Late onset hypogonadism

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“Male Menopause”

- Clinical AND biochemical syndrome
- Testosterone levels decline by 0.4-3% per year after the age of 30, as opposed to the more rapid decline that occurs in females
- Affects 40% of men aged over 45 (?)
- Signs and symptoms are often non-specific and patients will not often volunteer them
- Low testosterone can be a risk factor for CV events (although giving testosterone may not improve CV risk)
- Testosterone may increase PSA levels, *theoretical* risk of increase in prostate ca, need for biopsies etc

Signs & Symptoms

- ***Red flag symptoms:***
- *Low sex drive*
- *Difficulty with erection*
- *Low sperm count*
- *Unexplained loss of hair*
- *Hot flashes*
- *Low bone density*

Signs & Symptoms

- ***Additional signs:***
- *Testicular atrophy (changes in testes)*
- *Diminished lean muscle mass*
- *Increased body fat*
- *Elevated hbA1c**
- *Osteopenia or low trauma bone fracture*
- *Problems sleeping (insomnia)*
- *Fatigue*
- *Difficulty concentrating, lack of motivation, depression*

Signs & Symptoms

*International Diabetes Federation - central obesity, hypertriglyceridemia, low high-density lipid cholesterol, hypertension, or insulin resistance, has been highly associated with TD and low SHBG levels in up to 50–70% of patients

Adam Questionnaire - 97% specificity if yes to q1,7-10

(Q)Adam Questionnaire

ADAM questionnaire about symptoms of low testosterone (Androgen Deficiency in the Aging Male)

This basic questionnaire can be very useful for men to describe the kind and severity of their low testosterone symptoms.

1.	Do you have a decrease in libido (sex drive)?	Yes No
2.	Do you have a lack of energy?	Yes No
3.	Do you have a decrease in strength and/or endurance?	Yes No
4.	Have you lost height?	Yes No
5.	Have you noticed a decreased "enjoyment of life"	Yes No
6.	Are you sad and/or grumpy?	Yes No
7.	Are your erections less strong?	Yes No
8.	Have you noticed a recent deterioration in your ability to play sports?	Yes No
9.	Are you falling asleep after dinner?	Yes No
10.	Has there been a recent deterioration in your work performance?	Yes No

High risk patients

- prior treatment for testicular cancer
- prior testicular infection
- medications with gonadotoxic effects, eg – chemotherapy, (finasteride, beta blockers, statins, opioids)
- testicular trauma
- idiopathic testicular atrophy
- genetic conditions, eg - Klinefelter’s syndrome
- anatomic abnormalities, eg - varicoceles

Screening?

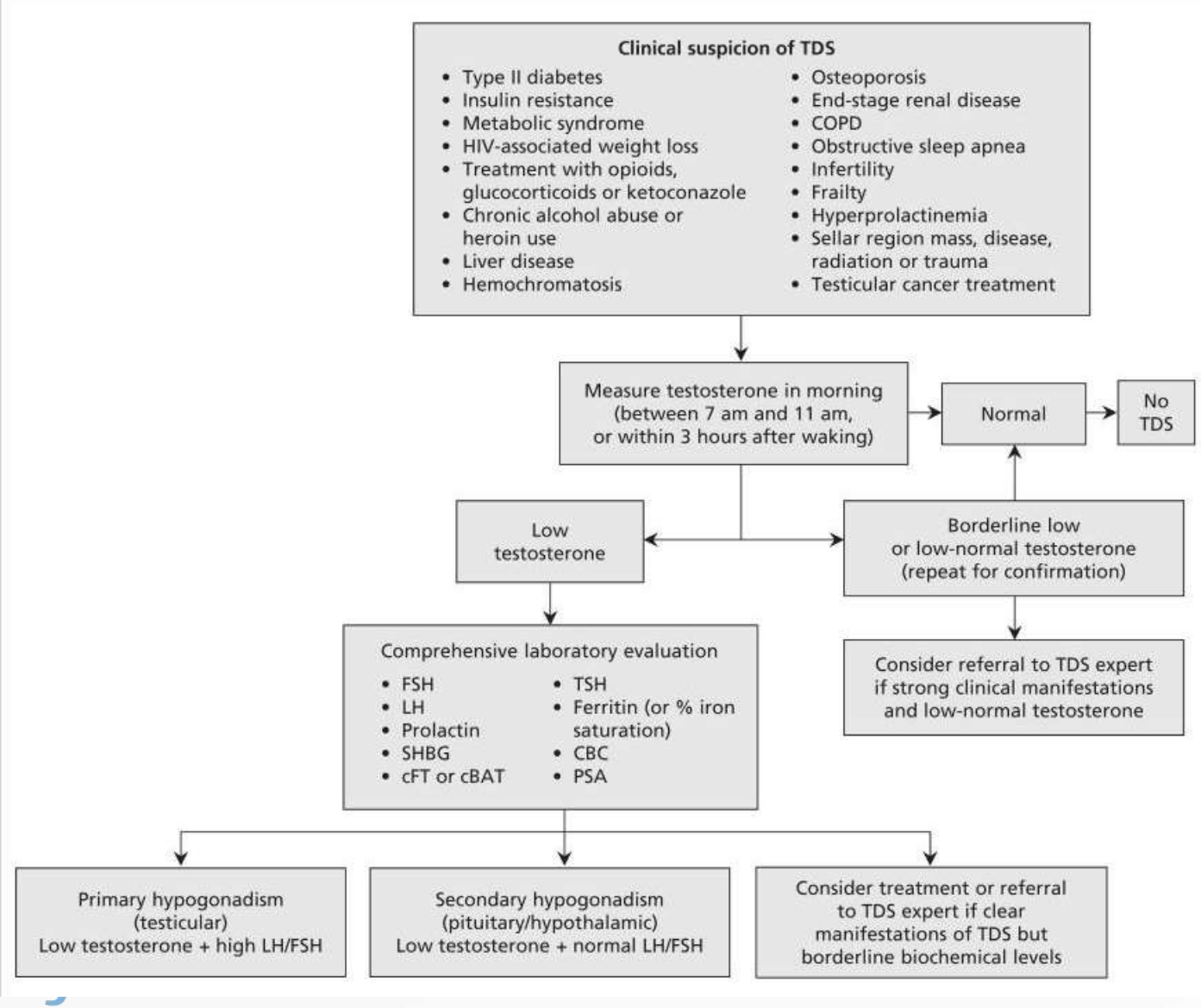
- Screen for TD in:

- adult men with consistent and multiple TD signs and symptoms
- all men with loss of spontaneous erections, ED, or low sexual desire
- all men with type 2 diabetes mellitus
- all men with BMI >=30 kg/m2 or waist circumference > 102 cm
- all men with on long-term opiate, anticonvulsant or antipsychotic medication

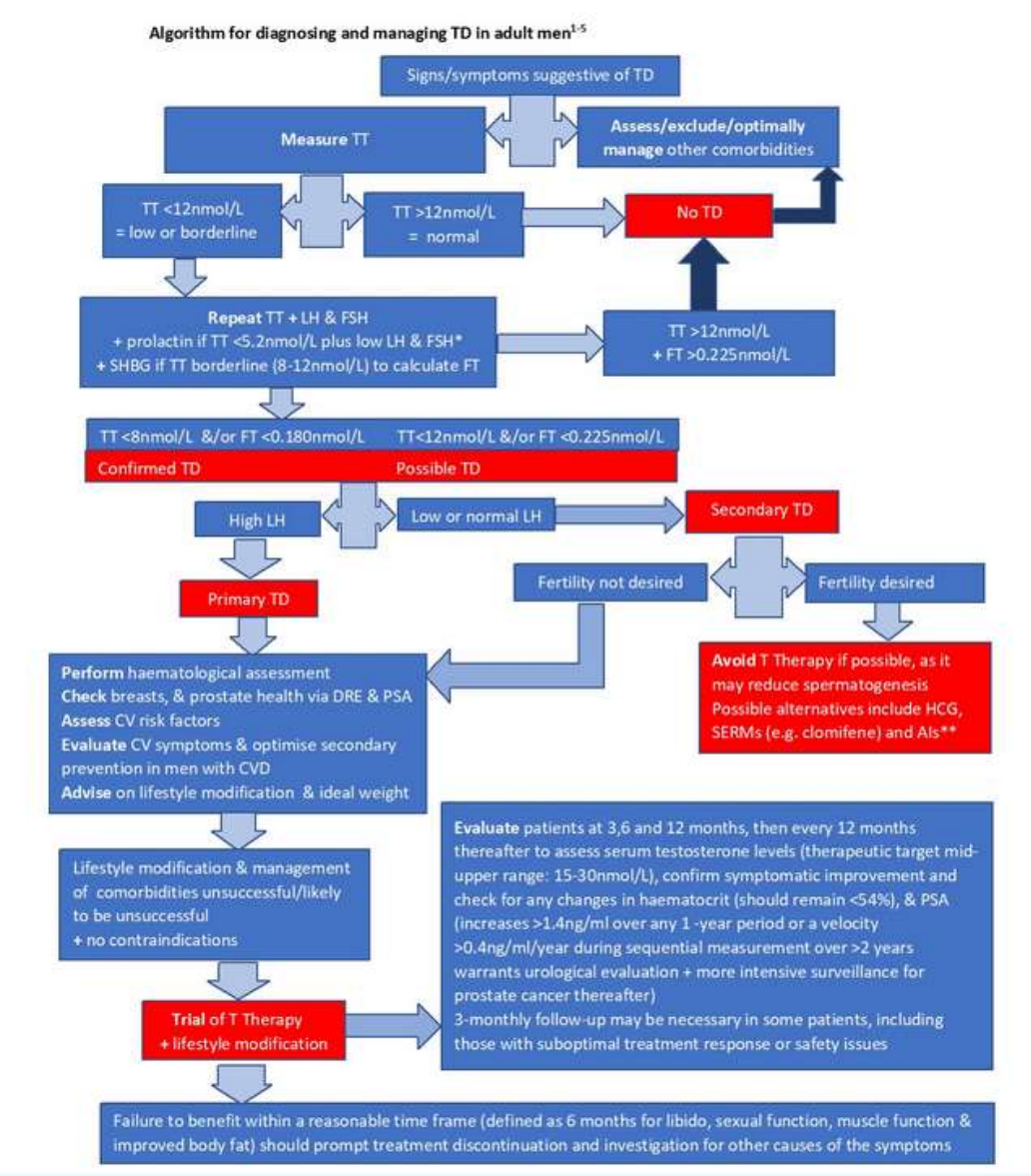
Investigations

- Testosterone levels – x2 FASTING samples 4 weeks apart taken at 7-11am (as levels can fluctuate throughout the day and are highest in a morning)
- Additional hormone tests to look for other causes: LH, FSH, TSH, prolactin
- No consensus agreement on abnormal values – some endrocrinologists will treat “low-normal” levels
  - 6 Different guidelines!

Pathway



More pathways



Treatment

Testosterone therapy options[6,15]

Formulation	Route of administration	Frequency of administration	Advantages	Disadvantages
Testosterone 1%, 1.62%* and 2% gel available *1.62% = 16.2 mg/g	Transdermal gel 1% (sachets/tubes) 1.62%* (pump) 2% (pump) *1.62% = 16.2 mg/g	• Applied daily[16] • May require dose titration	• Fast onset • Provides uniform and normal serum levels for 24 hours[7]	• Skin irritation at application site • Potential for interpersonal transfer • Compliance may be an issue long-term
Testosterone undecanoate	Intramuscular injection	Every 10–14 weeks, adjusted to maintain trough testosterone >12 nmol/L	• Steady state levels • Reduced frequency of administration improves compliance	• Possible injection site pain/reaction[17]
Testosterone enantate	Intramuscular injection	Every 2–3 weeks	Can be administered every 3–6 weeks for maintenance, according to individual requirement[18]	• Levels fluctuate • Possible injection site pain/reaction[18]
Mix of 4 testosterone esters (including propionate) as Sustanon 250	Intramuscular injection	Usually administered every 3 weeks May cause a reaction at the injection site[19]		

Adapted from Hackett et al. (2017)[6] and Dohle et al. (2017)[15]

Monitoring

- PR – at initiation, 6 months then annually
- Bloods - Haematocrit, testosterone, PSA – at initiation, 3 months, 6 months then annually

Main contraindications

- Prostate cancer
- Male breast cancer
- An active desire to have children
- Haematocrit >54%
- Severe chronic heart failure (NYHA) class IV

Risks vs Benefits

Potential benefits and harms of testosterone supplementation in men with testosterone deficiency syndrome*,[17,18]

Organ system	Benefits	Harms
Erectile function/libido	Improvement	None
Depression/mood/fatigue	Improvement	Aggressive behaviour
Erythropoiesis	Increase in hematocrit	Increased risk of polycythemia, embolism
Skeletal muscle	Increase in fat-free mass	None
Bone metabolism	Prevention of osteoporosis	None
Cardiovascular system	Improvement in congestive heart failure, exercise capacity	Increased risk of thromboembolic cardiovascular events
Prostate		
Benign prostatic hyperplasia	None beyond manifestations of testosterone deficiency syndrome	Marginal increase in volume and prostate-specific antigen level
Cancer (metastatic or high risk of recurrence)	Absolute contraindication	Recurrence and rapid progression
Cancer (localized and treated)	None beyond manifestations of testosterone deficiency syndrome	Potential exacerbation of subclinical residual cancer
Testicle	None beyond manifestations of testosterone deficiency syndrome	Atrophy or impairment of spermatogenesis

References/further info

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707424/
  - Testosterone deficiency in the aging male.
  - Therapeutic advances in Urology
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4674408/
  - Diagnosis and management of testosterone deficiency syndrome in men: clinical practice guideline.
  - Canadian Medical Association Journal
- http://www.pctag.uk/testosterone-calculator/
  - Primary Care Testosterone Advisory Group
- https://sexualadviceassociation.co.uk/testosterone-deficiency/
  - For patients

Quick summary

- http://www.pctag.uk/wp-content/uploads/2018/03/BSSM-Practical-Guide-High-Res-single-pp-view-final.pdf

Questions?