Evaluation and Management of Testosterone Deficiency: AUA Guideline

John P. Mulhall, Landon W. Trost, Robert E. Brannigan, Emily G. Kurtz, J. Bruce Redmon, Kelly A. Chiles, Deborah J. Lightner, Martin M. Miner, M. Hassan Murad, Christian J. Nelson, Elizabeth A. Platz, Lakshmi V. Ramanathan and Ronald W. Lewis

From the American Urological Association Education and Research, Inc., Linthicum, Maryland

Purpose: There has been a marked increase in testosterone prescriptions in the past decade resulting in a growing need to give practicing clinicians proper guidance on the evaluation and management of the testosterone deficient patient.

Materials and Methods: A systematic review utilized research from the Mayo Clinic Evidence Based Practice Center and additional supplementation by the authors. Evidence-based statements were based on body of evidence strength Grade A, B, or C and were designated as Strong, Moderate, and Conditional Recommendations with additional statements presented in the form of Clinical Principles or Expert Opinions (table 1 in supplementary unabridged guideline, http://jurology.com/).

Results: This guideline was developed by a multi-disciplinary panel to inform clinicians on the proper assessment of patients with testosterone deficiency and the safe and effective management of men on testosterone therapy. Additional statements were developed to guide the clinician on the appropriate care of patients who are at risk for or have cardiovascular disease or prostate cancer as well as patients who are interested in preserving fertility.

Conclusions: The care of testosterone deficient patients should focus on accurate assessment of total testosterone levels, symptoms, and signs as well as proper on-treatment monitoring to ensure therapeutic testosterone levels are reached and symptoms are ameliorated. Future longitudinal observational studies and clinical trials of significant duration in this space will improve diagnostic techniques and treatment of men with testosterone deficiency as well as provide more data on the adverse events that may be associated with testosterone therapy.

Key Words: testosterone, hypogonadism, men's health, androgens

Abbreviations and Acronyms

ASCVD = atherosclerotic cardiovascular disease

AUA = American Urological Association

FDA = U.S. Food and Drug Administration

Hct = hematocrit

hCG = human chorionic gonadotropin

LH = luteinizing hormone

MACE = major adverse cardiac event

RCTs = randomized controlled trials

RT = radiation therapy

VTE = venous thromboembolism

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The complete unabridged version of the guideline is available at http://jurology.com/.

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BACKGROUND

Testosterone testing and prescriptions have nearly tripled in recent years; however, it is clear from clinical practice that there are many men using testosterone without a clear indication.[1–3] Some studies estimate that up to 25% of men who receive testosterone therapy do not have their testosterone tested prior to initiation of treatment. Of men who are treated with testosterone, nearly half do not have their testosterone levels checked after therapy commences.[2,3] While up to a third of men who are placed on testosterone therapy do not meet the criteria to be diagnosed as testosterone deficient,[2,3]

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there are a large percentage of men in need of testosterone therapy who fail to receive it due to clinician concerns, mainly surrounding prostate cancer development and cardiovascular events, although current evidence fails to definitely support these concerns.

GUIDELINE STATEMENTS

Diagnosis of Testosterone Deficiency

1. **Clinicians should use a total testosterone level below 300 ng/dL as a reasonable cut-off in support of the diagnosis of low testosterone. (Moderate Recommendation; Evidence Level: Grade B)**

2. **The diagnosis of low testosterone should be made only after two total testosterone measurements are taken on separate occasions with both conducted in an early morning fashion. (Strong Recommendation; Evidence Level: Grade A)**

3. **The clinical diagnosis of testosterone deficiency is only made when patients have low total testosterone levels combined with symptoms and/or signs. (Moderate Recommendation; Evidence Level: Grade B)**

4. **Clinicians should consider measuring total testosterone in patients with a history of unexplained anemia, bone density loss, diabetes, exposure to chemotherapy, exposure to testicular radiation, HIV/AIDS, chronic narcotic use, male infertility, pituitary dysfunction, and chronic corticosteroid use even in the absence of symptoms or signs associated with testosterone deficiency. (Moderate Recommendation; Evidence Level: Grade B)**

5. **The use of validated questionnaires is not currently recommended to either define which patients are candidates for testosterone therapy or monitor symptom response in patients on testosterone therapy. (Conditional Recommendation; Evidence Level: Grade C)**

The diagnosis of testosterone deficiency requires both a low testosterone measurement as well as the presence of select symptoms and/or signs. The Panel defines the threshold for low testosterone as being consistently <300 ng/dL on *at least two* serum total testosterone measurements obtained in an early morning fashion, preferably using the same laboratory with the same method/instrumentation for measurement (fig. 1).[2,4]

Clinicians should make note of any patient-reported symptoms associated with low testosterone, such as reduced energy, reduced endurance, diminished work and/or physical performance, fatigue, visual field changes (bitemporal hemianopsia), anosmia, depression, reduced motivation, poor concentration, impaired memory, irritability, infertility, reduced sex drive, and changes in erectile function.[5,6]

Clinicians should also conduct a targeted physical exam to examine patients for signs that are associated with low testosterone. This assessment should include evaluation of general body habitus; virilization status (examination of body hair patterns and amounts in androgen dependent areas); body mass index or waist circumference; gynecomastia; testicular evaluation including presence, size, consistency and masses; varicocele presence; and prostate size and morphology.[5,6]

A meta-analysis of the literature suggests that men who have a history of unexplained anemia,[7] bone density loss,[8] diabetes,[9] exposure to chemotherapy,[10] direct or scatter radiation therapy to the testes,[11] HIV,[12] a history of chronic narcotic use,[13] infertility,[14] pituitary disorders,[15] and chronic corticosteroid use[16] are at risk for low testosterone. The Panel recommends measuring testosterone in all patients who have a history of these conditions, even in the absence of symptoms or signs listed above.

Screening questionnaires are not an appropriate tool to identify candidates for testosterone therapy and should not be used at the expense of a full patient evaluation and laboratory testosterone measurement. Specificities and sensitivities vary greatly amongst available questionnaires making them ill-suited for screening or for use as a surrogate for testosterone laboratory testing.[4]

Adjunctive Testing

6. **In patients with low testosterone, clinicians should measure serum luteinizing hormone levels. (Strong Recommendation; Evidence Level: Grade A)**

Measuring luteinizing hormone levels may help to establish the etiology of testosterone deficiency and may be an important factor in determining if adjunctive tests should be ordered (Appendix C in supplementary unabridged guideline, http://jurology.com/).[17] Testosterone deficient patients with low or low/normal LH levels are also candidates for selective estrogen receptor modulator use as a treatment for testosterone deficiency, particularly those wishing to preserve their fertility.[18]

7. **Serum prolactin levels should be measured in patients with low testosterone levels combined with low or low/normal luteinizing hormone levels. (Strong Recommendation; Evidence Level: Grade A)**

8. **Patients with persistently high prolactin levels of unknown etiology should undergo evaluation for endocrine disorders. (Strong Recommendation; Evidence Level: Grade A)**

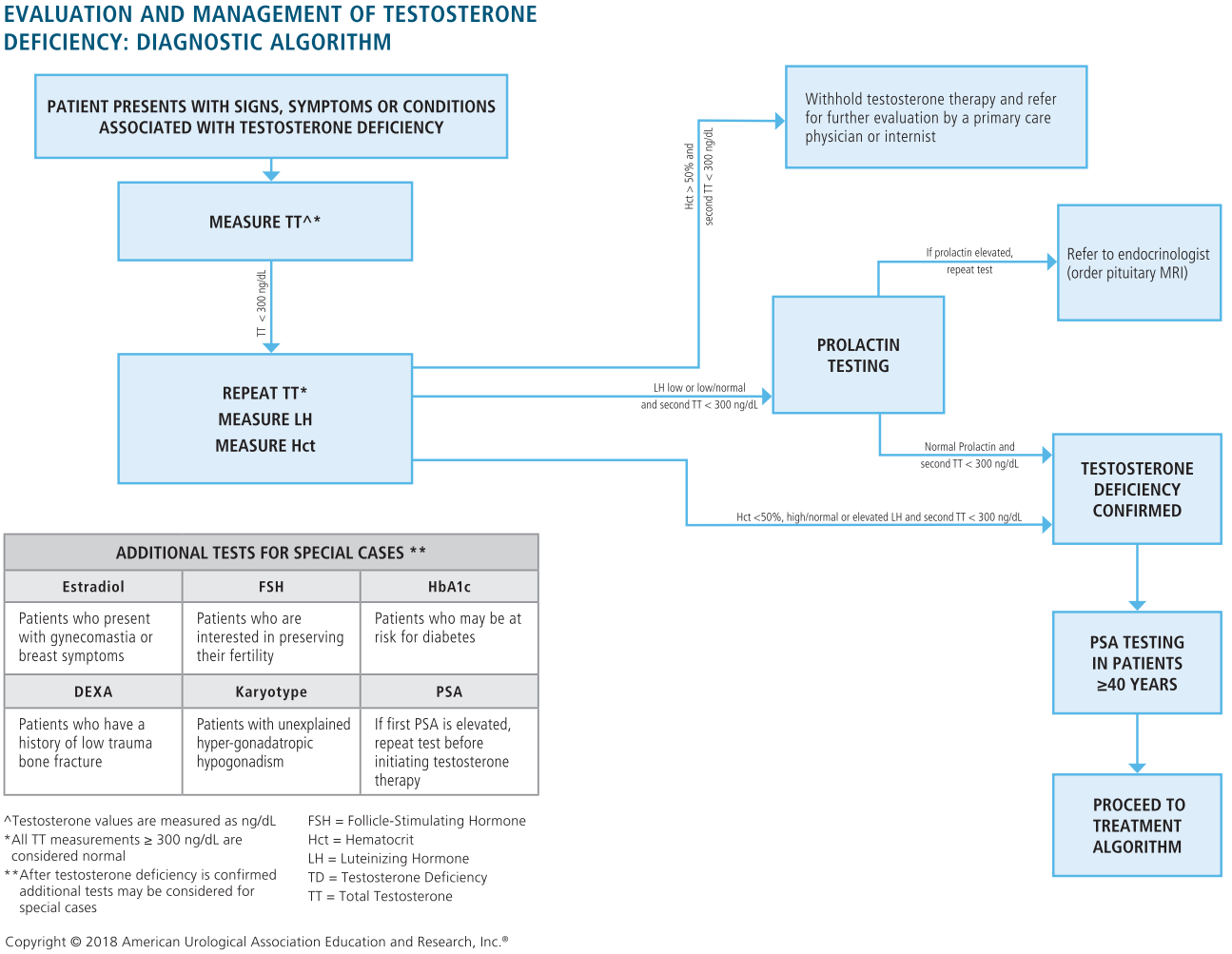


Figure 1. Diagnostic algorithm

Serum prolactin should be measured in patients who have low total testosterone and low or low/normal LH levels to screen for hyperprolactinemia. If patients have elevated prolactin levels, prolactin measurement should be repeated to ensure that the initial elevation was not spurious. Persistently elevated prolactin levels can indicate the presence of pituitary tumors, such as prolactinomas,[19] and the Panel recommends that such patients should be referred to an endocrinologist for further evaluation. Men with total testosterone levels of <150 ng/dL in combination with a low or low/normal LH should undergo a pituitary MRI regardless of prolactin levels, as non-secreting adenomas may be identified.[20]

9. **Serum estradiol should be measured in testosterone deficient patients who present with breast symptoms or gynecomastia prior to the commencement of testosterone therapy. (Expert Opinion)**

Men who have elevated baseline estradiol measurements should be referred to an endocrinologist. While it is not uncommon for estradiol levels to increase while patients are on testosterone therapy as total testosterone increases, clinicians should be aware that symptomatic gynecomastia or other breast symptoms are uncommon. For men who develop gynecomastia/breast symptoms on treatment (e.g., breast pain, breast tenderness, nipple tenderness), a period of monitoring based on clinical judgment should be considered as breast symptoms sometimes abate.

10. **Men with testosterone deficiency who are interested in fertility should have a reproductive health evaluation performed prior to treatment. (Moderate Recommendation; Evidence Level: Grade B)**

Men diagnosed with testosterone deficiency who are interested in preserving their current fertility should undergo testicular exam to evaluate testicular size, consistency, and descent and have their serum follicle-stimulating hormone measured to assess their underlying reproductive health status.[21]

Elevated follicle-stimulating hormone levels in the setting of testosterone deficiency (hypergonadatropic hypogonadism) is typically indicative of impaired spermatogenesis;[6] therefore, clinicians should consider adjunctive fertility testing, such as a semen analysis, in such patients. Patients who have severe oligospermia (sperm concentration <5 million sperm per mL) or non-obstructive azoospermia should be offered reproductive genetics testing consisting of karyotype testing and Y-chromosome analysis for microdeletions.[21]

11. **Prior to offering testosterone therapy, clinicians should measure hemoglobin and hematocrit and inform patients regarding the increased risk of polycythemia. (Strong Recommendation; Evidence Level: Grade A)**

Prior to commencing testosterone therapy, all patients should undergo a baseline measurement of hemoglobin/hematocrit. If the Hct exceeds 50%, clinicians should consider withholding testosterone therapy until the etiology is formally investigated. While on testosterone therapy, a Hct $\geq$54% warrants intervention, such as dose reduction or temporary discontinuation. While the incidence of polycythemia for one particular modality of testosterone compared to another cannot be determined, trials have indicated that injectable testosterone is associated with the greatest treatment-induced increases in hemoglobin/Hct.[22]

12. **PSA should be measured in men over 40 years of age prior to commencement of testosterone therapy to exclude a prostate cancer diagnosis. (Clinical Principle)**

It is the opinion of this Panel that serum PSA levels should be measured prior to the commencement of testosterone therapy in patients over 40 years of age in order to minimize the risk of prescribing testosterone therapy to men with occult prostate cancer.

For patients who have an elevated PSA at baseline, a second PSA test is recommended to rule out a spurious elevation. In patients who have two PSA levels at baseline that raise suspicion for the presence of prostate cancer, a more formal evaluation, potentially including reflex testing (e.g., 4K or phi), and prostate biopsy with/without MRI, should be considered before initiating testosterone therapy.

Patients who maintain on-treatment testosterone levels in the normal range should decide on PSA testing using a shared decision-making approach with their clinician in accordance with the American Urological Association's Early Detection of Prostate Cancer Guideline.

Counseling Regarding Treatment of Testosterone Deficiency

13. **Clinicians should inform testosterone deficient patients that low testosterone is a risk factor for cardiovascular disease. (Strong Recommendation; Evidence Level: Grade B)**

Currently available literature has consistently shown that low testosterone levels are associated with an increased incidence of major adverse cardiac events, such as myocardial infarction, stroke, and possible cardiovascular-related mortality and an increased prevalence of certain atherosclerotic cardiovascular disease risk factors.[23] Testosterone deficient patients should be informed that low testosterone levels place them at risk for these major cardiovascular events, and clinicians should assess all testosterone deficient patients for ASCVD risk factors, both fixed (e.g., older age, male gender) and modifiable (e.g., dyslipidemia, hypertension, diabetes, current cigarette smoking).

14. **Patients should be informed that testosterone therapy may result in improvements in erectile function, low sex drive, anemia, bone mineral density, lean body mass, and/or depressive symptoms. (Moderate Recommendation; Evidence Level: Grade B)**

15. **Patients should be informed that the evidence is inconclusive whether testosterone therapy improves cognitive function, measures of diabetes, energy, fatigue, lipid profiles, and quality of life measures. (Moderate Recommendation; Evidence Level: Grade B)**

The main purpose of testosterone therapy is to achieve therapeutic testosterone levels and provide relief of symptoms or signs. In trials, patients with low testosterone have demonstrated statistically significant improvements in erectile function,[24] sex drive,[24] anemia,[25] bone mineral density,[26] lean body mass,[27] and depressive symptoms.[24] However, given the limitations of the underlying studies and difficulties in assessing symptoms, it is unclear how clinically meaningful these improvements may be in some cases.

The evidence is less conclusive as to whether or not testosterone therapy improves cognitive function,[28] measures of diabetes,[29] energy,[30] fatigue,[30] lipid profiles,[29] and quality of life measures.[31] Despite the absence of definitive evidence, the Panel suggests that patients with these symptoms may be counseled regarding the possibility of improvement on testosterone therapy.

16. **The long-term impact of exogenous testosterone on spermatogenesis should be discussed with patients who are interested in future fertility. (Strong Recommendation; Evidence Level: Grade A)**

For men on exogenous testosterone who are planning future reproduction, testosterone cessation should occur in advance of initiation of any effort to conceive. Patients need to be made aware of the highly variable time course to recover sperm in

the ejaculate and the variable degree to which spermatogenesis returns after stopping exogenous testosterone.[32] While two-thirds of males in contraceptive studies recovered sperm in the ejaculate within six months of exogenous testosterone therapy cessation, 10% failed to do so until the second year after cessation.[32] The recovery of spermatogenesis after discontinuing use of exogenous testosterone is also not well-established in infertile males and this important risk should be discussed with patients before starting treatment.[33]

17. **Clinicians should inform patients of the absence of evidence linking testosterone therapy to the development of prostate cancer. (Strong Recommendation; Evidence Level: Grade B)**

The relationship between testosterone therapy and the development of prostate cancer has been debated. While the U.S. Food and Drug Administration retains a warning regarding the potential risk of prostate cancer in patients who are prescribed testosterone products, there is accumulating evidence against a link between testosterone therapy and prostate cancer development. Randomized controlled trials have shown that there is not a significant increase in the rate of a prostate cancer diagnosis in older, testosterone deficient men who were treated with testosterone compared to placebo.[24,30,34]

One meta-analysis by Calof et al.[35] (2005) pooled data from 19 RCTs to determine the number of all-cause prostate events in men who were on exogenous testosterone treatment as compared to men who were on placebo. At the end of study, the total number of prostate-related events was significantly greater in the testosterone arm than in the placebo arm (OR=1.79; CI: 1.07, 2.95). The authors conceded that it was not possible to determine if each individual prostate event occurred in unique individuals since the same person might have had more than one event leading to an overestimate in incidence. When individual prostate events were analyzed separately, there was not a statistically significant difference in incidence between the two groups in terms of prostate cancer (OR=1.09), PSA elevation to >4 ng/mL or PSA increase >1.5 ng/mL during treatment (OR=1.19), any increase in International Prostate Symptom Score (OR=1.08), or acute urinary retention (OR=0.99).

18. **Patients with testosterone deficiency and a history of prostate cancer should be informed that there is inadequate evidence to quantify the risk-benefit ratio of testosterone therapy. (Expert Opinion)**

It is the opinion of this Panel that the decision to commence testosterone therapy in men with in-situ prostate cancer on active surveillance or previously treated prostate cancer is a negotiated decision based on the perceived potential benefit of treatment weighed against the limited knowledge of potential risks. Testosterone therapy in men with locally advanced or metastatic disease remains poorly understood and administration of testosterone in these scenarios should ideally be performed under research settings.

Post-Radical Prostatectomy. Testosterone therapy can be considered in men who have undergone radical prostatectomy with favorable pathology (e.g., negative margins, negative seminal vesicles, negative lymph nodes), and who have undetectable PSA postoperatively. Limited data have demonstrated no significant increases in prostate cancer recurrence in men treated with testosterone compared to controls, although an increase in PSA among men in high-risk groups receiving testosterone has been shown, highlighting the need for appropriate patient selection.[36] It should be noted that currently available studies are underpowered and of too short of a duration to be able to detect any effects attributable to testosterone therapy.

Radiation Therapy. Available studies evaluating the safety of testosterone therapy in men treated with RT have suggested that after RT patients (with or without a history of androgen deprivation therapy) do not experience recurrence or progression of prostate cancer and experienced either a steady decline in PSA values to <0.1 ng/mL or had non-significant changes in PSA.[37]

Active Surveillance. There are limited data on men on active surveillance who are candidates for testosterone therapy. Available literature indicate that patients with and without high-grade prostatic intraepithelial neoplasias who were on testosterone therapy did not experience significant increases in PSA or subsequent cancer diagnosis compared to men not receiving testosterone.[38]

PSA Monitoring. Prostate cancer patients on testosterone therapy should have their PSA levels monitored on the same schedule as men without testosterone deficiency; however, clinicians may choose to increase the frequency of testing. PSA recurrence in men on testosterone therapy should be evaluated in the same fashion as untreated men. A discussion regarding the benefit of stopping testosterone therapy should include the possibility of a decline in PSA.

19. **Patients should be informed that there is no definitive evidence linking testosterone therapy to a higher incidence of venous thromboembolic events. (Moderate Recommendation; Evidence Level: Grade C)**

The literature examining the relationship between testosterone therapy and increased incidence of venous thromboembolic events has returned conflicting results. The concern about the possible association between testosterone therapy and VTE led the FDA to require pharmaceutical companies to add a warning to their product labeling regarding post-marketing reports of VTE; however, this decision was based on anecdotal cases and not peer-reviewed literature. Since the FDA warning in June 2014, observational studies have not shown an association between testosterone therapy and an increased risk of VTE.[39]

20. **Prior to initiating treatment, clinicians should counsel patients that, at this time, it cannot be stated definitively whether testosterone therapy increases or decreases the risk of cardiovascular events (e.g., myocardial infarction, stroke, cardiovascular-related death, all-cause mortality). (Moderate Recommendation; Evidence Level: Grade B)**

Current evidence consistently shows that untreated low testosterone levels are associated with an increased risk of MACE; however, studies that measure cardiovascular benefit or harm in men on testosterone therapy have returned inconsistent and controversial results.[23,40,41] Until there is definitive evidence proving an association between testosterone therapy and subsequent MACE, the Panel recommends that clinicians counsel patients that the current scientific literature does not definitively demonstrate that testosterone therapy increases the risk of MACE. Men who are on testosterone therapy should be advised to report the occurrence of any possible cardiovascular symptoms, such as chest pain, shortness of breath, dizziness, or transient loss of consciousness, during routine follow-up visits.

21. **All men with testosterone deficiency should be counseled regarding lifestyle modifications as a treatment strategy. (Conditional Recommendation; Evidence Level: Grade B)**

Men with testosterone deficiency should be counseled that lifestyle modifications, such as losing weight, or maintaining weight within the recommended range, along with increasing physical activity, has the potential to increase total testosterone levels and/or reduce signs and symptoms associated with testosterone deficiency.[42] High body mass index coupled with low testosterone could put the patient at risk for a cardiovascular event, and patients who are overweight or obese should be counseled regarding weight loss programs concurrent with testosterone therapy.

Treatment of Testosterone Deficiency

22. **Clinicians should adjust testosterone therapy dosing to achieve a total testosterone level in the middle tertile of the normal reference range. (Conditional Recommendation; Evidence Level: Grade C)**

The goal of testosterone therapy is the normalization of total testosterone levels combined with improvement in symptoms or signs.[5,43] The Panel recommends that testosterone treatment programs use the minimal dosing necessary to drive testosterone levels to the normal physiologic range of 450-600 ng/dL. In the event that patients do not experience symptomatic relief after reaching the specified target testosterone levels or remain testosterone deficient in the setting of symptom/sign improvement, testosterone therapy should be stopped.

23. **Exogenous testosterone therapy should not be prescribed to men who are currently trying to conceive. (Strong Recommendation; Evidence Level: Grade A)**

Exogenous testosterone therapy has been shown to interrupt normal spermatogenesis and can put patients in severely oligospermic or azoospermic states and should not be used in men trying to conceive. A systematic review of 33 RCTs suggested that although higher doses of testosterone were more likely to result in azoospermia than lower doses, a dose-response effect was not consistently seen.[44]

24. **Testosterone therapy should not be commenced for a period of three to six months in patients with a history of cardiovascular events. (Expert Opinion)**

The currently available literature does not provide enough evidence to offer clear guidance on the use of testosterone therapy in men with existing, stable ASCVD and/or a remote history of a myocardial infarction, or a cerebrovascular accident. It is the opinion of the Panel that testosterone therapy with close monitoring to ensure appropriate dosing and safety surveillance may be considered in these patients after a three to six month waiting period from most recent cardiac event.

25. **Clinicians should not prescribe alkylated oral testosterone. (Moderate Recommendation; Evidence Level: Grade B)**

Given the availability of other approved testosterone therapies, the use of 17-alpha-akylated androgens is not appropriate. Methyl testosterone is approved in the United States for treatment of testosterone deficiency. However, its use is associated with liver toxicity, including abnormal liver function tests, cholestasis, and jaundice.[45]

26. **Clinicians should discuss the risk of transference with patients using testosterone gels/creams. (Strong Recommendation; Evidence Level: Grade A)**

Topical testosterone preparations (e.g., gels, creams, liquids) have the potential to result in

transference to others. Women and children are at the highest risk for adverse events, such as virilization, precocious puberty, and hyperandrogenism. To address the issue, the FDA includes medication guides with topical testosterone preparations and recommends observing for signs and symptoms of early puberty in children as well as avoiding contact with the unwashed or uncovered areas where the drug has been applied.[46]

27. **Clinicians may use aromatase inhibitors, human chorionic gonadotropin, selective estrogen receptor modulators, or a combination thereof in men with testosterone deficiency desiring to maintain fertility. (Conditional Recommendation; Evidence Level: Grade C)**

Exogenous testosterone has inhibitory effects on the production of intratesticular testosterone, which is imperative to maintain normal spermatogenesis. For this reason, alternative therapies, including select estrogen receptor modulators,[47] human chorionic gonadotropin,[48] and aromatase inhibitors[49] are commonly used to promote the endogenous production of testosterone. While these agents share the common overall treatment effect of increasing intrinsic production of testosterone, there are substantial differences in pharmacologic characteristics and mechanisms of action between them. Clinicians should understand that of these agents, only hCG has been approved by the FDA for use in males.

28. **Commercially manufactured testosterone products should be prescribed rather than compounded testosterone, when possible. (Conditional Recommendation; Evidence Level: Grade C)**

While testosterone gels and creams are the most commonly used forms of compounded testosterone therapies and are routinely less expensive than branded forms of testosterone, individual pharmacies operate without direct FDA oversight and approval, resulting in considerable variation in potency and quality, even between samples from the same pharmacy. Clinicians issuing prescriptions for compounded testosterone need to consider performing additional monitoring and dose adjustments to assure appropriate therapeutic levels if compounded preparations are prescribed.[50]

Follow-up of Men on Testosterone Therapy

29. **Clinicians should measure an initial follow-up total testosterone level after an appropriate interval to ensure that target testosterone levels have been achieved. (Expert Opinion)**

30. **Testosterone levels should be measured every 6-12 months while on testosterone therapy. (Expert Opinion)**

31. **Clinicians should discuss the cessation of testosterone therapy three to six months after commencement of treatment in patients who experience normalization of total testosterone levels but fail to achieve symptom or sign improvement. (Clinical Principle)**

It is the opinion of this Panel that total testosterone should be tested after the commencement of therapy at a time point that allows a patient to be sufficiently established on a dosing regimen before determining if therapeutic levels have been achieved and if dosing alterations are required (fig. 2).

Patients on topical gels, patches, and intranasal formulations should have their testosterone checked between two to four weeks after commencement of therapy. The therapy should be applied on the day when testing is to be obtained. Patients using anastrozole, clomiphene citrate, or hCG should be tested no earlier than four weeks.

The Panel recommends that patients on short-acting intramuscular or subcutaneous testosterone (testosterone cypionate or enanthate) have their testosterone measured no earlier than three to four cycles.

Patients who are on long-acting intramuscular testosterone (testosterone undecanoate) should have blood work tested halfway between the first two 10-week injections.

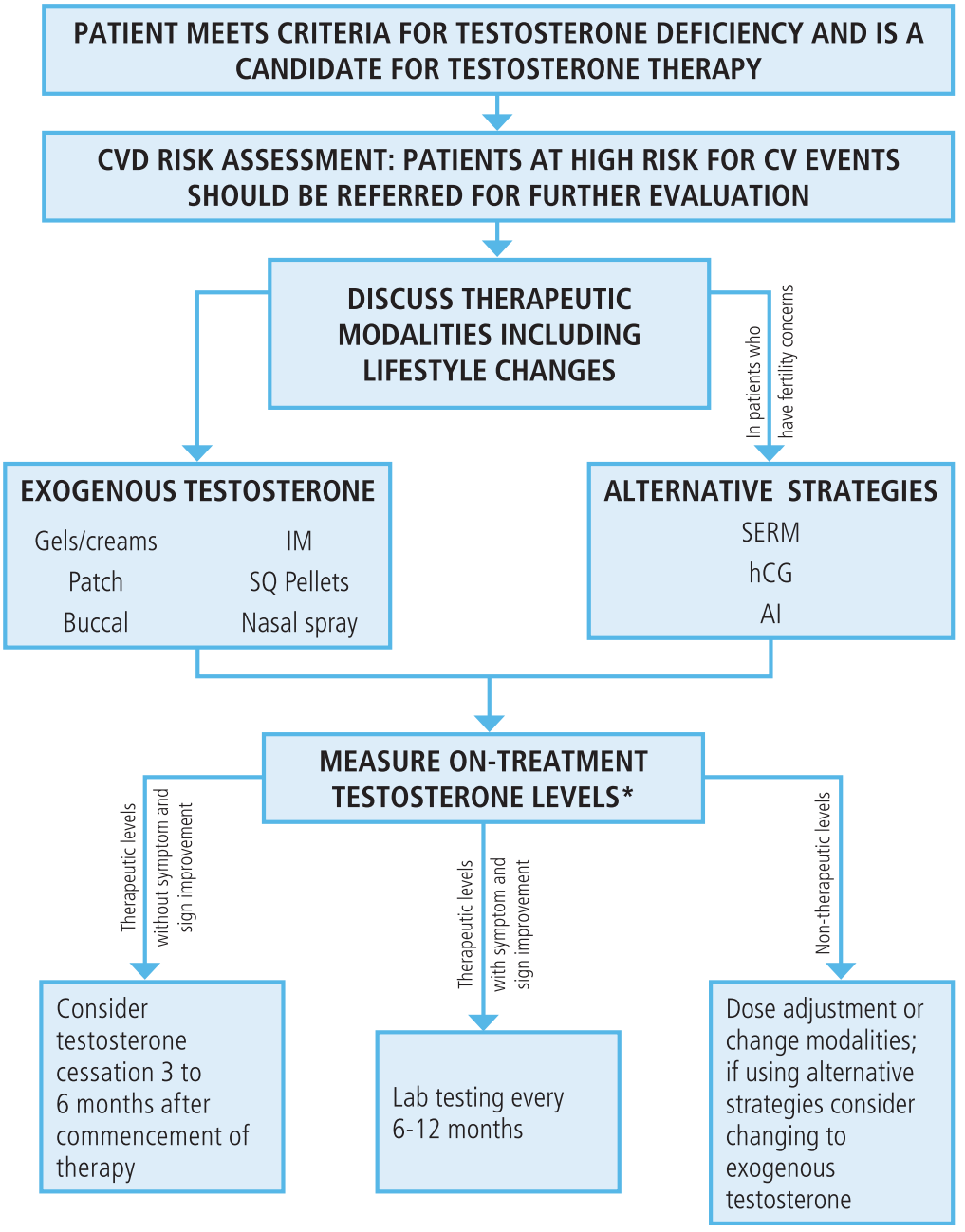
Patients who are on long-acting subcutaneous pellets require two separate testosterone assessments. The first testosterone measurement should be obtained two to four weeks after initial implant to determine if the number of inserted pellets needs to be increased or decreased to achieve the appropriate therapeutic level. Patients should then be tested after 10-12 weeks to determine when the next administration should occur.

After therapeutic levels have been achieved, all patients on testosterone therapy should have serum testosterone levels checked every 6-12 months to ensure maintenance of target levels.

Please refer to table 7 in the supplementary abridged guideline (http://jurology.com/) for a summary of follow-up testing for men being treated for testosterone deficiency. Testing intervals are the expert opinion of the Panel based on pharmacokinetic dosing principle of measuring steady state and with the intent of achieving therapeutic levels between 450-600 ng/dL. These are provided to guide clinicians in the follow-up of such patients. In cases where measurement falls outside of the recommended range, dose and/or frequency of administration may be adjusted accordingly.

If patients achieve target testosterone levels, but do not feel that they have sufficient improvement in their symptoms, clinicians should question whether testosterone deficiency is the etiology of their symptoms/signs. There is no utility in continuing testosterone therapy in men who achieve target

EVALUATION AND MANAGEMENT OF TESTOSTERONE DEFICIENCY: TREATMENT ALGORITHM



*Testosterone levels should be driven to the normal physiological range of 450-600 ng/dL (approximately equivalent to the middle tertile of the normal range).

AI = Aromatase Inhibitor
CVD = Cardiovascular Disease
hCG = Human Chorionic Gonadotropin
IM = Intramuscular Testosterone Injection
SERM = Selective Estrogen Receptor Modulator
SQ = Subcutaneous

Figure 2. Treatment algorithm

testosterone levels without symptom/sign improvement.

DISCLAIMER

This document was written by the Evaluation and Management of Testosterone Deficiency Guideline Panel of the American Urological Association Education and Research, Inc., which was created in 2016. The Practice Guidelines Committee (PGC) of the AUA selected the committee chair. Panel members were selected by the chair. Membership of the Panel included specialists in urology, cardiology, family medicine, and psychology with specific expertise on this disorder. The mission of the Panel was to develop recommendations that are analysis-based or consensus-based, depending on Panel processes and available data, for optimal clinical practices in the treatment of muscle-invasive bladder cancer.

Funding of the Panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the Panel provides an ongoing conflict of interest disclosure to the AUA.

While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ('off label') that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not intended to provide legal advice about use and misuse of these substances.

Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.

For this reason, the AUA does not regard technologies or management which are too new to be addressed by this guideline as necessarily experimental or investigational.

CONFLICT OF INTEREST (COI) DISCLOSURES

All panel members completed COI disclosures. Disclosures listed include topic and non-topic related relationships. Any author not listed had nothing to disclose.

Consultant/Advisor: John P. Mulhall, Pfizer, Lilly; Leadership Position: Robert E. Brannigan, The American Society for Reproductive Medicine; John P. Mulhall, Association of Peyronie's Disease Advocates; Scientific Study or Trial: Kelly A. Chiles, Pfizer; Christian J. Nelson, National Institutes of Health; Other: Robert E. Brannigan, National Institutes of Health.

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