

HYPOGONADISM AND TESTOSTERONE REPLACEMENT

NOV 2019

Attitudes are significantly changing towards replacing testosterone in men who have a range of symptoms typical of low testosterone production. Nevertheless, established guidelines may not necessarily keep up with current information. Indeed, many doctors remain uncertain and even misinformed about the scientific evidence that indicates significant benefits both in quality of life as well as prevention of certain important medical conditions. In fact, testosterone is now recognised as having wide-ranging health effects and even critical for important biochemistry processes for example heart health. So, it is not just about sex!



WHAT IS HYPOGONADISM?

Also known as testosterone deficiency. The cause may be directly attributable to the testicles or from lack of stimulation by hormones from the pituitary gland and/or specific areas of the brain responsible for maintaining a healthy control of hormone levels. Other names given to this status include age-related hypogonadism, late onset hypogonadism, and andropause (comparing this to menopause in women). Men have a gradual decline in testosterone and the onset of symptoms whereas for women it occurs rather rapidly. Hypogonadism can be primary, which indicates the fault lies with the testicles themselves perhaps from trauma or past infection et cetera. Secondary or central hypogonadism is where the stimulation from the brain and pituitary glands declines. There are many reasons for that including ageing, environmental chemicals, stress and so on.

WHAT ARE THE HEALTH IMPACTS OF DEFICIENCY?

Symptoms and consequences of testosterone deficiency have been well described over many years. Of course, some many men may have few, if any, symptoms. Good for them.



So, you can see that testosterone previously believed to be only for reproduction and sexuality now has a huge range of health

Impact on:	Adverse Effect:
Sexual function	Decreased libido Increased ED Diminished ejaculatory function
Glycemic control and diabetes mellitus	Increase in blood glucose levels, insulin resistance, HbA1c levels Increased risk for diabetes mellitus
Inflammatory responses	Increase in CRP levels Increase in inflammatory cytokines
Lipid profile	Increase in levels of total cholesterol, LDL-cholesterol, and triglycerides
Body composition	Reduced muscle mass Increase in visceral fat and total fat mass
Bone mineral density	Reduced bone mineral density
Blood pressure	Increase in blood pressure
Endothelial function	Increase in endothelial dysfunction
Cardiovascular function	Increased risk for CVD, stroke, and hypertension Increase in intima-media thickness
Mortality	Increased risk for mortality
Quality of life	Diminished physical activity and energy Depressed mood Decreased vitality

benefits and that deficiency may result in loss of vitality, mood problems, sexuality, obesity, loss of muscle mass (1) and even an increased risk of heart disease and its consequences (2) (3). Therefore, there is an argument for testosterone replacement to not only relieve symptoms but perhaps also

prevent later consequences of heart disease and even prostate cancer (the latter is still under investigation). Recent studies have suggested that testosterone replacement therapy (TRT) may reduce death by half in men with heart or other conditions. (4) (5)

HOW IS IT DIAGNOSED

The most important evidence are the actual symptoms and appearance of the patient. Laboratory tests for serum testosterone and other hormones as well as general metabolic evaluations are necessary obviously.

Note that the diagnosis is not just about a blood test as numerous factors including actual laboratory accuracy, may influence the testosterone value. Moreover, testosterone levels can vary during the day, week and time of year.

WHAT ARE THE TYPICAL SYMPTOMS OF TESTOSTERONE DEFICIENCY?

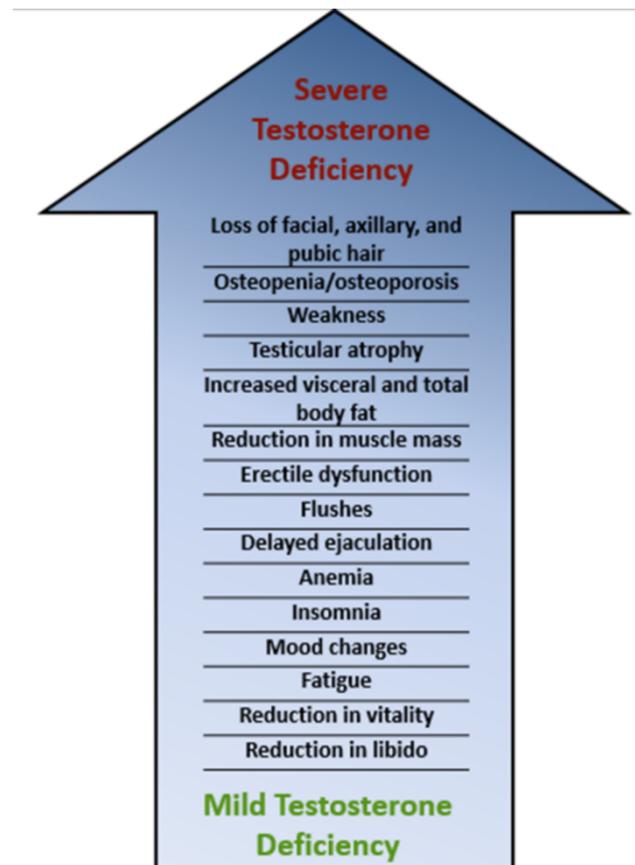
Some men may have very few symptoms whereas others have, over the years, had a gradual decline in overall health, function, appearance which has not been considered a consequence of testosterone deficiency. They put it down to simply the inevitability of ageing which is quite tragic for both the male, his partner/wife as well as family members. In addition, his attitude and abilities to work can be significantly impaired.

The chart shows some of those symptoms from mild to severe. (6)

TESTOSTERONE REPLACEMENT THERAPY - TRT

Here are the options:

- Do nothing and just go with that.
- There are herbal preparations which may help stimulate testosterone production assuming the testes are still capable.
- Treatment with Testosterone - options
 - Testosterone given as a cream or gel applied daily (Transdermal) – 'Bio-identical Testosterone - BHRT'.
 - Testosterone patches - and adhesive patch applied once a day.
 - Testosterone given by injection – widely used, non BHRT – but converts to T.



- Long acting injection every 6-12 weeks (Reandron 1000)
- Short-acting given every 2-3 weeks
- Short-acting given from twice weekly 2 weekly. (Testosterone Cypionate)
Easily self-injected – tiny needle like a diabetic uses.

Choice can depend on several factors:

1. Effectiveness
2. All allowing a relatively steady testosterone level over days, weeks.
3. Ease of use
4. Flexibility of dosing, absorption
5. Risks and side effects particularly conversion into too much DHT (a byproduct of testosterone which in itself is vital for health but not too much, and also conversion to oestrogen).
6. Ability to measure and monitor testosterone levels
7. Cross contamination with other family members esp female when using topical creams.
8. Cost

None satisfies all requirements. It comes down to individual preference and often a trial of one then another to find the most suitable overtime. The Dr will discuss all these factors during your assessment.

PREFERRED OPTION:

With a lot more information from experts around the world, I am coming to accept that the reference option is frequent injections, self given and given at least weekly.

WHAT ARE THE RISKS?

Testosterone discussions in the medical world have been very active in the last decades. Many new studies have been completed that confirm the safety of testosterone replacement and indeed the risks of not doing so! The older ideas that it may cause cancer of the prostate and heart attacks have now been firmly refuted. (REDUCE Trial 2010, EHPCCG Study 2008). There is perhaps some small risk for men over 75 concerning heart, that would not be unsurprising!



Nevertheless, proper assessment is required, appropriate laboratory investigations completed and an informed discussion must take place. (7) (8) (9) (10) (11).

It is believed that TRT will not cause prostate cancer, PCa, but may accelerate an existing prostate cancer– new information is starting to suggest this may be at low levels – at higher levels it may be protective.

(12). In fact the link to PCa may include low testosterone, excess oestrogen and other chemical factors. Therefore testosterone may be PROTECTIVE against getting PCa.

1 in 10 men will be diagnosed with prostate cancer in their lifetime



3000

NZ men are diagnosed each year with prostate cancer

600

men a year will die from prostate cancer

Are there men who should not have testosterone replacement?

Currently the absolute contraindications (must not have) are:

- Advanced prostate cancer; it may be that man with mild but treated prostate cancer who have major issues with testosterone insufficiency could have testosterone replacement therapy, TRT. But that would involve significant amount of discussion.
- Elevated PSA (prostate test) for the patient's age and prostate size. These man need investigating first.
- Prostate nodule on examination
- A blood count greater than 50%--because testosterone therapy may increase the blood count i.e. make the blood a bit thicker.
- Male breast cancer

Cautions for some men (these may not necessarily mean no testosterone replacement)

- Severe symptoms of enlarged, noncancerous prostate
- Severe obstructive sleep apnoea
- Uncontrolled heart failure
- Men who still require fertility (consider Clomiphene or HCG).
- Men experiencing angina of the heart. (But refer to notes below).
- Old men over 75.

(Note: Even the above cautions are being doubted by latest research) (13)

ABOUT HEART DISEASE AND TESTOSTERONE

Two years ago, some studies came out suggesting that testosterone replacement may increase the risk of heart attacks and stroke. Opponents of testosterone therapy immediately condemned the use of testosterone treatment. The media got hold of it and the whole process got negative publicity.

Fortunately these medical trial reports were carefully analysed by experts and found to be very poorly done and did not pass reliability checks and therefore dismissed (14). The multitude of previous and later clinical trials has proven that testosterone replacement is safe providing appropriate evaluation, investigations are done. (8) (15)

Interesting results from clinical trials regarding heart disease

1. TRT in men with stable heart disease is safe
2. In men **not taking** statin drugs, the yearly rate of change in heart artery disease was lower in men taking testosterone compared with those not.
3. 3 clinical trials in men with angina (heart pain) showed increased time before they got chest pain with exertion. In other words an improvement.
4. Four clinical trials in men with heart failure found significant improvement in symptoms
5. 2017 Study claims increase heart risk – but this study seems very flawed – [read this rebuttal!](#) (20)

ABOUT TESTOSTERONE AND METABOLIC SYNDROME RISKS



Metabolic syndrome is becoming extremely prevalent. What is it? Is a gradual increase in abdominal obesity especially that may lead to diabetes, worsening blood pressure and the consequences of heart disease, stroke et cetera. These men need to be on testosterone replacement. But also, it is critical to change eating habits, alcohol intake, exercise habits and so on. Testosterone is important but not a Magic Bullet.

There are some men, who, when they are on testosterone take this as an open ticket to an unhealthy lifestyle thinking one good thing will neutralise a bad thing! Wrong.

Here are the criteria for this important diagnosis - need to have 3 or more to meet the International criteria for the diagnosis.

1. Waist circumference > 94-102 cm
2. Elevated triglycerides (a type of fat measured as part of the cholesterol assessment) > 1.69
3. Reduced good HDL cholesterol < 1.04
4. Blood pressure elevated >130 systolic and/or > 85 diastolic or patient on treatment
5. Fasting blood glucose elevated > 5.55

WHEN YOU THINK ABOUT IT AND LOOK AROUND YOU WILL SEE MANY MEN WITH UN-DIAGNOSED MILD TO SEVERE METABOLIC SYNDROME.

The importance in hypogonadism for metabolic syndrome is firmly established and if left untreated, the condition may have detrimental health effects.

In fact the benefits for men who are obese who have type 2 diabetes and very significant with reduction in HbA1c (blood sugar levels), metabolic risk factors and improvement in AMS score and depression. In addition, there was a reduction in all cause mortality (16) (17) (18).

TREATMENT GUIDELINES AND MONITORING TRT

- If a man has no obvious prostate cancer or other contraindications or precautions, proceed to TRT- and as previously mentioned my preference would be injectable testosterone every week, preferably twice a week to avoid conversion to estrogens and the peaks and troughs. Some men prefer topical transdermal cream.
- If the T level is <8, the PSA may rise in first 3-6 months to new base-line.
- If the PSA is >4 may need referral to a urologist.

ESSENTIAL READING!

I highly recommend that you obtain the following book from Amazon and download onto your Kindle. This will give you an excellent guideline not only for testosterone but for general health

TITLE: The Testosterone Optimization Therapy Bible. Author: J Campbell. 2018

For men 35 and under where fertility is an issue I recommend the following book as well from Amazon.

TITLE: Optimised Under 35. Author: Daniel Kelly

Monitoring:

Follow up	Monitoring	Outcome
3-6 months for the first year then every year thereafter. Of course if that are any changes or concerns then a review is required.	Baseline DRE	Trial of 3-6 months, longer if on long acting Depot T types
	PSA 1.4 rise in any year or 0.4 per year	Refer urologist
	Haematocrit =>54%	needs phlebotomy esp if on depot T
	Serum T levels	
	Check symptom relief, AMS and ADAM scores	

REFERENCES

1. *A Vascular Hormone in Health and Disease.* **Kelly DM, Jones TH.**, 2013, J.Endocrinology.
2. *Androgen therapy in men with testosterone deficiency: can testosterone reduce the risk of cardiovascular disease?* **Androgen, Saad F.** s.l. : Diabetes Metab Res Rev, 2012, Vol. 28.
3. *Endogenous sex hormones and the prospective association with cardiovascular disease and mortality in men; the Tromso Study.* **Vikan T, Schirmer H, Njolstad I, Svarthberg J.** s.l. : Eur J Endocrinol, 2009, Vol. 161.
4. *Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes.* **Muraleedharan V, Marsh H, Kapoor D, Channer KS, Jones TH.** s.l. : Eur J Endocrinol., 2013, Vol. 169.
5. *Testosterone treatment and mortality in men with low testosterone levels.* **Shores MM, Smith NL, Forsberg CW, Anawalt BD, Matsumoto AM.** s.l. : J Clin Endocrinol Metab., 2012, Vol. 97.
6. *A practical guide to diagnosis, management and treatment of testosterone deficiency for Canadian physicians.* **Morales A, Bella AJ, Chun S, et al.** s.l. : Can Urol Assoc J., 2010, Vol. 4.
7. *An update on male hypogonadism therapy.* **Surampudi P, Swerdloff RS, Wang C.** s.l. : Expert Opin Pharmacother., 2014, Vol. 15.
8. *Diagnosis and management of testosterone deficiency syndrome in men: clinical practice guideline.* **Morales A, et al.** s.l. : CMAJ, 2015, Vol. 187.
9. *Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline.* **Bhasin S, Cunningham GR, Hayes FJ, et al.** s.l. : J Clin Endocrinol Metab, 2010, Vol. 95.
10. *The International Society for Sexual Medicine's process of care for the assessment and management of testosterone deficiency in adult men.* **Dean JD, McMahon CG, Guay AT.** s.l. : J Sex Med, 2015, Vol. 2015.
11. *EAU Guidelines on Male Hypogonadism.* **al, Dohle GR et.** s.l. : European Association of Urology, 2015.
12. *Effect of Androgens on Prostate Cancer.* **A, Morgentaler.** s.l. : Eur Urol, 2009, Vol. 55.
13. *Shifting the paradigm of testosterone and prostate cancer.* **Morgentaler A, Traish AM.** s.l. : Eur Urol, 2009, Vol. 55.

14. *Testosterone therapy and cardiovascular risk: advances and controversies.* **A, Morgentaler.** s.l. : Mayo Clin Proc, 2015, Vol. 90.
15. *American Association of Clinical Endocrinologists and American College of Endocrinology position statement on the association of testosterone and cardiovascular risk.* **Goodman N, Guay A, Dandona P, et al.** s.l. : Endocr Pract., 2015, Vol. 21.
16. **G, Hackett.** s.l. : J Sex Med, 2014, Vol. 11.
17. *BLAST Study.* **Hackett G.** s.l. : Int J Clin Pract, 2014, Vol. 68.
18. *BLAST Study Follow Up.* **Hackett G.** s.l. : Int J Clin Pract, 2014, Vol. 70.
19. Is Testosterone safe in older men? <http://jeffreydachmd.com/2017/02/testosterone-therapy-coronary-plaque-calcium-score/>