TABLE 7e-2 POTENTIAL ADVERSE EFFECTS ASSOCIATED WITH THE USE OF ANABOLIC-ANDROGENIC STEROIDS (AAS)

Organ System Effect	
Cardiovascular	Dyslipidemia
	Atherosclerotic disease
	Sudden death
	Myocardial fibrosis, cardiomyopathy
	Cardiac conduction abnormalities
	Hypertension
Neuroendocrine	HPT axis suppression
	Hypogonadism after AAS withdrawal
	Gynecomastia
Females	Virilizing effects
Neuropsychiatric	Major mood disorders (mania, hypomania, depression)
	Aggression, violence
	AAS dependence
	Neuronal apoptosis
	Cognitive deficits
Hematologic	Polycythemia
	Hypercoagulability and thrombosis
Hepatic	Inflammatory and cholestatic effects
	Peliosis hepatis (rare)
	Neoplasms (rare)
Musculoskeletal	Premature epiphyseal closure (in adolescents)
	Tendon rupture
Kidney	Renal failure secondary to rhabdomyolysis
	Focal segmental glomerulosclerosis
Dermatologic	Acne
	Striae

Abbreviation: HPT axis, hypothalamic-pituitary-testicular axis.

Source: Modified with permission from HG Pope Jr et al: Adverse health consequences of performance-enhancing drugs: an endocrine society scientific statement. *Endocr Rev* 35:341, 2014.

more likely to engage in other high-risk behaviors than nonusers. The adverse events associated with AAS use may be due to AAS themselves, concomitant use of other drugs, high-risk behaviors, and host characteristics that may render these individuals more susceptible to AAS use or to other high-risk behaviors.

The high rates of mortality and morbidities observed in AAS users are alarming. The risk of death among elite powerlifters has been reported to be fivefold greater than in age-matched men from the general population. The causes of death among powerlifters included suicides, myocardial infarction, hepatic coma, and non-Hodgkin's lymphoma.

Numerous reports of cardiac death among young AAS users raise concerns about the adverse cardiovascular effects of AAS. High doses of AAS may induce proatherogenic dyslipidemia, increase thrombosis risk via effects on clotting factors and platelets, induce vasospasm through their effects on vascular nitric oxide, and induce myocardial hypertrophy and fibrosis.

Replacement doses of testosterone, when administered parenterally, are associated with only a small decrease in high-density lipoprotein (HDL) cholesterol and little or no effect on total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels. In contrast, supraphysiologic doses of testosterone and orally administered, 17-α-alkylated, nonaromatizable AAS are associated with marked reductions in HDL cholesterol and increases in LDL cholesterol.

Long-term AAS use may be associated with myocardial hypertrophy and fibrosis as well as shortening of QT intervals. AAS use suppresses LH and FSH secretion and inhibits endogenous testosterone production and spermatogenesis. Consequently, stopping AAS may be associated with sexual dysfunction, fatigue, infertility, and depressive symptoms. In some AAS users, hypothalamic-pituitary-testicular axis suppression may last more than a year, and in a few individuals, complete recovery may not occur. The symptoms of androgen deficiency during AAS withdrawal may cause some men to revert back to using AAS, leading to continued use and AAS dependence. As many as 30% of AAS users develop a syndrome of AAS dependence, characterized by long-term AAS use, despite adverse medical and psychiatric effects. Supraphysiologic doses of testosterone may also impair insulin sensitivity, predisposing to diabetes. Elevated liver enzymes, cholestatic jaundice, hepatic neoplasms, and peliosis hepatis have been reported with oral 17-α-alkylated AAS. AAS use may cause muscle hypertrophy without compensatory adaptations in tendons, ligaments, and joints, thus increasing the risk of tendon and joint injuries. AAS use is associated with acne, baldness, and increased body hair.

Unsafe injection practices, high-risk behaviors, and increased rates of incarceration render AAS users at increased risk of HIV and hepatitis B and C. In one survey, nearly 1 in 10 gay men had injected AAS or other substances, and AAS users were more likely to report high-risk unprotected anal sex than other men.

Some AAS users develop hypomanic and manic symptoms during AAS exposure (irritability, aggressiveness, reckless behavior, and occasional psychotic symptoms, sometimes associated with violence) and major depression (sometimes associated with suicidality) during AAS withdrawal. Users may also develop other forms of illicit drug use, which may be potentiated or exacerbated by AAS.

APPROACH TO THE PATIENT: AAS Use

AAS users generally mistrust physicians and seek medical help infrequently; when they do seek medical help, it is often for the treatment of AAS withdrawal syndrome, infertility, gynecomastia, or other medical or psychiatric complications of AAS use. The suspicion of AAS use should be raised by increased hemoglobin and hematocrit levels; suppressed luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone levels; low HDL cholesterol; and low testicular volume and sperm density in a person who looks highly muscular (Table 7e-3). A combination of these findings and a self-report of AAS use by the patient, which usually can be elicited by a tactful interview, are often sufficient to establish a diagnosis in clinical practice.

Accredited laboratories use gas chromatography and mass spectrometry or liquid chromatography and mass spectrometry to detect AAS abuse. In recent years, the availability of high-resolution mass spectrometry and tandem mass spectrometry has further improved the sensitivity of detecting AAS abuse. Illicit testosterone use is most often detected by the urinary testosterone-to-epitestosterone ratio and further confirmed by the use of the ^{13}C:^{12}C

TABLE 7e-3 DETECTION OF THE USE OF ANABOLIC-ANDROGENIC STEROIDS

Clinical indicators that should raise suspicion of anabolic-androgenic steroid use
Very muscular phenotype
Reduced testicular volume (<15 mL)
Laboratory indicators
Suppressed LH and FSH levels
Increased hematocrit
Detection of anabolic-androgenic steroids
LC-MS/MS analysis of urine
Detection of exogenous testosterone use
Urinary testosterone-to-epitestosterone ratio
Isotope ratio mass spectrometry analysis to detect differences in ^{13}C:^{12}C ratio in exogenous and endogenous testosterone

Abbreviations: FSH, follicle-stimulating hormone; LC-MS/MS, liquid chromatography and tandem mass spectrometry; LH, luteinizing hormone.