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County Durham & Tees Valley CCGs Primary Care Guidance for the Management of Hypogonadism

This document is designed to guide the investigation and referral process for patients presenting with testosterone deficiency symptoms and require treatment initiation by secondary care. Annual monitoring guidance is listed for primary care for the ongoing prescribing and management of the patient upon discharge from secondary care services.

County Durham & Tees Valley CCGs Primary Care Management of Hypogonadism	**Status**: Approved by CD&T APC	**Author:** Alda Hummelinck
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Diagnosing Testosterone Deficiency (TD) [1]

Diagnosed on signs and symptoms AND reduced serum levels of total or free testosterone.

Signs and symptoms are non-specific, multifactorial in origin and can be associated with lifestyle and psychological factors, and the normal aging process. It is essential therefore to take a full history and order relevant bloods, when considering a diagnosis of TD.

Initial Investigations [1]

- Total testosterone (TT) levels taken between 7-11 am (≤ 12 nmol/L then follow-up)
- HbA1c & lipid profile – to consider any underlying metabolic syndrome
- PSA – consider the need in young patients
- FBC
- LFT

Follow-Up Investigations (minimum of 1 week from initial tests) [1]

- Repeat TT
- LH – if low referral to endocrinology, if high consider referral to urology
- FSH
- SHBG
- Albumin
- **Fracture risk assessment using Q-fracture® (https://qfracture.org/)**
- Calculate Free Testosterone using a "Free Testosterone Calculator"
- FT <0.225 nmol/L then refer to secondary care to asses and treat
- FT >0.225 nmol/L is not considered hypogonadal, however if there is any ongoing concern despite this result consider advice and guidance (A&G) from endocrinology

Risk Factors [1]

- Adult men with consistent and multiple TD signs and symptoms
- All men with loss of spontaneous erections, ED and/or low libido
- All men with T2DM
- All men with BMI ≥ 30kg/m^2 or waist circumference > 102cm
- All men on long term opiate, anticonvulsant or antipsychotic therapy

Signs and Symptoms Suggestive of TD: [1]

Psychological:

Changes in mood
Poor self-related health
Diminished cognitive function

Cardio metabolic:

Increased BMI/ Obesity
Metabolic Syndrome
Insulin Resistance/T2DM

Physical:

Decreased body hair
Gynecomastia
Decreased muscle mass
Sweats/hot flushes
Osteoporosis/height loss

Sexual:

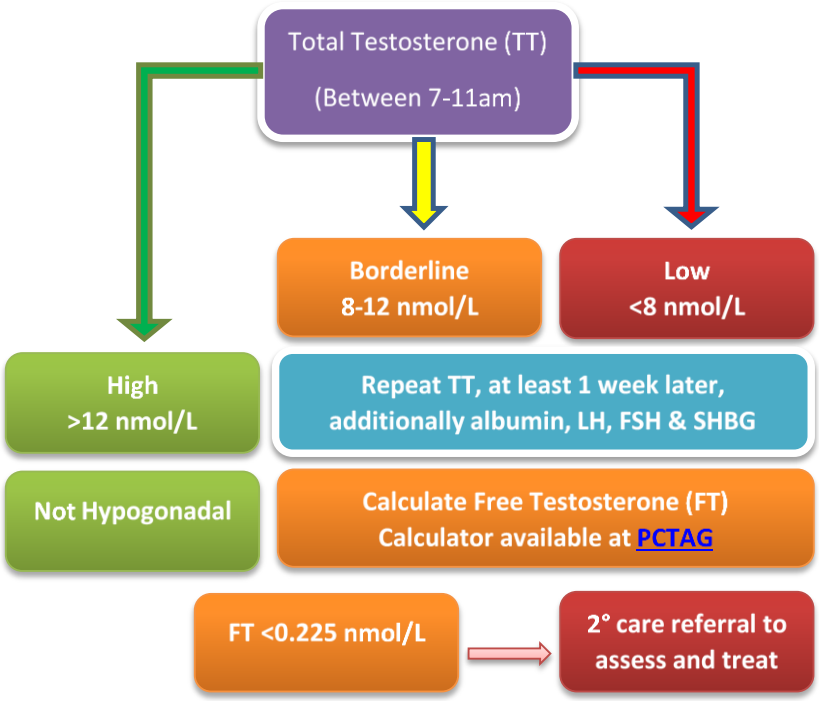
Delayed puberty/small testes
Decrease libido/infertility
Erectile dysfunction
Decrease morning erection
Delayed ejaculation

Patient History [1]

- Identify any risk factors
- Identify any signs and symptoms suggestive of TD
- Take full drug history; including current, previous, prescribed, OTC and recreational
- Confirm alcohol intake

Physical Examination [1]

1. Record patient height, weight, BMI and waist circumference
2. Assess amount of body hair (including facial and pubic)
3. Examine for any breast enlargement
4. Examine for any abnormalities of penis, testicles and scrotum
5. Check prostate through a digital rectal exam (DRE) (if clinically justified)



Drugs that may cause Hypogonadism: [2]

- Opioids (including methadone)
- Antipsychotics
- Anticonvulsants
- Glucocorticoids

As part of a review considering de-prescribing where possible

Discharging Back To Primary Care

- Regular review appointments will occur in secondary care, who will communicate any dose or formulation changes to primary care
- After no longer than 9 months of secondary care involvement the patient should be stabilised on dose and formulation and if there remains no further concern the patient will be discharged back into primary care
- Upon receiving the discharge letter, primary care should arrange for the patient to attend for annual monitoring for testosterone from month 12
- Ensure monitoring takes place annually
- Failure to attend for monitoring, allow up to 1 further treatment but failure to engage again should warrant treatment being stopped

Primary Care Annual Monitoring [1]

- Monitor for any misuse potential
- Total Testosterone (therapeutic target range; 15-30 nmol/L – IM injection "Nebido" acts over a longer period of time and a lower range is to be expected; 12-18 nmol/L)
- FBC; looking at haematocrit (should remain <54%) - any significant increase seek haematology advice (or urology/endocrinology as appropriate)
- PSA; either >1.4 ng/mL increase over any 1-year period or a velocity increase of >0.4 ng/mL over two sequential years seek urology advice/referral
- DRE should be considered if abnormal PSA; make a 2 week wait referral if necessary, based on clinical judgement
- Fracture risk assessment using Q-fracture® (https://qfracture.org/)

Secondary Care Referral

- All young males should be referred to secondary care, however, still investigate in primary care to see if hypogonadal
- Consider a 2 week wait referral if there are clinical signs suggestive of cancer
- Refer patient into secondary care service to further assess and commence treatment as necessary
- Include patient history, examination findings and blood results from primary care investigations
- It is essential to have two repeated values for total testosterone, at least a week apart and between 7-11 am, to support primary referral for treatment initiation
- If appropriate, secondary care will write to primary care to suggest commencement of testosterone replacement therapy
- Primary care to issue medication or arrange for IM injection based on recommendation

Testosterone BNF [3] See formulation table page 3

- Green plus on prescribing formulary
  - Requires specialist initiation however prescribing is done purely in primary care
- Available in gel forms, under various brandings
- Some patients prefer IM injection
  - Lasts between 10-14 weeks or 2-3 weeks depending on choice of injection
- Choice is based on patient preference
- Most common side effects for gel formulations involved skin reactions, whilst injection site pain is commonly noted for the IM injection
- Monitoring serum total testosterone to check effectiveness of treatment;
  - Gel Formulations – Target 15-30 nmol/L
  - IM Injections – Target 12-18 nmol/L
  - Failing to reach target range may require dose adjustments and/or further investigation

Considering Treatment Discontinuation

- Testosterone is usually a lifelong treatment
- If annual monitoring results suggest a further need to investigate – seek advice and guidance at first instance and consider discontinuing treatment as appropriate
- If considering discontinuation of treatment regimen, advice and guidance should be sought to confer specialist opinion on a case by case basis

Formulation *(Schedule 4 CD Anab)*	Qty	Cost per month at Usual Dose	Usual Dose of Testosterone	Administration	Monitoring
Transdermal Gel					
Tostran 2% Gel ***0.5g per actuation (10mg of testosterone)***	60g	£42.95	60mg OD (Max 80mg)	Applied Once daily, adjusted according to response	*Fast Onset (provides uniform serum levels for 24h)* Serum TT levels *should be taken **2 to 4 hours** after application.* **(Target range 15-30 nmol/L)**
Testogel 50mg/5g Gel unit dose Sachet ***5g sachet contains 50mg of testosterone***	30 Sachet	£31.11	50mg OD (Max 100mg)		
Testogel 16.2mg/g Gel ***1.25 g per actuation (20.25mg of testosterone)***	88g (60 actuations)	£31.11	40.5mg OD (Max 81mg)		
Testevan 20mg/g Gel ***1.15g per actuation (23mg of testosterone)***	85.5g (56 actuations)	£25.22 based on 46mg dose OD	23mg OD (Max 69mg)		
Testim 50mg/5g Gel unit dose tube ***5g tube contains 50mg of testosterone***	30 Single Dose Tubes	£30.50	50mg OD (Max 100mg)		
Solution for injections					**(Trough level - lower target range 12-18 nmol/L)**
Nebido 1g/4ml **(Testosterone Undecanoate)**	1 Vial	£87.11 per vial	1g	Deep IM injection every 10-14 weeks	Long-acting preparation. Serum TT levels should be checked **prior** to an injection
Testosterone Enantate 250mg/1ml	3 Ampoules	£85.74 per 3 amps	250mg	Slow IM injection every 2-3 weeks	Short-acting preparation. Serum TT levels should be checked **1 week after** an injection
Sustanon 250mg/1ml **Mix of 4 testosterone esters**	1 Ampoule	£2.45 per amp	1mL	Deep IM injection every 3 weeks	

Choice of formulation should be based on patient discussion. Transdermal gel **choice should be based on lowest NHS acquisition cost**; prices listed are subject to fluctuations and are correct at time of publication based on April 2021 Drug Tariff. Clinician first choice gel formulations should be Testevan or Tostran. Supply issues may require prescribing of other choices, as long as dosage remains equivalent.

For further information on individual products please consult individual SPCs at www.medicines.org.uk

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