Testosterone Deficiency: Case Study & British Society for Sexual Medicine Guidelines

Dr Jonny Coxon MA MD MRCS MRCGP DRCOG FECSM
GP Partner
Special Interest in Sexual & Gender Medicine
Clinical Assistant in Urology
Clinical Assistant (Endocrinology), Gender Identity Clinic
Declarations of Interest

I have received recent honoraria from:

• Prostate Cancer UK
• Besins
• Bayer
• Ferring
Mr Jonny Future, 55 years old

- Number of symptoms:
  - Fatigue
  - Decreased “zest for life”, irritable
  - Weight gain (BMI 35)
  - Low libido, poor erections
  - Spots on face
  - Night sweats, poor sleep

- PMH:
  - HT, ↑cholesterol, anaemia, back pain

- Meds:
  - Atorvastatin, losartan, tramadol
What could be the diagnosis / cause?

Choose any that could apply:
1. Hypothyroidism
2. Vitamin D deficiency
3. Testosterone deficiency
4. Depression
5. Side effects of medication
What could be the diagnosis / cause?

Choose any that could apply:

1. Hypothyroidism
2. Vitamin D deficiency
3. Testosterone deficiency
4. Depression
5. Side effects of medication
British Society for Sexual Medicine Guidelines on Adult Testosterone Deficiency, With Statements for UK Practice

Geoff Hackett, MD, Michael Kirby, MD, David Edwards, MD, Thomas Hugh Jones, MD, Kevan Wylie, MD, Nick Ossei-Gerning, MD, Janine David, MD, and Asif Muneer, MD

ABSTRACT

Background: Testosterone deficiency (TD) is an increasingly common problem with significant health implications, but its diagnosis and management can be challenging.

Aim: To review the available literature on TD and provide evidence-based statements for UK clinical practice.

Methods: Evidence was derived from Medline, EMBASE, and Cochrane searches on hypogonadism, testosterone (T) therapy, and cardiovascular safety from May 2005 to May 2015. Further searches continued until May 2017.

Outcomes: To provide a guideline on diagnosing and managing TD, with levels of evidence and grades of recommendation, based on a critical review of the literature and consensus of the British Society of Sexual Medicine panel.

Results: 25 statements are provided, relating to 5 key areas: screening, diagnosis, initiating T therapy, benefits and risks of T therapy, and follow-up. 7 statements are supported by level 1, 8 by level 2, 5 by level 3, and 5 by...
"Testosterone deficiency (TD) is a **clinical** and **biochemical** syndrome characterized by a deficiency of testosterone, or testosterone action,  

AND  

relevant symptoms and signs"
Epidemiology of Testosterone Deficiency

• Estimates for prevalence vary
• Ranges from 2-12% of men over 40 / 50
• Increases with age

Which features here are **not** linked to TD?

Choose any that apply:

1. Fatigue
2. Weight gain
3. Spots on face
4. Night sweats
5. Anaemia
Which features here are **not** linked to TD?

Choose any that apply:

1. Fatigue
2. Weight gain
3. Spots on face
4. Night sweats
5. Anaemia
Clinical signs and symptoms suggestive of TD

- Sexual dysfunction symptoms prominent
- Also:
  - night sweats
  - sleep disturbance
  - other changes in mood

**Depression**
- Depressed mood
- Cognitive impairment

**Cardiovascular disorders**
- Hyperlipidaemia
- Hypertension

**Physical decline**
- BMD: Loss of bone mineral density
- Fatigue: Decreased energy levels
- Sarcopaenia: Loss of muscle mass and strength

**Metabolic disorders**
- Abdominal obesity
- Poor insulin regulation
- Poor glycaemic control

**Sexual dysfunction**
- Reduced sexual desire and activity
- Erectile dysfunction (ED)
## Screening for TD

<table>
<thead>
<tr>
<th>Recommendations—screening</th>
<th>LoE</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen for TD in adult men with consistent and multiple signs of TD</td>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td>Screen all men presenting with ED, loss of spontaneous erections, or low sexual desire</td>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>Screen for TD in all men with T2DM, BMI &gt; 30 kg/m² or waist circumference &gt; 102 cm</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Screen for TD in all men on long-term opiate, antipsychotic, or anticonvulsant medication</td>
<td>2</td>
<td>B</td>
</tr>
</tbody>
</table>

ADAM Questionnaire

Your answers to the following questionnaire will help to identify whether you have the features of Testosterone Deficiency Syndrome (TDS).

Please answer the questions honestly.

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

If the answer is YES to question 1 or 7, or at least three of the other questions:

Further evaluate for symptoms of TD & consider testing

Google “testosterone questionnaire”
• Mr JF comes in during his lunch break for blood tests
• Routine ‘fatigue bloods’ done: normal
• Recalling a great talk (😊!) about TD, you included these:

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum testosterone level (XE2dr)</td>
<td>7.1 nmol/L [6.68 - 25.7]</td>
</tr>
<tr>
<td>Serum sex hormone binding globulin level (44CD.)</td>
<td>24 nmol/L [19.3 - 76.4]</td>
</tr>
<tr>
<td>Serum free testosterone level (XabD9)</td>
<td>168 pmol/L [163 - 473]</td>
</tr>
</tbody>
</table>
What do you advise him?

Choose the best answer(s):

1. Reassure him bloods are normal this time
2. Test again, in another convenient lunch break
3. Test again, on a morning fasting sample
4. Diagnose testosterone deficiency

<table>
<thead>
<tr>
<th>Testosterone Level</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum testosterone level (XE2dr)</td>
<td>7.1 nmol/L [6.68 - 25.7]</td>
</tr>
<tr>
<td>Serum sex hormone binding</td>
<td>24 nmol/L [19.3 - 76.4]</td>
</tr>
<tr>
<td>globulin level (44CD.)</td>
<td></td>
</tr>
<tr>
<td>Serum free testosterone level</td>
<td>168 pmol/L [163 - 473]</td>
</tr>
<tr>
<td>(XabD9)</td>
<td></td>
</tr>
</tbody>
</table>
What do you advise him?

Choose the best answer(s):
1. Reassure him bloods are normal this time
2. Test again, in another convenient lunch break
3. Test again, on a morning fasting sample
4. Diagnose testosterone deficiency

<table>
<thead>
<tr>
<th>Testosterone Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum testosterone level (XE2dr)</td>
<td>7.1 nmol/L</td>
</tr>
<tr>
<td>Serum sex hormone binding globulin level (44CD)</td>
<td>24 nmol/L</td>
</tr>
<tr>
<td>Serum free testosterone level (XabD9)</td>
<td>168 pmol/L</td>
</tr>
</tbody>
</table>
Laboratory Diagnosis of TD

- Measure **testosterone**: fasting sample, before 11am
- Need at least 2 results, preferably 4 weeks apart

Laboratory Diagnosis of TD

• If 1\textsuperscript{st} test low/borderline:
  • repeat & measure LH (+/- FSH)
  • plus SHBG to calculate free testosterone

• Clinical symptoms more closely related to free testosterone than total

Diagnosis of TD

Welcome to the Free & Bioavailable Testosterone Calculator

Also available on Apple Appstore and Google Play

Free & Bioavailable Testosterone Calculator

This website has been developed in part through an educational grant from Besins Healthcare (UK) Ltd. The company has no editorial control on its content.

IMPORTANT LIMITATIONS: This calculator is an educational tool and should not be solely relied upon in making any clinical decision. No responsibility whatsoever is assumed for its correctness or suitability for any given purpose. Please consult your healthcare provider first for any health concerns.

Additionally, the calculated free and bioavailable testosterone should not be relied upon in situations with potential massive interference by steroids binding to SHBG.

---

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>g/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SHBG</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nmol/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Testosterone</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nmol/L</td>
</tr>
</tbody>
</table>

Calculate

Free Testosterone:
Thresholds for T Therapy

- BEWARE LABORATORY REFERENCES RANGES
  - Vary considerably across the country

- Use “action levels” instead

**Thresholds** for T Therapy

- **Total T level < 8 nmol/L or free T < 180 pmol/L**
  - Usually requires T Therapy

- **Total T level > 12 nmol/L or free T > 225 pmol/L**
  - Does not require T Therapy

- **Total T 8-12 nmol/L or free T 180-225 pmol/L**
  - May require a **trial** of T Therapy for a minimum of 6 months

Diagnosis of TD

• If these low levels are confirmed, **in combination** with his symptoms, testosterone deficiency can be diagnosed.
Testosterone therapy (TT)

• Choice usually = gel vs injection

• No justification for selecting one over another except patient choice

Testosterone gels

• Daily, may need titrating

• Advantages:
  • Fast onset
  • Levels peak 2-4 hours then slow ↓

• Disadvantages:
  • Skin irritation
  • Potential interpersonal transfer
  • Possible non-compliance long-term?
Testosterone injections

1. Short-acting:
   • Usually 3-weekly
   • **Advantages:**
     • Low cost prescription (Sustanon)
     • Short duration allows quick withdrawal
   • **Disadvantages:**
     • More frequent injections (cost?)
     • Fluctuating testosterone levels between injections
Testosterone *injections*

2. Long-acting:
   - Every 10-14 weeks
   - **Advantages:**
     - Fewer injections – ↑ compliance
     - Maintains better steady state
   - **Disadvantages:**
     - Slower drug withdrawal if needed
     - Possible painful injection site (4ml, needs to be SLOW)
Does T therapy work?

- Good evidence cited in guidelines for improvements in:
  - Sexual desire, activity, erections
  - Waist circumference
  - BMI
  - Lean mass vs fat mass
  - Insulin resistance
  - Lipid profile
  - BP
  - Walking distances
  - Bone mineral density
  - Anaemia
  - Lower urinary tract symptoms
  - Depression scores

How long to trial treatment?

• Different symptoms improve at different rates

• Should trial for **MINIMUM 6 MONTHS**

• Most commonly, **lifelong therapy**

## Follow-up and monitoring

<table>
<thead>
<tr>
<th>Recommendations – Follow-up</th>
<th>LoE</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess the response to therapy at 3, 6 and <strong>12 months</strong>, and every <strong>12 months</strong> thereafter</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>Aim for a target level of <strong>total testosterone 15-30 nmol/l</strong> to achieve optimal response</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td><strong>Monitor haematocrit</strong> before treatment, at 3-6 months, 12 months and every 12 months thereafter. Decrease dosage, or switch preparation, if haematocrit &gt;0.54. If haematocrit remains elevated, consider stopping and re-introduce at a lower dose.</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>Assess prostate health by PSA and DRE before commencing TRT followed by PSA at 3-6 months, 12 months and every 12 months thereafter</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td><strong>Assess cardiovascular risk before TRT is initiated and monitor cardiovascular risk factors throughout therapy</strong></td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>

Risks of Testosterone Therapy

• 12 months after starting treatment, Mr JF is a “new man”:
  • Lost 4kg weight, 5cm waist circumference
  • BP & cholesterol improved
  • Better sexual function
  • Energy ↑
  • Hb ↑

• However, he says he thinks he might want to stop TT: he’s read about risks of heart disease and prostate cancer

• What can you tell him?

Testosterone and CV risk

- BSSM Guideline gives full review of evidence

- Body of evidence links *low T* to ↑ *CV risk*

Testosterone and CV risk

- Individual studies with TT cited:
  - ↓ major CV events
  - ↓ mortality
- Meta-analyses:
  - **No** increased CV risk with TT
- European Medicines Agency 2014
  - No concerns re CV risk

Engrained belief that testosterone is linked to prostate cancer (pCa) growth

Now think of SATURATION MODEL:
- Beyond a low T level, receptors saturated, no further growth stimulated

No evidence that T Therapy increases risk of pCa, or pCa progression

Adverse effects of TT

• Changes in mood, energy, sexual desire
• Polycythaemia
• Acne
• ↓ fertility

Adverse effects of TT

• Changes in mood, energy, sexual desire
• Polycythaemia
• Acne
• ↓ fertility

• Sustained supraphysiological levels should be avoided
The British Society for Sexual Medicine (BSSM) was founded to promote research and exchange of knowledge of impotence and other aspects of sexual function and dysfunction.

Join BSSM
Latest resources

**A Practical Guide** – On The Assessment and Management of Testosterone Deficiency in Adult Men
2018

British Society for Sexual Medicine Guidelines on Adult Testosterone Deficiency, With Statements for UK Practice
2018

**A Practical Guide** – On Managing Erectile Dysfunction
2018

British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men
2018
A practical guide on the assessment and management of testosterone deficiency in adult men

Based on the 2017 British Society for Sexual Medicine (BSSM) guidelines on adult testosterone deficiency, with statements for UK practice

Why does it occur?
Testosterone deficiency (TD), also known as hypogonadism, may result from:²⁻⁴

- Problems with the testes [primary (hypogonadotropic) TD]
- Problems with the hypothalamus and pituitary gland [secondary (hypogonadotropic) TD]
- Problems with the hypothalamus/pituitary and testes (combined primary and secondary TD)
- Impaired action/suppression of testosterone

How is it diagnosed?

- The diagnosis of symptomatic TD requires the presence of characteristic signs and symptoms,²⁵⁻⁸ PLUS reduced serum concentrations of total testosterone (TT) or free testosterone (FT).

Psychological
- Changes in mood (e.g. anger, irritability, sadness, depression)
- Decreased well-being/poor self-rated health
- Diminished cognitive function (including impaired concentration, memory, and problem-solving skills)
Conclusions

• TD is a well-established and significant medical condition, encompassing somatic, sexual and psychological effects

• Associated with increased CV & all-cause mortality

• Testosterone therapy is evidence-based & effective in TD, improving a number of clinical features