

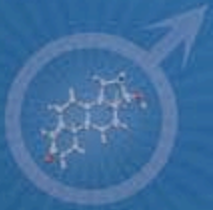
Managing Testosterone Deficiency: A Practical Guide

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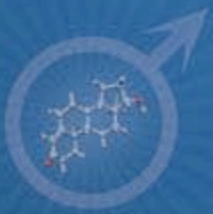
Case Study #1

A 59-Year-Old Man
with Erectile Dysfunction



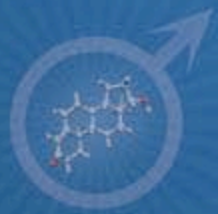
Case History

- Robert is a 59-year-old man who was recently divorced. He was experiencing erectile dysfunction and decided to try to correct the problem on his own by ordering sildenafil off the internet. He used a 50 mg dose of the phosphodiesterase-5 inhibitor (PDE5i) four times over the past few months.
- He comes to visit you complaining that the medication has been ineffective for him.



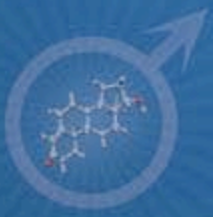
Patient History

- Robert is overweight, has hypertension and is a newly diagnosed type 2 diabetic. He exercises by walking 3 times a week for 40 minutes. Robert is a nonsmoker but does drink alcohol – a glass of wine and a beer to relax at night.
- Robert complains of difficulties in the last 9 months in getting and maintaining a full erection, but he has no difficulties with ejaculation. His sexual drive is reduced.
- He also complains of slight difficulties to initiate urination.



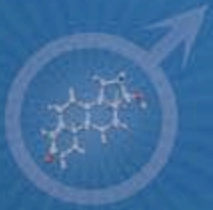
Physical Examination

- His genitourinary exam is normal but his prostate is mildly enlarged.



Question

1. What would you do in this situation?
 - A. Change to another PDE5i
 - B. Raise the dose of sildenafil to 100 mg
 - C. Put him on intracavernous prostaglandin E1 (PGE1)
 - D. Perform other tests



Discussion Points

- **D** is the best choice – laboratory tests should be performed. Robert has symptoms of an underlying testosterone (T) deficiency: he has decreased libido and his diabetes puts him at risk of having hypogonadism.¹ All men with type 2 diabetes should be screened for T deficiency.²
- Increasing the dose of sildenafil or prescribing a PGE1 may only improve his erectile function and not his libido.

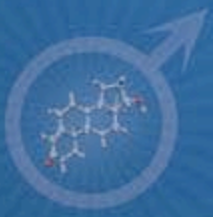
1. Dhindsa S, Prabhakar S, Sethi M, Bandyopadhyay A, Chaudhuri A, Dandona P. *J Clin Endocrinol Metab.* 2004;89:5462-5468.

2. Bhasin S, Cunningham GR, Hayes FJ, et al. *J Clin Endocrinol Metab.* 2006;91:1995-2010.



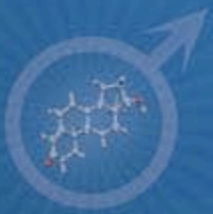
Laboratory Test Results

Test	Result	Normal Range
Complete blood count (CBC)	Normal	
Lipid profile	Normal	
Hemoglobin A1C	6.8%	4.5-6%
Total testosterone (TT)	10.1 nmol/L	10-30 nmol/L
Sex hormone-binding globulin (SHBG)	25 nmol/L	10-70 nmol/L
Calculated free testosterone (cFT)	183 pmol/L	200-800 pmol/L
Prolactin	7.3 μ g/L	<15 μ g/L
Prostate-specific antigen (PSA)	2.0 μ g/L	<3.5 μ g/L



Question

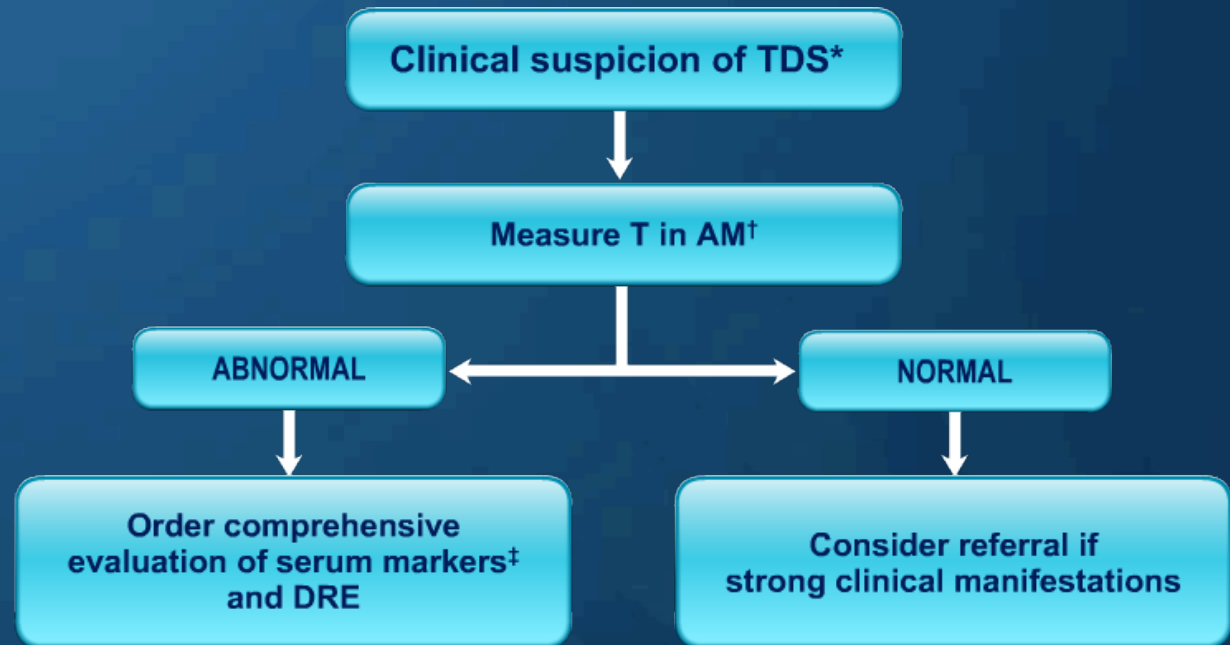
2. What should you do next?
 - A. Prescribe T
 - B. Repeat T test with measured bioavailable T (BT)
 - C. Repeat T, plus add tests for luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH)



Discussion Points

- **C** is the best choice – borderline or low T readings should be repeated with the addition of LH, FSH and TSH.

- A digital rectal exam (DRE) should be performed if T therapy is being considered.



- As determined from a thorough evaluation of clinical manifestations or the presence of disorders/conditions associated with a high prevalence of low T levels .

† Measured BT is the gold standard. If this test is unavailable in your region use TT, cFT or cBT.

‡ Tests to be included:

- | | | |
|------------------------------------|------------------------------|-----------------------------------|
| <input type="checkbox"/> Repeat T | <input type="checkbox"/> FSH | <input type="checkbox"/> CBC |
| <input type="checkbox"/> SHBG | <input type="checkbox"/> LH | <input type="checkbox"/> Ferritin |
| <input type="checkbox"/> Prolactin | <input type="checkbox"/> TSH | <input type="checkbox"/> PSA/DRE |

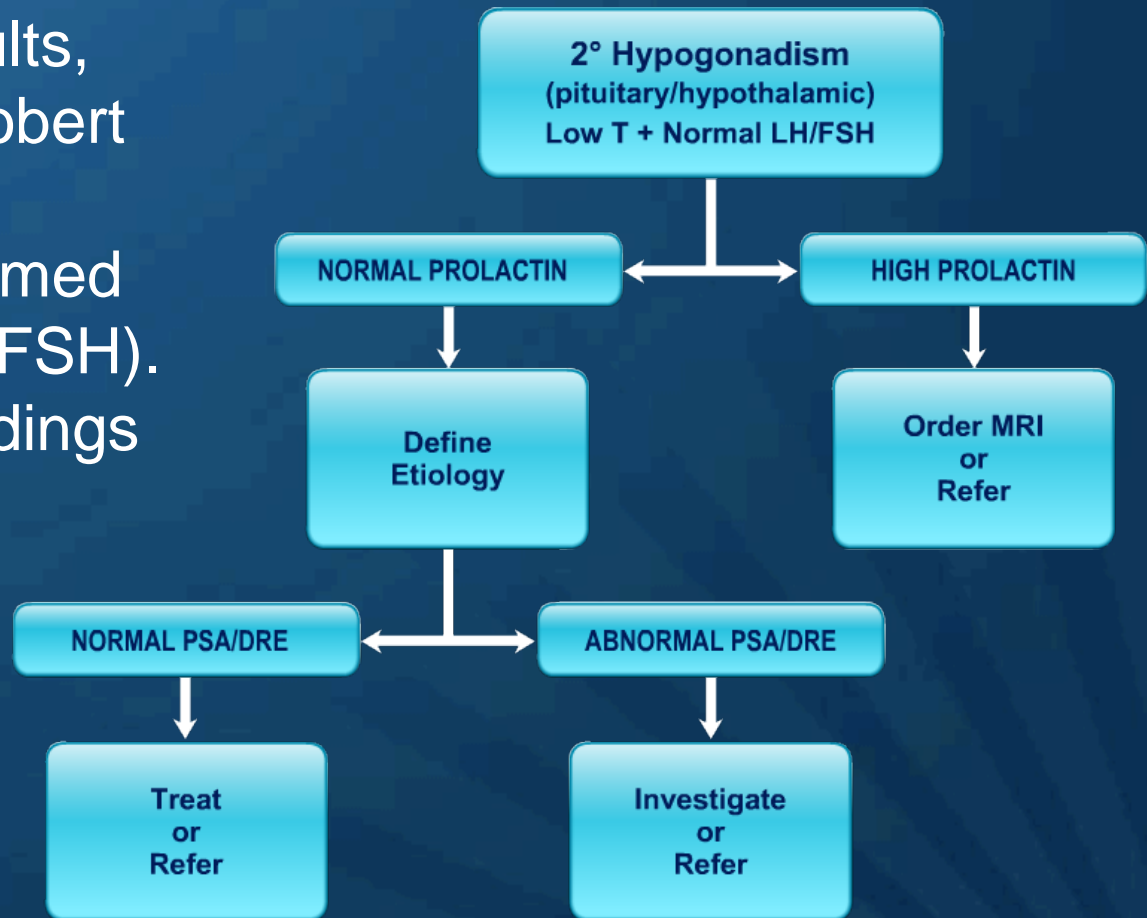


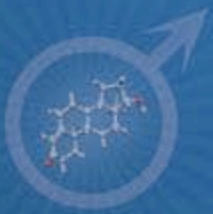
Repeat Laboratory Results

Test	Result	Normal Range
TT	9.5 nmol/L	10-30 nmol/L
BT	3.4 nmol/L	5-20 nmol/L
LH	9 IU/L	<10 IU/L
FSH	8.5 IU/L	<10 IU/L
DRE	Normal	

Diagnosis and Treatment Decision

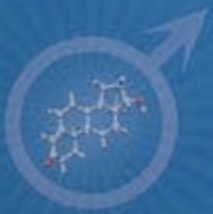
- Based on the lab results, you determine that Robert has **secondary hypogonadism** (confirmed low T and normal LH/FSH). His PSA and DRE findings are normal, as is his prolactin level.





Question

3. What would be your choice of treatment?
- A. Prescribe testosterone replacement therapy (TRT) and stop sildenafil
 - B. Prescribe sildenafil at a higher dosage
 - C. Give TRT plus sildenafil
 - D. Refer the patient to another physician specializing in sexual medicine
 - E. Do nothing and tell the patient that you can't help him



Discussion Points

- **C** is the best choice – for most older men, TRT alone is not sufficient to treat ED. Combination therapy with a PDE5i is recommended.
- Because of the possible vascular component of Robert's ED (diabetes mellitus and hypertension), combination therapy may be beneficial in improving erectile function.^{1,2}

1. Shabsigh R, et al. *J Urol.* 2004;172:658-663.
2. Greenstein A, et al. *J Urol.* 2005;173:530-532.

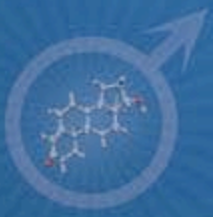


Choice of T Formulation

- You and Robert discuss the choice of T formulation based on the ASTEP algorithm:
- **A**vailability, **S**afety, **T**olerability, **E**fficacy, **P**reference
- What formulation would you recommend for Robert?
 - A. Oral testosterone
 - B. Testosterone patch
 - C. Testosterone gel
 - D. Intramuscular formulation

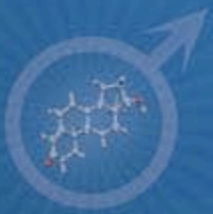
T Formulations in Canada

Generic Name	Trade Name	Dosage	Advantage(s)/ Disadvantage(s)
Intramuscular Injections			
Testosterone cypionate	Depo-testosterone ¹	200 mg every 2 weeks (400 mg max per month)	<ul style="list-style-type: none"> • Effective • Long-acting • Supraphysiologic T • Waning effect (2-3 weeks)
Testosterone enanthate	Delatestryl ²	100-400 mg every 1-4 weeks	
Oral Medications			
Testosterone undecanoate	Andriol ³ pms-Testosterone ⁴	120-160 mg daily divided in 2 doses ^a	<ul style="list-style-type: none"> • Convenient • Absorption issues • Supraphysiologic DHT
Transdermals			
Testosterone patch	Androderm ⁵	2.5 or 5 mg patch applied daily	<ul style="list-style-type: none"> • Consistent T levels • Visibility • Significant skin reactions
Testosterone gels	AndroGel ⁶ Testim ⁷	5-10 mg daily	<ul style="list-style-type: none"> • Consistent T levels • Minor skin reactions • Secondary exposure



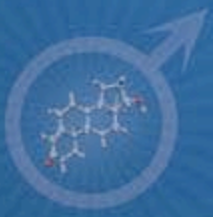
Initiation of TRT Regimen

- You recommend to continue sildenafil and initiate TRT. Robert decides he'd rather just start TRT now and consider sildenafil later.



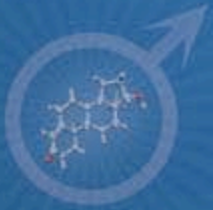
Twelve weeks later...

- Robert returns to visit you and he tells you that his sexual desire is very high but his erections are of poor quality.



Question

4. What do you do now?
 - A. Stop testosterone and give sildenafil
 - B. Maintain testosterone and add sildenafil
 - C. Continue testosterone and switch to another PDE5i
 - D. Maintain testosterone and add intracavernous PGE1 injections



Discussion Points

- **B** is the best choice – TRT should be maintained because Robert's libido has improved. TRT taken with a PDE5i may be beneficial in improving erectile function in hypogonadal men with ED who are unresponsive to TRT alone.^{1,2}
- While the original dose of sildenafil (50 mg) did not work, this dose may work now that he is on TRT. Otherwise, Robert could try an elevated dose (100 mg) or switch to a different PDE5i or intracavernous injection of PGE1.
- You remind Robert to return in 3 months – you want to check for symptom response and safety.

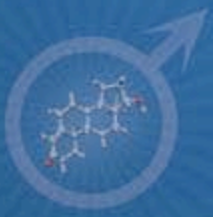
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6-Month Follow-Up Visit

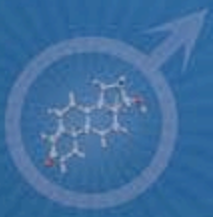
- At 6 months following initiation of TRT you perform a follow-up. Robert is very satisfied with the treatment and has full erections and good sexual drive.
- You perform a follow-up assessment:

Test	Result	Normal Range
Lipid profile	Normal	
Hemoglobin A1C	5.8%	4.5-6%
Hematocrit	0.40	0.38-0.50
TT	12 nmol/L	10-30 nmol/L
PSA	3.6 \uparrow g/L	<3.5 \uparrow g/L
DRE	Normal	



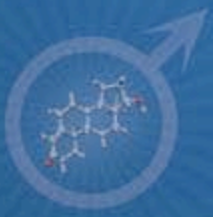
Question

5. What do you do now?
- A. Maintain same treatment and ask for a control test in 3 months
 - B. Maintain sildenafil alone and ask for a control test in 3 months
 - C. Stop TRT and refer to a urologist for further assessment



Discussion Points

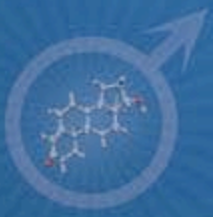
- **C** is the best choice – an increase in PSA can indicate the presence of a prostate tumour, therefore this patient needs to be referred to a urologist.



Follow-Up

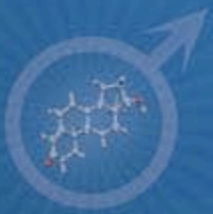
- Robert had a PSA increase of 1.6 ng/mL within 6 months of starting TRT. Urological consultation is suggested with PSA increments >0.75 ng/mL per year.¹ PSA velocity is appropriately measured when at least 3 values are recorded over a period of 18 months.^{2,3}

1. Carter HB, et al. *JAMA*. 1992;267:2215-2220.
2. D'Amico AV, et al. *N Engl J Med*. 2004;351:125-135.
3. Carter HB, et al. *J Natl Cancer Inst*. 2006;98:1521-1527.



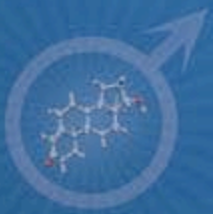
Biopsy Results

- The prostate biopsy shows no cancer.



Question

6. What do you do now?
 - A. Repeat the biopsy
 - B. Reinstigate TRT and continue surveillance with PSA and DRE
 - C. Stop TRT and tell the patient that maintaining TRT is too risky for prostate cancer
 - D. Tell the patient to see another physician

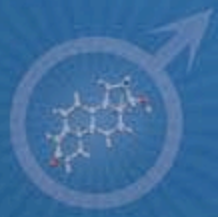


Discussion Points

- **B** is the best choice – prostate cancer has been ruled out. There is no contraindication to resume T replacement. However, there is a risk of a false-negative biopsy, thus surveillance with PSA and DRE should be continued.
- Age-adjusted PSA “threshold” levels should be utilized.¹ For Robert, at age 59, his PSA level should remain below 3.5 ng/mL.

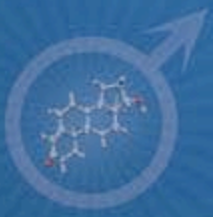
Age (years)	Recommended PSA Reference Range (ng/mL)
40 to 49	0.0 – 2.5
50 to 59	0.0 – 3.5
60 to 69	0.0 – 4.5
70 to 79	0.0 – 6.5

1. Oesterling JE, et al. *JAMA*. 1993;270:860-864.



Long-Term Follow-Up

- The patient continued TRT and came to his follow-up appointments every 6 months. Robert has a new sexual partner named Mary. His libido and erectile function are normal. His testosterone is maintained at 14 nmol/L. His PSA is stable around 2.93.



Key Teaching Points

- Men with sexual dysfunction and co-morbid conditions are at high risk for hypogonadism.
- Combination therapy with TRT and PDE5i may be used to treat decreased libido and erectile dysfunction in men identified with hypogonadism.
- Ensure appropriate prostate assessment before and during treatment.