Testosterone Replacement

A 10 Minute Update for 2019

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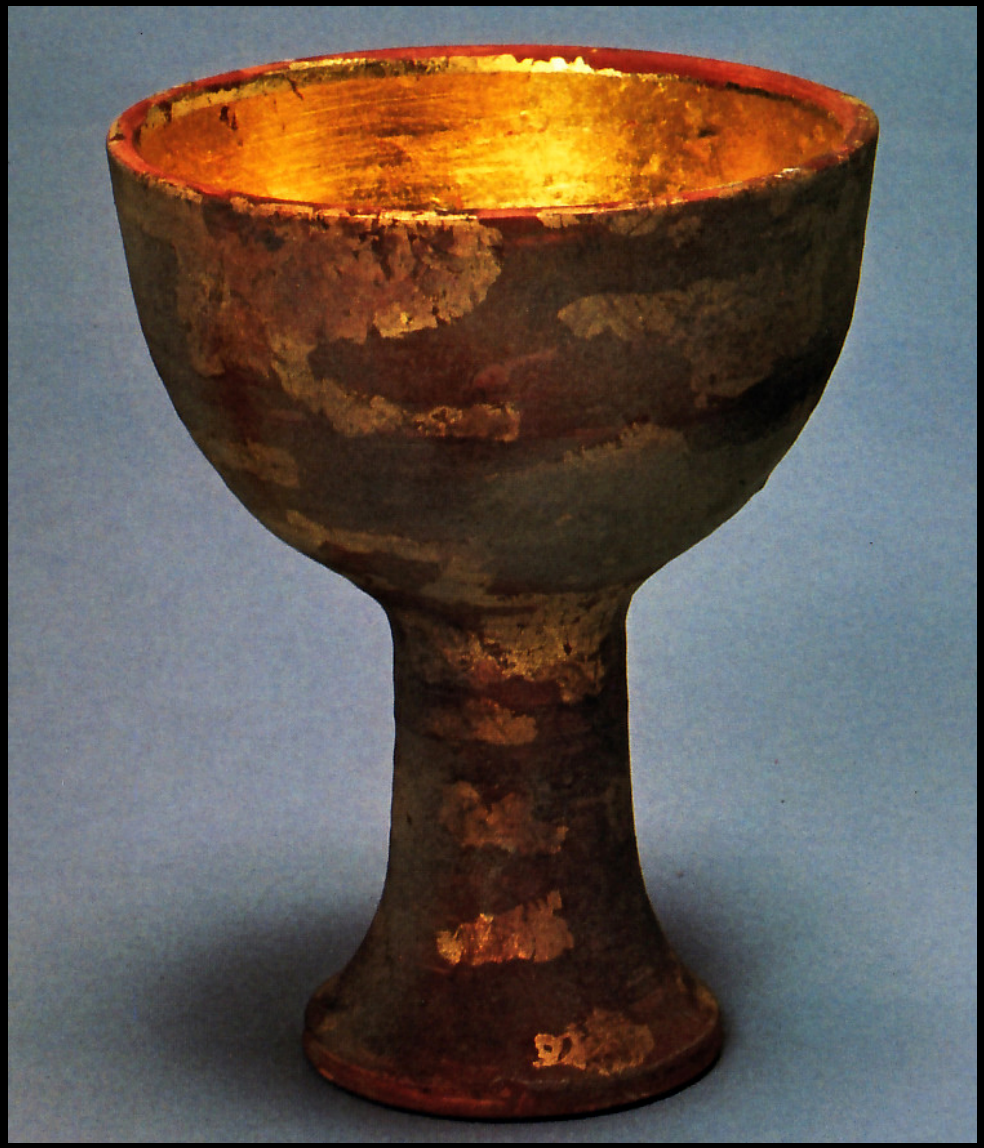
Maybe it’s simpler than you think



Seven T Trials

- Physical Function Trial
- Sexual Function Trial
- Vitality Trial (for fatigue)
- Cognitive Function Trial
- Anemia Trial (hemoglobin)
- Bone Trial (bone density)
- Cardiovascular Trial (coronary artery plaque volume)

Snyder et al. Clinical Trials 2014; 11:362-375

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T Trials Data: Summary

- Sexual function improved (less than a dose of Viagra; 2.64 pts on full length IIEF)
- Walking distance improved by small amount
- Vitality did not improve
- Cognition did not improve
- Mood/depressive symptoms improved slightly
- Mild to moderate anemia improved
- PSA went up
- Bone density and estimated bone strength improved

T Trials Data: Summary

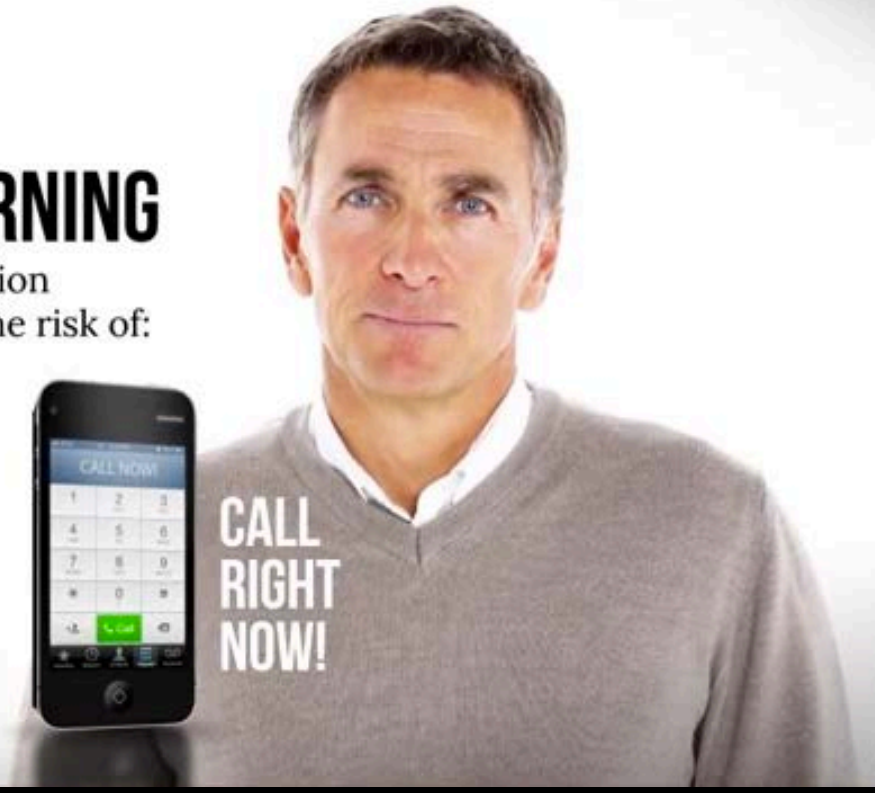
- Plaque in coronary arteries increased (concerning)
- Unclear if TRT increases risk of MI, CVA, Cancer
- Oct 2016, FDA approved labeling to highlight potential for heart-related side effects and mental health/abuse risks

Topical Gel & Injectable

TESTOSTERONE WARNING

A new study shows that prescription testosterone products increase the risk of:

- STROKES
- HEART ATTACKS
- BLOOD CLOTS
- PULMONARY EMBOLISM
- DEEP VEIN THROMBOSIS



Enthusiasm waning

- Prescriptions on the downswing
- 2013 study (JAMA Internal Medicine) reviewed insurance Rx data on >10 million men >40y from 2001-2011 and TRT RX tripled (nearly ¼ didn't even have T levels checked)
- From 2013-2018, Rx for men >/= 30 decreased by 48% (JAMA July 10, 2018)

Potential Factors

- Reasonable dropout rate based on patient expectations
- Many who report the nonspecific symptoms seen on TV ads are **actually hoping for correction of ED** w/o being stigmatized
- Providers may be frustrated by time involved with educating/managing patients relative to reimbursement
- Patient/partner health concerns, bother with inconvenience/discomfort/etc

Areas for improvement

- Uneducated physicians using TRT when men want to maintain **fertility**
- Lack of proper w/u (two early AM values, rule out problematic causes, men >/=65 w/o symptoms should not be treated per Endocrine Society)
- Knowing side effects of drugs like clomid
- Knowing when to use HCG/HMG
- Guidance on managing high Hgb/Hct
- **The shot-clinic epidemic**

The Withdrawal

- Many men treated apart from guidelines by PCPs, ‘naturopaths’/’integrative health’, or shot clinics despite normal/low normal levels b/c they want to try treatment
- Many providers don’t understand the **negative feedback** (and patients don’t know)
- When men don’t see any clinical difference, they stop TRT, level plummet to well below baseline, they feel awful and erroneously assume it WAS helping and stay on indefinitely

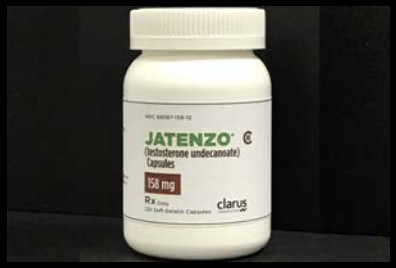
PSA issue

- Many of the men seeking TRT may be younger than the recommended age for screening per AUA Guideline, but get PSA baseline before TRT
- No established **T-adjusted PSA**
- If PSA rises when T normalized, logic suggests the PSA should be considered as in other men with normal T since we don't treat elevated PSA with ADT
- However, many men are simply taken off TRT (withdrawal…miserable)

Common Treatment Options

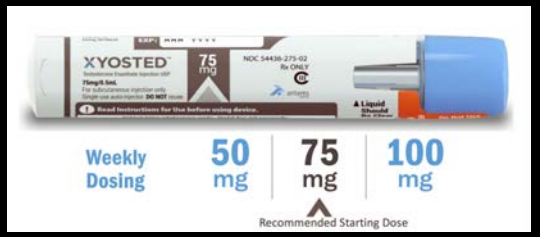
- Topicals (Androgel/Testim/Fortesta/Axiron, Compounded pharmacy versions)
- Patches (Androderm, Striant)
- Pellets (Testopel, Compounded versions in blister packs may be safer)
- Injections
  - Testosterone enanthate
  - Testosterone cypionate (one more carbon ester chain, so longer half-life)
  - Testosterone undecanoate (Aveed)

Newer Products



- Oral T undecanoate (Jatenzo, Clarus Therapeutics):
- Approved by FDA 3/27/19. First new oral TRT in over 60 years.
- For men with low T due to Klinefelter's or pituitary tumors.
- Less affected by food (dietary fat) than prior oral formulations (such as Andriol).
- Box warning notes it can cause HTN. Not for LOH.

Newer Products



- Testosterone enanthate injection (Xyosted, Antares Pharma):
- Once weekly single-use autoinjector for primary or hypogonadotropic hypogonadism.
- Comes in 50 mg, 75 mg, and 100 mg subcutaneous doses.
- Phase 3 study noted 5.4% rise in HCT and increased BP.
- Box warning highlights HTN.

Newer Products

- Testosterone nasal gel (Natesto, Aytu BioScience):
- Approved by FDA in 2014 for primary or HGHG, congenital or acquired.
- Avoids first-pass metabolism. Max concentration 45 minutes after administration with clearance in 2-6 hours.
- Each pump is 5.5 mg, with recommendation of one pump per nostril (11 mg) **three times per day** (33 mg daily dose). Not for men with chronic nasal conditions.

Conclusions

- T Trials Data show TRT isn't a cure-all and enthusiasm may be waning
- Much of the data seems to suggest we are safe to treat from heart/CA perspective, but we need to document discussion (saturation model is not gospel and cardiovascular risk still on the box)
- Forward thinking practices can consider multidisciplinary collaboratives and noninvasive wellness screenings (e.g., EndoPAT)

Conclusions

- As far as future directions, several opportunities:
  - Physician education on workup and management still seems important
  - Fertility management strategies
  - Hgb/Hct management strategies
  - Concept of T-adjusted PSA
  - Future combo clomid/arimidex?
  - Weaning protocols to mitigate withdrawal

Have you chosen wisely??

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