ratio in testosterone by the use of isotope ratio combustion mass spectrometry. Exogenous testosterone administration increases urinary testosterone glucuronide excretion and, consequently, the testosterone-to-epitestosterone ratio. Ratios above 4 suggest exogenous testosterone use but can also reflect genetic variation. Genetic variations in the uridine diphosphoglucuronyl transferase 2B17 (*UGT2B17*), the major enzyme for testosterone glucuronidation, affect the testosterone-to-epitestosterone ratio. Synthetic testosterone has a lower ^{13}C:^{12}C ratio than endogenously produced testosterone, and these differences can be detected by isotope ratio combustion mass spectrometry.

TREATMENT COMPLICATIONS ASSOCIATED WITH AAS USE

The nonathlete weightlifters who abuse AAS rarely seek medical treatment and do not typically view these drugs and the associated lifestyle as deleterious to their health. In turn, many internists erroneously view AAS abuse as largely a problem of cheating in competitive sports, whereas, in fact, most AAS users are not athletes. Also, physicians often have a poor understanding of the factors motivating the use of these performance-enhancing drugs, the long-term health effects of AAS, and the associated psychopathologies that may affect treatment choices.

In addition to treating the underlying body dysmorphia disorder that motivates the use of these drugs, the treatment should be directed at the symptoms or the condition for which the patient seeks therapy, such as infertility, sexual dysfunction, gynecomastia, or depressive symptoms. Accordingly, therapy may include some combination of cognitive and behavioral therapy for the muscle dysmorphia syndrome, antidepressant therapy for depression, selective phosphodiesterase-5 inhibitors for erectile dysfunction, selective estrogen receptor modulators or aromatase inhibitors to reactivate the hypothalamic-pituitary-testicular axis, or hCG to restore testosterone levels. Clomiphene citrate, a partial estrogen receptor agonist, administered in a dose of 25–50 mg on alternate days, can increase LH and FSH levels and restore testosterone levels in a vast majority of men with AAS withdrawal syndrome. However, the recovery of sexual function during clomiphene administration is variable despite improvements in testosterone levels. Anecdotally, other aromatase inhibitors, such as anastrozole, have also been used. hCG, administered by intramuscular injections of 750–1500 IU three times each week, can raise testosterone levels into the normal range. Some patients may not respond to either clomiphene or hCG therapy, raising the possibility of irreversible long-term toxic effects of AAS on Leydig cell function.

MALE LOWER URINARY TRACT SYMPTOMS

Lower urinary tract symptoms (LUTS) in men include storage symptoms (urgency, daytime and nighttime frequency, and urgency incontinence), voiding disturbances (slow or intermittent stream, difficulty in initiating micturition, straining to void, pain or discomfort during the passage of urine, and terminal dribbling), or postmicturition symptoms (a sense of incomplete voiding after passing urine and postmicturition dribble). The overactive bladder syndrome refers to urgency with or without urgency incontinence, usually with urinary frequency and nocturia, and is often due to detrusor muscle overactivity. LUTS have historically been attributed to benign prostatic hyperplasia, although it has become apparent that the pathophysiologic mechanisms of LUTS are complex and multifactorial and may include structural or functional abnormalities of the bladder, bladder neck, prostate, distal sphincter mechanism, and urethra, as well as abnormalities in the neural control to the lower urinary tract. A presumptive diagnosis of benign prostatic hyperplasia should be made only in men with LUTS who have demonstrable evidence of prostate enlargement and obstruction based on the size of the prostate. Diuretics, antihistamines, antidepressants, and other medications that have anticholinergic properties can cause or exacerbate LUTS in older men. The intensity of LUTS symptoms tends to fluctuate over time.

LUTS is highly prevalent in older men, affecting nearly 50% of men over the age of 65 and 70% of men over the age of 80. LUTS adversely affects quality of life because of its impact on sleep, ability to perform activities of daily living, and depressive symptoms. LUTS is often associated with erectile dysfunction.

APPROACH TO THE PATIENT: LUTS

Medical evaluation should include assessment of the symptom severity using the International Prostate Symptom Score and, in some patients, a frequency-volume chart. The impact of LUTS on sleep and activities of daily living and quality of life should be evaluated. Evaluation should also include verification of medications that may contribute to LUTS, digital prostate examination, neurologic examination focused on perineum and lower extremities, urinalysis, fasting blood glucose, electrolytes, creatinine, and prostate-specific antigen (PSA). Urodynamic studies are not required in most patients but are recommended when invasive surgical therapies are being considered.

TREATMENT LUTS

Men who have mild symptoms can be reassured and followed. Men with mild to moderate LUTS can be treated effectively using α-adrenergic antagonists, phosphodiesterase-5 (PDE5) inhibitors, steroid 5α-reductase inhibitors, or anticholinergic agents alone or in combination. Selective α-adrenergic antagonists are typically the first line of therapy. In men with probable benign prostate obstruction with gland enlargement and LUTS, therapy using a steroid 5α-reductase inhibitor, such as finasteride or dutasteride, for 1 or more years improves urinary symptoms and flow rate and reduces prostatic volume. Long-term treatment with 5α-reductase inhibitors can reduce progression to acute urinary retention and need for prostate surgery. Combined administration of a steroid 5α-reductase inhibitor and α_1-adrenergic blocker can rapidly improve urinary symptoms and reduce the relative risk of acute urinary retention and surgery. PDE5 inhibitors, when administered chronically alone or in combination with α-adrenergic blockers, are effective in improving LUTS and erectile dysfunction through their effects on nitric oxide–cyclic guanosine monophosphate (cGMP) in the bladder, urethra, and prostate. PDE5 inhibitors do not improve urinary flow parameters. Anticholinergic drugs are used for the treatment of overactive bladder in men with prominent urgency symptoms and no evidence of elevated postvoid residual urine. Surgery is indicated when medical therapy fails or if symptoms progress despite medical therapy.

MEDICAL COMPLICATIONS OF PROSTATE CANCER THERAPY

Prostate cancer is the most common malignancy in American men, accounting for 29% of all diagnosed cancers and approximately 13% of all cancer deaths; its incidence is on the rise, partly due to increased screening with PSA. In 2013, approximately 233,000 new cases of prostate cancer were diagnosed in the United States and there were 29,480 deaths related to prostate cancer. The majority of these men have low-grade, organ-confined prostate cancer and excellent prospects of long-term survival. Substantial improvement in survival in men with prostate cancer has focused attention on the high prevalence of sexual dysfunction, physical dysfunction, and low vitality, which are important contributors to poor quality of life among patients treated for prostate cancer. The pathophysiology of these symptoms after radical prostatectomy is multifactorial, but denervation and androgen deficiency are important contributors to these symptoms.

Androgen deficiency is common in men with prostate cancer. Testosterone levels decline with age, and men with prostate cancer are at risk of having low testosterone levels simply by virtue of their age.