicators
- Measure testosterone in the morning (between 7-11am) or within 3 hours after waking
- Comprehensive laboratory evaluation – FSH, LH, prolactin, SHBG, cFT/cBAT, TSH, ferritin, CBC, PSA

Treatment: exogenous testosterone

- Oral testosterone (convenient, but must be taken with fatty food)
  - Andriol (80mg AM + 40mg PM)
- Injectable testosterone (cheap, but wide fluctuation in serum T)
  - Depo-testosterone (100mg IM/SC q1-2 wks)
  - Delatestryl (100mg IM/SC q1-2 wks)
- Transdermal testosterone
  - Transdermal patch (mimics T circadian rhythm, but skin irritation)
    - Androderm patch (2.5-7.5mg HS, apply between 8-12pm)
  - Transdermal gel (stable T, but possible transfer to others)
    - Androgel 1% gel, Testim 1% gel (5g-10g qAM)
- Intranasal gel testosterone (rapid absorption/no 1st pass, but multiple daily dosing)
  - Natesto 4.5% gel (TID, 1 pump per nostril)

Monitoring:

- Symptom response and ADR of treatment (at 3 months, 6 months after starting therapy)
  - Psychological/sexual symptoms improve in 1-3 months
  - Somatic symptoms improve in 6-12 months
- Testosterone (at 3 months, 6 months after starting therapy, then annually)
- Hematocrit (at baseline, 3 months, 6 months after starting therapy, then annually)
- PSA – prostate specific antigen (at baseline, 3 months, 6 months after starting therapy, annually)
- DRE (at baseline, 6 months, then annually)
- BMD (after 1-2 years in hypogonadal men with osteoporosis)

Androgenic Alopecia

What is it?

- Male pattern baldness, or male-pattern hair loss
- The growth phase responds to androgens (5α-reductase + testosterone in bloodstream = DHT) → shorter growth phase, miniaturisation of the follicle
- Androgens and genetics both play an important role
- 3 areas of the scalp are most affected:
  - Temples (side of the head)
  - Vertex (transition point where scalp goes from horizontal to vertical)
  - Mid-frontal

Treatment:

- Minoxidil (topical – non-Rx) – effective as long as used (don't discontinue), may take 2-12 months
  - 2% solution (Rogaine – apply 1mL BID, leave on scalp at least 4 h)
  - 5% foam (Rogaine – apply ½ capful BID, leave on scalp at least 4 h)
- 5-α reductase inhibitors (if discontinued, hair regrowth lost in 6-9 months)
  - Finasteride (1mg/day, selective for Type 2, metabolized by liver – ↑ effective than minoxidil)
  - Dutasteride (0.5-2.5mg/day, both Type 1 and 2, ↑ potent than finasteride, no indication)
- Surgery
  - Follicular unit transplantation
  - Follicular unit extraction

BPH (Benign Prostate Hyperplasia)

What is it?

- Common cause of urinary dysfunction symptoms in elderly men
- Includes adaptive cell changes [hypertrophy increase in cell size, hyperplasia increases in cell number]
- DHT (dihydrotestosterone) and type 2 5-α reductase are thought to play a central role in the development of BPH
- BPH pathogenesis progression:
  - BPH = benign prostatic hyperplasia
  - BPE = benign prostatic enlargement
  - BPO = benign prostatic obstruction

To diagnose:

- Signs and symptoms (including LUTS) – categorize BPH severity (mild, moderate, severe)
- Mandatory investigations (History, urinalysis, DRE – digital rectal exam, PSA, symptoms survey AUA)

Treatment:

- Watchful waiting (little to no symptoms, regular follow-up @ 6-12 months, education, behaviour)
- α-1 adrenergic blockers (rapid symptom relief – reduces dynamic factor, fast onset, all 6 agents have similar efficacy) *first-dose phenomenon*
  - Alfuzosin (selective for α-1A, 10mg QD after same meal, doesn't cross BBB, less ADR, CI in liver disease)
  - Prazosin (not selective = cause orthostatic hypotension, no BPH indication, 0.5-5mg BID, start low titrate q 2 weeks, start QD if renal impairment)
  - Tamsulosin (selective for α-1A, 0.4mg QD with/without food, caution in renal/liver impaired)
- 5 α-reductase inhibitors (impact underlying disease, ↓ prostate volume – reduces static factor, 3-6 months for onset of effect, use with caution in liver impairment, 50% reduction in PSA in 6 months, teratogenic)
  - Finasteride (0.5 mg QD, no interactions)
  - Dutasteride (5mg QD, potent CYP3A4 agents may increase dutasteride levels)
- Anti-muscarinic agents (relaxes detrusor muscle)
  - Tolterodine [Detrol IR, ER]: ER – 2-4mg QD, cholinergic ADR
  - Oxybutynin [Ditropan IR, ER, 10% gel, patch]: IR: 2.5-5mg QID, anticholinergic ADR, renal caution
  - Trospium [Trosec]: 20mg BID on empty stomach, cholinergic ADR, less CNS ADR
  - Darifenacin, Solifenacin: uroselective (preferentially inhibit M3 muscarinic receptors, use with caution if residual volume is > 200 mL, avoid in severe liver failure)
- Phosphodiesterase-5 inhibitors (relaxes smooth muscle around prostate)
  - Tadalafil [Cialis] – 5mg QD, 4 weeks' onset, can combine with α-1 adrenergic blockers
- Selective beta-3 adrenergic agonist (for LUTS irritative symptoms)
  - Mirabegron [Myrbetriq] – 25mg QD, 2-8 weeks' onset, for overactive bladder with urgency

- Desmopressin (replaces endogenous anti-diuretic hormone): for problematic nocturia
- Surgery
    - Prostatectomy: gold standard (TURP, open surgical for > 80 mL prostate)
    - TUIP: for moderate-severe voiding symptoms + prostate < 30 g
    - Minimally invasive surgical procedures (transurethral needle, green light laser, microwave)

Erectile Dysfunction (ED)

What is it?

- Persistent (> 3 months) failure to achieve a penile erection to allow for satisfactory sexual intercourse
    - May be psychogenic, organic, or drug-induced
    - Normal penile erection requires 3 systems: vascular, nervous, and hormonal systems to be functioning properly

Diagnosis:

- Clinical presentation: signs, symptoms, lab tests (testosterone, DRE, PSA)
- Investigation: sexual history (SHIM), medical history, medication history, physical exam, lab tests (FBG, HbA1C, lipids, serum testosterone if > 50 y/o, or younger patient with ↓ libido)

Treatment: [try 1st line oral therapy PDE-5i, but if on nitroglycerines/nitrates, trial ICI, VED, intra-urethral therapy

- PDE-5 (phosphodiesterase-5) inhibitors (need to adjust if > 65 y/o or hepatic impairment, or CYP450, 3A4 inhibitors) – most common ADR is headache and flushing, also PDE-6 visual anomalies, NAION, hearing loss, priapism
    - Sildenafil [Viagra]: faster onset, 12 h half-life, food delays Tmax, inhibits PDE-6 most
        - 50-100mg PO ~60 min before sex, not for daily use, renal impairment adjustment
    - Tadalafil [Cialis]: slower onset, 36 h half-life, not affected by food, doesn't inhibit PDE-6
        - 10-20mg PO ~60 min before sex, or 2.5-5mg PO QD, renal impairment adjustment
    - Vardenafil, ODT [Levitra, Staxyn]: fastest onset, 12 h half-life, fatty meal reduces Cmax
        - 10-20mg PO ~60 min before sex, not for daily use
- Prostaglandin E1 (2nd line)
    - Alprostadil [Caverject]: 2.5 mcg intra-cavernosally 5-10 mins before sex, limit to QD, sterile technique important
- Local therapy including intra-cavernous/intra-urethral agents (2nd line)
    - Alprostadil [MUSE]: trans-urethral suppository, lower efficacy, onset is 5-10 min after administration
- Non-drug treatments
    - Sexual counselling
    - Vacuum erection devices [VED] (3rd line): always effective, poorly tolerated
    - Penile prostheses (3rd line): corpora cavernosa permanently altered, no natural erections
    - Vascular surgery (penile implant, Peyronie's surgical repair, vascular bypass procedure)
- Testosterone therapy (men with documented hypogonadism)
- Lifestyle modifications: smoking cessation, heart healthy diet, discontinue/lower dose of drugs associated with ED