2016 Testosterone International Expert Consensus Recommendations: Mayo Clinic

by Abraham Morgenthaler, M.D. (Harvard Medical School), et. al, published in 2016 Mayo Foundation for Medical Education and Research. In order to address widespread concerns regarding the medical condition of testosterone deficiency (TD) or male hypogonadism, an international expert consensus conference was convened in Prague, Czechoslovakia on October 1, 2015. Experts included a wide range of medical specialties including urology, endocrinology, diabetology, internal medicine, and basic science research. Nine resolutions were debated with unanimous approval, with commentary after each.

TD = Testosterone Deficiency, and T= Testosterone as abbreviations.

These Nine Resolutions:

1. **TD is a well-established, significant medical condition that negatively affects male sexuality, reproduction, general health, and quality of life.** Low T levels may predict increase risk of developing diabetes and metabolic syndrome. It is associated with increased all-cause and cardiovascular mortality.

2. **The symptoms and signs of TD occur as a result of low levels of T, and may benefit from treatment regardless of whether there is an identified underlying origin. Symptoms of low T resolve with testosterone normalization.** Historically recognized causes of TD are rare (eg., anorchia, craniopharyngioma, pituitary tumor), recently termed ***classical hypogonadism***. These conditions account for only a tiny fraction of men with TD**. TD occurs frequently with conditions other than these classical causes. No evidence supports restriction of T therapy only to men with known underlying origin.**

3. **TD is a global health concern**. **Deficiency prevalence rates in men range from 2-38% in studies from four continents.** Variation in prevalence rates can be explained by differences in definition and biochemical thresholds. A U.S. study estimates an additional $190-525 billion in healthcare expenditures over the next 20 years from TD.

4. **T therapy for men with TD is effective, rational, and evidence-based.** High levels of T effectively increase sexual desire (libido), as well as assists erectile dysfunction and orgasmic function. T increases lean body mass, decreases fat mass, and improves bone mineral density. There is strong suggestive evidence for the role of testosterone's improvement in mood and energy.

5. **There is no specific testosterone (T) concentration that reliably distinguishes those who will biologically respond to T therapy from those who will not respond.** Total T concentration interpretation is confounded by inter-individual variation, variation in serum SBHG (Sex Hormone Binding Globulin levels), and genetic variation in androgen sensitivity due to AR gene polymorphisms. **Free T levels can be a reliable indicator of androgen status.**

6. **There is no scientific basis for any age-specific recommendations against the use of T therapy**. The term age-related hypogonadism is of questionable validity since the decline of serum T levels in men with age is minor, and is primarily attributable to co-morbidities, especially obesity. Both younger and older men respond to T therapy. The increased risk of erythrocytosis in older men requires monitoring, but does not merit withholding of T therapy if indicated. It is illogical to single out TD as the one medical condition

among many others (like diabetes, hypertension, heart disease, cancer, and arthritis) that does not merit treatment because it becomes more prevalent with age.

7. **The evidence does NOT support increased risks of cardiovascular events with T therapy**. Two observational studies several years ago received intense media attention after reporting increased cardiovascular risks. **Both studies had major flaws and limitations**. One study misreported its results and the other group had no control group. Low serum testosterone levels are associated with increased atherosclerosis, coronary arterial disease, obesity, diabetes, and increased mortality. Several RCTs (Randomized Controlled Trials) in men with known heart disease (angina and heart failure) showed greater benefits with T vs. placebo therapy (greater time to ischemia and greater exercise capacity). The largest metaanalysis showed no increased risk with T therapy and reduced risk was noted with metabolic conditions. There was NO increased risk of venothrombotic events with T therapy.

8. **The evidence does NOT support an increased risk of prostate cancer with T therapy.** Serum androgen concentrations are not associated with increased risk of prostate cancer than placebo. T therapy has no greater risk of prostate cancer than placebo. Aggressive/ high grade prostate cancers are associated with LOW T levels. Early data suggest there is no increased risk of recurrence or progression with T therapy in men previously treated for prostate cancer.

9. **The evidence supports a major research initiative is needed to explore possible benefits of T therapy for cardiometabolic diseases, including diabetes.** A large body of evidence suggests lower serum T levels are associated with increased cardiovascular risk and higher T levels are protective. T therapy reliably increases lean body mass, decreases fat mass, and may improve glycemic control. Mortality rates are reduced by half in men with TD who received T therapy compared with untreated men in observational studies. Among men who received T therapy, those with normalized T levels had a reduced rate of cardiovascular events and mortality vs. men with persistently low T levels.