11 - 20.11 Anabolic Androgenic Steroid Abuse

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nicotine effects on the fMRI BOLD response are related to nicotine effects on behavioral performance. Psychopharmacology. 2011;215:333. Weinberger AH, Desai RA, McKee SA. Nicotine withdrawal in U.S. smokers with current mood, anxiety, alcohol use, and substance use disorders. Drug Alcohol Depend. 2010;108:7. Weinberger AH, Sofuoglu M. The impact of cigarette smoking on stimulant addiction. Am J Drug Abuse. 2009;35:12. 20.11 Anabolic-Androgenic Steroid Abuse The anabolic-androgenic steroids (AAS) are a family of hormones that includes testosterone, the natural male hormone, which together with numerous synthetic analogs of testosterone have been developed over the last 70 years (Table 20.11-1). These drugs exhibit various degrees of anabolic (muscle building) and androgenic (masculinizing) effects; none of these drugs display purely anabolic effects in the absence of androgenic effects. It is important not to confuse the anabolic-androgenic steroids (AAS) (testosterone-like hormones) with corticosteroids (cortisol-like hormones such as hydrocortisone and prednisone). Corticosteroids are hormones secreted by the adrenal gland, rather than by the testes. Corticosteroids have no muscle-building properties and, hence, little abuse potential; they are widely prescribed to treat numerous inflammatory conditions such as poison ivy or asthma. AAS, by contrast, have only limited legitimate medical applications, such as in the treatment of hypogonadal men, the wasting syndrome associated with human immunodeficiency virus (HIV) infection, and a few specific diseases such as hereditary angioedema and Fanconi’s anemia. AAS, however, are widely used illicitly, especially by boys and young men seeking to gain increased muscle mass and strength, either for athletic purposes or simply to improve personal appearance. Table 20.11-1 Examples of Commonly Used Anabolic Steroids

AAS does not have its own diagnostic category in the fifth edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-5); rather it is coded as one of the other or unknown substance related disorders. EPIDEMIOLOGY Use of AAS is widespread among men in the United States, but are much less frequently used by women. Approximately 890,000 American men and approximately 190,000 American women reported having used AAS at some time during their lives. Approximately 286,000 men and 26,000 women are estimated to use steroids each year. Among this number, nearly one third, or 98,000, were between 12 and 17 years

of age. Various studies of high school students in the United States have produced even higher estimates of the prevalence of anabolic steroid use among adolescents. Across studies of high school students, it is estimated that 3 to 12 percent of males and 0.5 to 2.0 percent of females have used AAS during their lifetimes. The current high rates of steroid use among younger individuals appear to represent an important shift in the epidemiology of steroid use. In the 1970s, use of these drugs was largely confined to competition bodybuilders, other elite weight-training athletes, and elite athletes in other sports. Since then, however, it appears that an increasing number of young men, and occasionally even young women, may be using these drugs purely to enhance personal appearance rather than for any athletic purpose. PHARMACOLOGY All steroid drugs—including AAS, estrogens, and corticosteroids—are synthesized in vivo

from cholesterol and resemble cholesterol in their chemical structure. Testosterone has a four-ring chemical structure containing 19 carbon atoms (Fig. 20.11-1). FIGURE 20.11-1 Molecular structure of testosterone. Normal testosterone plasma concentrations for men range from 300 to 1,000 ng/dL. Generally, 200 mg of testosterone cypionate taken every 2 weeks restores physiological testosterone concentrations in a hypogonadal male. A eugonadal male who initiates physiological dosages of testosterone has no net gain in testosterone concentrations because exogenously administered AAS shut down endogenous testosterone production via feedback inhibition of the hypothalamic-pituitary-gonadal axis. Consequently, illicit users take higher than therapeutic dosages to achieve supraphysiological effects. The dose–response curve for anabolic effects may be logarithmic, which could explain why illicit users generally take 10 to 100 times the therapeutic dosages. Doses in this range are most easily achieved by taking combinations of oral and injected AAS, which illicit AAS users often do. Transdermal testosterone, available by prescription for testosterone replacement therapy, may also be used. Therapeutic Indications The AAS are indicated primarily for testosterone deficiency (male hypogonadism), hereditary angioedema (a congenital skin disorder), and some uncommon forms of anemia caused by bone marrow or renal failure. In women, AAS are given, although not as first-choice agents, for metastatic breast cancer, osteoporosis, endometriosis, and adjunctive treatment of menopausal symptoms. In men, they have been used experimentally as a male contraceptive and for treating major depressive disorder and sexual disorders in eugonadal men. Recently, they have been used to treat wasting syndromes associated with acquired immunodeficiency syndrome (AIDS). Controlled studies have also suggested that testosterone has antidepressant effects in some men infected with HIV with major depressive disorder, and is also a supplementary (augmentation) treatment in some depressed men with low endogenous testosterone levels who are refractory to conventional antidepressants.

Adverse Reactions The most common adverse medical effects of AAS involve the cardiovascular, hepatic, reproductive, and dermatological systems. The AAS produce an adverse cholesterol profile by increasing levels of low-density lipoprotein cholesterol and decreasing levels of high-density lipoprotein cholesterol. High-dose use of AAS can also activate hemostasis and increase blood pressure. Isolated case reports of myocardial infarction, cardiomyopathy, left ventricular hypertrophy, and stroke among users of AAS, including fatalities, have appeared, Among the AAS-induced endocrine effects in men are testicular atrophy and sterility, both usually reversible after discontinuing AAS, and gynecomastia, which may persist until surgical removal. In women, shrinkage of breast tissue, irregular menses (diminution or cessation), and masculinization (clitoral hypertrophy, hirsutism, and deepened voice) can occur. Masculinizing effects in women may be irreversible. Androgens taken during pregnancy could cause masculinization of a female fetus.

Dermatological effects include acne and male pattern baldness. Abuse of AAS by children has led to concerns that AAS-induced premature closure of bony epiphyses could cause shortened stature. Other uncommon adverse effects include edema of the extremities caused by water retention, exacerbation of tic disorders, sleep apnea, and polycythemia. ETIOLOGY The major reason for taking illicit AAS is to enhance either athletic performance or physical appearance. Taking AAS is reinforced because they can produce the athletic and physical effects that users desire, especially when combined with proper diet and training. Further reinforcement derives from winning competitions and from social admiration for physical appearance. AAS users also perceive that they can train more intensively for longer durations with less fatigue and with decreased recovery times between workouts. The dramatic effects of AAS on muscle growth are illustrated in Figure 20.11-2, which compares a “natural” bodybuilder who has never used these drugs with a bodybuilder of identical height and body fat who has used AAS extensively.

FIGURE 20.11-2 Physical effects of anabolic steroid use. The photographs compare a “natural” bodybuilder who has never used anabolic steroids (left) with a man who has used large doses of anabolic steroids over several years (right). Both men are 67 inches tall and have 7 percent body fat. The man on the left weighs 170 lbs and represents approximately the maximum degree of muscularity obtainable without drugs. His fatfree mass index is 25.4 kg/m2 by the formula of Elana Kouri, et al. The man on the right weighs 213 lbs and has a fat-free mass index of 31.7 kg/m2. Note the muscle hypertrophy from steroid use is particularly marked in the upper body in the pectoralis, deltoid, trapezius, and biceps muscles. Any man significantly more muscular than the man on the left has almost certainly abused anabolic steroids. (Courtesy of H.G. Pope M.D.) Although the anabolic or muscle-building properties of AAS are clearly important to those seeking to enhance athletic performance and physical appearance, psychoactive effects may also be important in the persistent and dependent use of AAS. Anecdotally, some AAS users report feelings of power, aggressiveness, and euphoria, which become associated with, and can reinforce, AAS taking. In general, males are more likely to take AAS than females, and athletes are more likely to take AAS than nonathletes. Some male and female weight lifters may have muscle dysmorphia, a form of body dysmorphic disorder in which the individual feels that he or she is not sufficiently muscular and lean. DIAGNOSIS AND CLINICAL FEATURES Steroids may initially induce euphoria and hyperactivity. After relatively short periods, however, their use can become associated with increased anger, arousal, irritability, hostility, anxiety, somatization, and depression (especially during times when steroids

are not used). Several studies have demonstrated that 2 to 15 percent of anabolic steroid abusers experience hypomanic or manic episodes, and a smaller percentage may have clearly psychotic symptoms. Also disturbing is a correlation between steroid abuse and violence (“roid rage” in the parlance of users). Steroid abusers with no record of antisocial behavior or violence have committed murders and other violent crimes. Steroids are addictive substances. When abusers stop taking steroids, they can become depressed, anxious, and concerned about the physical state of their bodies. Some similarities have been noted between athletes’ views of their muscles and the views of patients with anorexia nervosa about their bodies; to an observer, both groups seem to distort realistic assessment of the body. Iatrogenic addiction is a consideration in view of the increasing number of geriatric patients who are receiving testosterone from their physicians in an attempt to increase libido and reverse some aspects of aging. Mr. A is a 26-year-old single man. He is 69 inches tall and presently weighs 204 pounds, with a body fat of 11 percent. He reports that he

began lifting weights at age 17, at which time he weighed 155 pounds. About 2 years after beginning his weight lifting, he began taking AAS, which he obtained through a friend at his gymnasium. His first “cycle” (course) of AAS, lasting for 9 weeks, involved methandienone (Methanabol), 30 mg a day, orally, and testosterone cypionate, 600 mg a week, intramuscularly. During these 9 weeks he gained 20 pounds of muscle mass. He was so pleased with these results that he took five further cycles of AAS over the course of the next 6 years. During his most ambitious cycle, approximately 1 year ago, he used testosterone cypionate, 600 mg per week; nandrolone decanoate, 400 mg a week; stanozolol (Winstrol), 12 mg a day; and oxandrolone (Anavar), 10 mg a day. During each of the cycles Mr. A has noted euphoria, irritability, and grandiose feelings. These symptoms were most prominent during his most recent cycle, when he felt “invincible.” During this cycle he also noted a decreased need for sleep, racing thoughts, and a tendency to spend excessive amounts of money. For example, he impulsively purchased a $2,700 stereo system when he realistically could not afford to spend more than $500. He also became uncharacteristically irritable with his girlfriend, and on one occasion put his fist through the side window of her car during an argument, an act inconsistent with his normally mild-mannered personality. After this cycle of AAS ended, he became mildly depressed for about 2 months. Mr. A has used a number of drugs to lose weight in preparation for bodybuilding contests. These include ephedrine, amphetamine, triiodothyronine, and thyroxin. Recently, he has also begun to use the opioid agonist–antagonist nalbuphine intravenously (IV) to treat muscle aches from weight lifting. He also used oral opioids, such as controlled-release oxycodone (OxyContin), at least once a week. He uses oral opioids sometimes to treat muscle aches, but often simply to get high. He reports that use of nalbuphine and other opioids is widespread among other AAS users of his acquaintance.

Mr. A exhibits characteristic features of muscle dysmorphia. He checks his appearance dozens of times a day in mirrors, or when he sees his reflection in a store window or even in the back of a spoon. He becomes anxious if he misses even one day of working out at the gym, and acknowledges that his preoccupation with weight lifting has cost him both social and occupational opportunities. Although he has a 48inch chest and 19-inch biceps, he has frequently declined invitations to go to the beach or a swimming pool for fear that he would look too small when seen in a bathing suit. He is anxious because he has lost some weight since the end of his previous cycle of AAS and is eager to resume another cycle of AAS in the near future. (Adapted from Harrison G. Pope, Jr., M.D., and Kirk J. Brower, M.D.) TREATMENT Abstinence is the treatment goal of choice for patients manifesting AAS abuse or dependence. To the extent that users of AAS abuse other addictive substances (including alcohol), traditional treatment approaches for substance-related disorders may be used. Nevertheless, AAS users may differ from other addicted patients in several ways that have implications for treatment. First, the euphorigenic and reinforcing effects of AAS may only become apparent after weeks or months of use in conjunction with intensive exercising. When compared with immediately and passively reinforcing drugs, such as cocaine, heroin, and alcohol, AAS use may entail more delayed gratification. Second, AAS users may manifest greater commitment to culturally endorsed values of physical fitness, success, victory, and goal directness than users of other illicit drugs. Finally, AAS users are often preoccupied with their physical attributes and may rely excessively on these attributes for self-esteem. Treatment therefore depends on a therapeutic alliance that is based on a thorough and nonjudgmental understanding of the patient’s values and motivations for using AAS. AAS Withdrawal Supportive therapy and monitoring are essential for treating AAS withdrawal because suicidal depressions can occur. Hospitalization may be required when suicidal ideation is severe. Patients should be educated

about the possible course of withdrawal and reassured that symptoms are time-limited and manageable. Antidepressant agents are best reserved for patients whose depressive symptomatology persists for several weeks after AAS discontinuation and who meet criteria for major depressive disorder. Selective serotonin reuptake inhibitors (SSRIs) are the preferred agents because of their favorable adverse effect profile and their effectiveness in the only reported case series of treated AAS users with major depressive disorder. Physical withdrawal symptoms are not lifethreatening and do not ordinarily require pharmacotherapy. Nonsteroidal antiinflammatory drugs (NSAIDs) may be useful to treat musculoskeletal pain and headaches.

ANABOLIC STEROID–INDUCED MOOD DISORDERS Irritability, aggressiveness, hypomania, and frank mania associated with anabolic steroid use probably represent one of the most important public health issues associated with these drugs. Although athletes using these drugs have long recognized that syndromes of anger and irritability could be associated with AAS use, these syndromes were little recognized in the scientific literature until the late 1980s and 1990s. Since then, a series of observational field studies of athletes has suggested that some AAS users develop prominent hypomanic or even manic symptoms during AAS use. A possible serious consequence of AAS-induced mood disorders may be violent or even homicidal behavior. Several published reports have anecdotally described individuals with no apparent history of psychiatric disorder, no criminal record, and no history of violence, who committed violent crimes, including murder, while under the influence of AAS. In a number of cases, AAS use has been cited in criminal trials as a possible mitigating factor in the defense of such individuals. Although a causal link is difficult to establish in these cases, evidence of AAS use has frequently been presented in forensic settings as a possible mitigating factor in criminal behavior. Depressive syndromes induced by AAS have occurred and suicide is a risk. A brief and self-limited syndrome of depression occurs on AAS withdrawal, probably as a result of the depression of the hypothalamic-pituitary-gonadal axis after exogenous AAS administration. ANABOLIC STEROID–INDUCED PSYCHOTIC DISORDER Psychotic symptoms are rare in association with anabolic steroid use, but they have been described in a few cases, primarily in individuals who were using the equivalent of more than 1,000 mg of testosterone a week. Usually, these symptoms have consisted of grandiose or paranoid delusions, generally occurring in the context of a manic episode, although occasionally occurring in the absence of a frank manic syndrome. In most cases reported, psychotic symptoms have disappeared promptly (within a few weeks) after the discontinuation of the offending agent, although temporary treatment with antipsychotic agents was sometimes required. OTHER ANABOLIC STEROID–RELATED DISORDERS Symptoms of anxiety disorders, such as panic disorder and social phobia can occur during AAS use. AAS use may serve as a “gateway to the use of opioid agonist or antagonists, such as nalbuphine, or to use of frank opioid agonists, such as heroin.” A study of men admitted for substance dependence treatment in Massachusetts produced similar findings. DEHYDROEPIANDROSTERONE AND ANDROSTENEDIONE Dehydroepiandrosterone (DHEA), a precursor hormone for both estrogens and

androgens, is available over the counter. Recent years have seen an interest in DHEA for improving cognition, depression, sex drive, and general well-being in elderly adults. Some reports suggest that DHEA in dosages of 50 to 100 mg per day increases the sense of physical and social well-being in women aged 40 to 70 years. Reports also exist of androgenic effects, including irreversible hirsutism, hair loss, voice deepening, and other undesirable sequelae. In addition, DHEA has at least a theoretical potential of enhancing tumor growth in persons with latent, hormone-sensitive malignancies, such as prostate, cervical, and breast cancer. Despite its significant popularity, few

controlled data exist on the safety or efficacy of DHEA. REFERENCES Achar S, Rostamian A, Narayan SM. Cardiac and metabolic effects of anabolic-androgenic steroid abuse on lipids, blood pressure, left ventricular dimensions, and rhythm. Am J Cardiol. 2010;106(6):893. Baggish AL, Weiner RB, Kanayama G, Hudson JI, Picard MH, Hutter AM Jr., Pope HJ Jr.. Long-term anabolic-androgenic steroid use is associated with left ventricular dysfunction. Circulation Heart Fail. 2010;3:472. Basile JR, Binmadi NO, Zhou H, Yang Y-H, Paoli A, Proia P. Supraphysiological doses of performance enhancing anabolicandrogenic steroids exert direct toxic effects on neuron-like cells. Front Cell Neurosci. 2013;7:69. Caraci F, Pistarà V, Corsaro A, Tomasello F, Giuffrida ML, Sortino MA, Nicoletti F, Copani A. Neurotoxic properties of the anabolic androgenic steroids nandrolone and methandrostenolone in primary neuronal cultures. J Neurosci Res. 2011;89(4):592. Driscoll MD, Arora A, Brennan ML. Intramuscular anabolic steroid injection leading to life-threatening clostridial myonecrosis: A case report. J Bone Joint Surg. 2001;93:1. Herlitz LC, Markowitz GS, Farris AB, Schwimmer JA, Stokes MB, Kunis C, Colvin RB, D'Agati VD. Development of focal segmental glomerulosclerosis after anabolic steroid abuse. J Am Soc Nephrol. 2010;21:163. Kanayama G, Brower KJ, Wood RI, Hudson JI, Pope HG Jr.. Issues for DSM-V: Clarifying the diagnostic criteria for anabolic–androgenic steroid dependence. Am J Psychiatry. 2009;166:642. Kanayama G, Hudson JI, Pope HG. Demographic and psychiatric features of men with anabolic–androgenic steroid dependence: a comparative study. Drug Alcohol Depend. 2009;102:130. Kanayama G, Hudson JI, Pope HG Jr.. Illicit anabolic–androgenic steroid use. Horm Behav. 2010;58:111. Kanayama G, Hudson JI, Pope HG Jr.. Long-term psychiatric and medical consequences of anabolic–androgenic steroid abuse: a looming public health concern? Drug Alcohol Depend. 2008;98:1. Kanayama G, Kean J, Hudson JI, Pope HG, Jr. Cognitive deficits in long-term anabolic-androgenic steroid users. Drug Alcohol Depend. 2013;130(1–3):208–214. Larance B, Degenhardt L, Copeland J, Dillon P. Injecting risk behaviour and related harm among men who use performance- and image-enhancing drugs. Drug Alcohol Rev. 2008;27:679. Pope HG Jr, Brower KJ. Anabolic-androgenic steroid abuse. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Vol. 1. Philadelphia: Lippincott Williams & Wilkins; 2009:1419. Pope HG, Brower KJ. Treatment of anabolic–androgenic steroid-related disorders. In: Galanter M, Kleber H, eds. The American Psychiatric Publishing Textbook of Substance Abuse Treatment. 4th ed. Washington, DC: American Psychiatric Publishing; 2008:237. Pope HG Jr., Kanayama G, Hudson JI. Risk Factors for illicit anabolic-androgenic steroid use in male weightlifters: A crosssectional cohort study. Biol Psychiatry. 2012;71:254.

Revision #1
Created 2026-01-04 19:51:16 UTC by Omar Ayman
Updated 2026-01-04 19:51:16 UTC by Omar Ayman