The Health Threat Posed by the Hidden Epidemic of Anabolic Steroid Use and Body Image Disorders Among Young Men

Anna L. Goldman,[1,2] Harrison G. Pope, Jr.,[2,3] and Shalender Bhasin[1,2,4]

[1]Research Program in Men's Health: Aging and Metabolism, Brigham and Women's Hospital, Boston, Massachusetts 02115; [2]Harvard Medical School, Boston, Massachusetts 02115; [3]Biological Psychiatry Laboratory, McLean Hospital, Belmont, Massachusetts 02478; and [4]Boston Claude D. Pepper Older Americans Independence Center, Boston, Massachusetts 02115

ORCiD numbers: 0000-0002-3982-6200 (S. Bhasin); 0000-0003-4359-5131 (A. L. Goldman); 0000-0003-1298-6439 (H. G. Pope, Jr.).

Context: The prevalence of body image disorders and anabolic-androgenic steroid (AAS) use is increasing, despite the evidence of their serious adverse health effects and despite the passage of laws regulating their sales. Here we review the evolution of the dual emerging epidemics of body image disorders and AAS use, adverse health effects of AASs, and the need for an integrated health policy and regulatory response.

Evidence Acquisition: We searched for studies published prior to June 2018. Quality of evidence was low to moderate because of its observational nature; heterogeneity of eligibility criteria; variable doses; reliance on retrospective self-reported data in many studies; and variable quality of outcome ascertainment.

Evidence Synthesis: Most AAS users are nonathlete young men, who use these substances to look lean and more muscular. Some of these men suffer from "muscle dysmorphia," a form of body dysmorphic disorder. AASs has been associated with cardiovascular disorders, psychiatric disorders, AAS-withdrawal hypogonadism, infertility, neurotoxic effects, musculoskeletal injuries, liver toxicity, and needle-borne infections. Potential adverse effects may be compounded by the use of other substances (*e.g.,* opioids) and high-risk behaviors. Unregulated Internet sales of AASs and selective androgen receptor modulators, which are easily purchased without a prescription, are of concern because of their potential to fuel the epidemic among adolescents and the military.

Conclusions: Integrated nationwide efforts are necessary to raise public awareness of this epidemic, to study long-term health effects of AASs and treatment strategies, and to reform regulations to stem the epidemics of AAS use and body image disorders. (***J Clin Endocrinol Metab*** **104: 1069–1074, 2019)**

The anabolic-androgenic steroids (AASs) are a class of pharmacological substances, sharing a cyclopenta phenanthrene steroidal ring structure, that includes testosterone and many synthetic compounds structurally related to testosterone. The anabolic effects of AASs include promotion of nitrogen retention and muscle growth, whereas the androgenic effects include the development of male secondary sexual characteristics such as facial hair, deepening of the voice, and the growth and development of external genitalia. According to the Controlled Substances Act, a substance may be classified as an AAS if it is (1) chemically related to testosterone; (2) pharmacologically related to testosterone (*i.e.*, it produces biological effects similar to those of testosterone);

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Abbreviations: AAS, anabolic-androgenic steroid; HPT, hypothalamic-pituitary-testicular; SARM, selective androgen receptor modulator.

and (3) not an estrogen, progestin, or a corticosteroid (1). Another family of compounds with similar effects, the nonsteroidal selective androgen receptor modulators (SARMs), has entered development over the last two decades. SARMs are substances that bind to the androgen receptor and regulate the transcription of androgen-dependent genes in a tissue-specific manner (2, 3).

In the United States, several AASs have been approved for a limited number of medical indications, such as treatment of hypogonadism and some types of anemia (1). Nonsteroidal SARMs have not yet been approved for human use, but are being developed for their potential anabolic applications (2, 3). However, the legitimate medical use of these compounds is overshadowed by the emerging epidemics of AAS and SARM use among weightlifters, most of whom are men and between 18 and 50 years of age (4–7). Contrary to popular belief, most AAS users are not competitive athletes, but simply men who use these drugs to enhance personal appearance, sometimes because of underlying body image disorders (4, 6, 8). Regulatory efforts have largely failed to check these substance use disorders, but instead have managed to create headwinds for the clinical use of androgens and for the pharmaceutical development of these compounds as function-promoting anabolic therapies.

Historical Evolution of the Dual Epidemics of AAS Use and Body Image Disorders

Prior to the 1980s, illicit AAS use in the United States was limited largely to elite competitive athletes (4, 6). In the early 1980s, however, with the availability of books on how to obtain and use these substances, AAS use spilled over into the nonathletic community. The growth of AAS use by nonathletes appears to have paralleled an increasing prevalence of concerns about body image among young men—a trend fueled in part by a growing emphasis on a lean and muscular male body appearance in modern societies (6, 8). Men with body image concerns appear to be increasingly susceptible to developing "muscle dysmorphia," recognized in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, as a form of body dysmorphic disorder characterized by a pathological preoccupation with muscularity (8–12). Individuals with muscle dysmorphia typically spend long hours weightlifting in the gym, and often develop compulsive behaviors such as constantly checking their appearance in the mirror, covering their body with clothes to disguise their perceived "smallness," or refusing to be seen in public situations where their bodies would be visible (9–11). First described in the 1990s, and now the subject of a growing literature, muscle dysmorphia often significantly compromises social and occupational functioning, is associated with an elevated prevalence of mood and anxiety disorders, and is well established to be a risk factor for AAS use and probably the use of other appearance- and performance-enhancing drugs such as SARMs (4, 9–11).

The Epidemiology of AAS Use

A recent analysis suggests that 2.9 to 4.0 million Americans have used AASs at some time; ~98% of these individuals are men (4, 6, 7). Approximately one-third of the members of this group, some 1 million men, are estimated to have experienced AAS dependence, where they have continued to use AASs for many years, often despite adverse medical and psychiatric effects. Although the attention of the public, media, and policymakers has remained focused on AAS use among competitive athletes, more than 80% of AAS users have never used these drugs for any competitive athletic purpose (4). These nonathlete AAS users remain largely invisible, because they rarely disclose their AAS use to any clinicians that they see and are not subjected to the scrutiny or testing that the athletes face (4). Thus, despite the high prevalence of AAS use, this epidemic has remained hidden and not received the attention that it deserves either because it has escaped the attention of public health authorities, or not risen to a level of priority for action because of the current preoccupation with the opioid epidemic.

AAS use in the US military also appears to have risen, as soldiers have attempted to become more muscular and to improve recovery as they prepare for tours of combat duty (13–16). The prevalence of AAS use in the military is unknown; a small 2012 study using in-depth interviews found that nearly one-third of those surveyed admitted to use of these drugs (13), whereas Web-based surveys by the Department of Defense have reported a lower but increasing prevalence of AAS use during the past decade (14). Elite military forces (US Army Rangers, Special Forces, and Navy SEALs) show a higher prevalence of dietary supplement use than other military personnel (15, 16), and thus, by extension, may be at even higher risk for AAS use than other soldiers. In response to concerns from the field about AAS use by US service members, the Consortium of Health and Military Performance hosted a symposium in April 2015 where participants recommended connecting with users, education and intervention, improving knowledge and filling research gaps, and establishing an information clearinghouse and clinical repository (16).

Adverse Health Effects of AAS Use

There are few systematically collected data from prospective observational studies on the adverse health

outcomes associated with AAS use. Data from randomized controlled trials of testosterone have sometimes been extrapolated to infer that AAS use produces few adverse effects. However, these conclusions are misleading, because clinical trials have typically used physiologic doses in the range of 100 mg of testosterone per week, with only a handful of studies using as much as 600 mg per week. By contrast, AAS users may often use the equivalent of 1000 to 5000 mg of testosterone per week. Moreover, users often combine AASs with multiple other appearance- and performance-enhancing drugs, adjunctive drugs to counteract the side effects of AASs, and other classical drugs of abuse (*e.g.,* opioids, cocaine, and amphetamines). Potential adverse effects among these individuals may be compounded further by AAS-associated high-risk behaviors such as sharing of needles, unprotected sex, or involvement in violent behaviors. Thus, the full magnitude of AAS-associated morbidity and mortality is likely much greater than was generally believed two or three decades ago (Table 1).

Evolving data have implicated four categories of adverse AAS effects that appear particularly concerning: cardiovascular disorders, psychiatric disorders, AAS-withdrawal hypogonadism, and neurotoxic effects (4). Long-term AAS use is clearly associated with cardiomyopathy and acceleration of coronary atherosclerosis (17–19), very likely causing an increased risk of myocardial infarction, cerebrovascular accidents, and death. Psychiatric effects of AAS use may include mania and hypomania, aggression, and violent behavior during AAS use; and depression, sometimes associated with suicidality, during AAS withdrawal (4, 20–22). Another psychiatric consequence of AAS use is possible progression to use of other classical drugs of abuse. For example, a recent analysis of 233 AAS users and nonusers, assessing potential causal pathways using directed acyclic graphs, found that AAS use substantially increased the risk for subsequent development of opioid use disorders (23). Exogenous AASs suppress the hypothalamic-pituitary-testicular (HPT) axis, and the HPT axis may take months or even years to recover when AASs are discontinued (24, 25). Recent evidence suggests that HPT recovery may remain incomplete or fail entirely in some men (24, 25). In some men's health clinics, prior AAS abuse has emerged as a frequent cause of hypogonadism and infertility (26). Some men whose testosterone levels remain low even after prolonged withdrawal from AASs may have had underlying hypogonadism that had not been detected prior to the initiation of AAS use. The distressing symptoms of AAS-withdrawal hypogonadism, including loss of libido, erectile dysfunction, fatigue, and sometimes serious depression, may lead some men to resume AAS use, perpetuating a vicious cycle of AAS dependence (4). Finally, supraphysiologic doses of AASs have been observed to exert toxic effects on neuronal cells *in vitro*, raising the concern that long-term use of high doses of these compounds could lead to early-onset dementia (27, 28). In a preliminary neuroimaging study, AAS users displayed substantial deficits of scyllo-inositol in the anterior cingulate region of the brain as compared with otherwise similar nonusing weightlifters (29). Scyllo-inositol protects against the toxicity of β-amyloid, a protein implicated in Alzheimer's disease, suggesting that depletion of scyllo-inositol could be one potential mechanism whereby AASs might contribute to early dementia.

Additional potential adverse effects of AAS abuse include gynecomastia, acne, hair loss, nephrotoxicity, hepatotoxicity, and musculoskeletal injuries such as tendon ruptures (Table 1) (4). Marked muscle hypertrophy may render AAS-using weightlifters susceptible to injuries of articular and juxta-articular soft tissues, such as tendons and ligaments (30). Upper extremity tendon ruptures are almost always associated with AAS abuse. Needle-sharing practices can increase the risk of needle-borne infections such as the human immunodeficiency virus, hepatitis C, and skin and muscle abscesses (31).

Table 1. Potential Adverse Health Consequences of AAS in Humans

- Cardiovascular
  - Cardiomyopathy
  - Accelerated atherosclerosis and premature coronary artery disease
- Suicidal, homicidal, and sudden unexplained deaths
- Reproductive adverse effects
  - Anabolic steroid withdrawal hypogonadism
  - Infertility
  - Gynecomastia
  - Sexual dysfunction
- Mood and psychiatric disorders
  - Mania and hypomania during AAS use
  - Depression during AAS withdrawal
  - Higher frequency of other substance use disorders
- Risks associated with needle use:
  - Skin and muscle abscesses
  - Increased risk of HIV and hepatitis C
- Liver toxicity with 17-α alkylated, oral androgens or with halogenated AAS
- Musculoskeletal injuries
  - Tendon injuries
  - Articular and juxta-articular soft tissue injuries
- Growth retardation in children
- High risk behaviors
  - Unprotected sex
  - Impulsive behaviors
  - Aggression and acts of violence
- Acne and balding

Gaps in Federal Laws That Weaken Consumer Protection and Law Enforcement

AASs were once readily available as prescription drugs with minimal federal enforcement until reports began to emerge in the media in the 1980s, describing a rising epidemic of use among competitive athletes and high school students who used these drugs to manipulate their appearance. In response, the US Congress passed the Anabolic Steroid Control Act of 1990 (32), which classified AASs as Schedule III controlled substances, thereby criminalizing possession without a prescription (Fig. 1). The gaps in this law still allowed for the possession of unlisted steroidal compounds and "prohormones," precursors that are metabolized by enzymes in the body into an active androgenic compound. These prohormones and other substances also became classified as Schedule III substances in 2004 via the successor to the 1990 law, the Anabolic Steroid Control Act of 2004 (33). The Ryan Haight Online Pharmacy Consumer Protection Act of 2008 made it illegal to purchase controlled substances online without a prescription (34). Eventually, the Designer Steroid Control Act of 2014 closed additional loopholes in the former Steroid Control Acts and gave full jurisdiction of the regulation of these compounds to the Justice Department (35). Despite these laws, the abuse of AASs and SARMs by nonathlete weightlifters has continued to grow; the increasing demand for these substances is being filled by a burgeoning underground marketplace that exists outside the bounds of the consumer protection laws and the normal regulatory oversight that governs the sales of pharmaceuticals and other consumer products. Regrettably, these same laws have made it increasingly difficult for physicians to prescribe testosterone and other compounds even for approved indications. Similar laws have been passed in other countries with parallel outcomes. For example, Queensland, sometimes called the "steroid capital" of Australia, reclassified AASs as Schedule 1 drugs in 2014, increasing penalties for possession and distribution. Despite this tough legislation, the Australian Crime Commission reported an increase in steroid seizures due to increased domestic production and easy Internet access (36).

Three recent developments have further challenged detection and regulatory oversight by the US Food and Drug Administration and the US Drug Enforcement Agency. First, recent years have seen the synthesis and distribution of novel AASs, such as tetrahydrogestrinone and madol, that had no medicinal applications, and which were produced solely for illicit use. Because these novel molecules had not been known or tested previously, their detection remained elusive for several years. Second, various novel compounds have appeared that represent precursor molecules with no androgenic or anabolic activity of their own, but which are converted in the body into active androgenic compounds. Third, during the past decade, the use of other appearance- and performance-enhancing drugs such as nonsteroidal SARMs has been growing among athletes, recreational bodybuilders, and members of US armed forces (12–15).

Internet Sales of AASs and Nonsteroidal SARMs

Even though no oral SARM has yet been approved by the Food and Drug Administration for any indication, these compounds are being sold on the Internet. In a systematic investigation of products marketed as SARMs through the Internet, we found that only 52% contained genuine SARMs, and many were inaccurately labeled (37). Some products marketed as SARMs contained other drugs, whereas other products contained amounts that differed from that listed on the label. Other studies of various dietary supplements have found that many contain

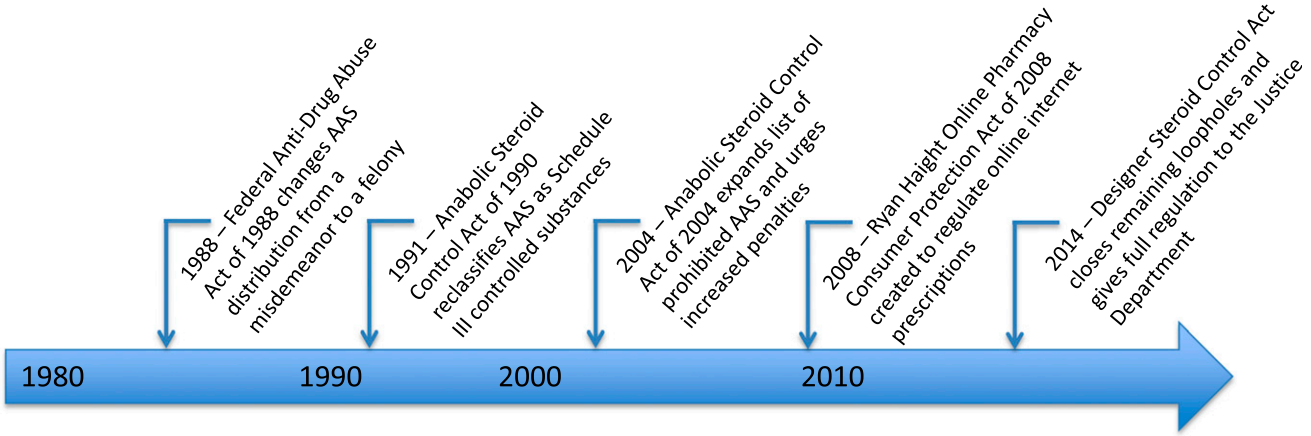

Figure 1. Timeline of laws passed by the United States Congress regulating the use and distribution of AASs. Many other countries have their own laws for AAS prescriptions, sales, and distribution, which are not shown in this figure.

surreptitious AAS or AAS precursor molecules. These findings suggest that greater regulatory oversight is needed for dietary supplements sold on the Internet.

The ease of purchasing AASs without a prescription through the Internet represents a growing source of concern. The Internet has enabled small unlicensed laboratories in and outside the United States to synthesize and package these compounds, disseminate information about their products, and to sell them to potential users around the globe. These suppliers easily operate outside the usual network of licensed pharmacies, and they can create and remove Web sites as often as needed to stay ahead of law enforcement and regulators. A recent study identified eight leading Internet sites accessed by the search term "buy steroids" (38). Among these sites, seven offered injectable testosterone, other commonly used forms of AASs, and non-AAS hormone therapies; six offered recommendations for stacking and cycling regimens, and accepted common forms of payment such as credit cards. No site required a prescription for purchase of any substance, and all sites were supplied by unregulated international pharmacies providing shipment to home addresses with disclaimers that consumers are liable to local laws. Although many countries have their own laws to regulate the dispensing, sales, and distribution of AASs, illegal distribution of these compounds into the United States via unregulated, international pharmacies continues. Enforcement efforts to shutdown Internet sales of narcotics and other illicit substances have proven challenging as new vendors and Internet sites quickly replace the sites that are shut down. Harmonization of global efforts to combat underground AAS sales and distribution is needed.

Steps to Bridge the Gaps in Our Knowledge and Health Policy—the Path Forward

Despite the health threats posed by the rapid growth of AAS use among young people, there is a surprising dearth of studies on the long-term health consequences of AASs. Hardly any major national or regional initiatives have addressed this looming public health crisis. Several expert panels have emphasized the urgent need for AAS research, with particular emphasis on prospective longitudinal studies to gather outcome data on the health effects of these drugs. Randomized trials cannot ethically duplicate the large doses of AASs used by nonathlete weightlifters, the multiplicity of drugs used, and the many high-risk behaviors associated with AAS use. Therefore, the highest priority should be assigned to prospective observational studies, which may be the only feasible approach to collecting valid outcome data on the health risks associated with AAS use. In addition, we need further studies regarding the prevalence of AAS use in children, adults, and among men and women in the armed forces; the mechanisms by which AASs and other appearance- and performance-enhancing drugs exert their adverse health effects; and the interactive effects of AASs with sports injuries and other high-risk behaviors. We also need randomized trials to assess therapeutic interventions for treating the adverse effects these drugs. It seems particularly important to assess treatment strategies for the AAS-withdrawal syndrome, because such treatment is often necessary to break the vicious cycle of AAS-withdrawal hypogonadism, relapse, and dependence. Although human chorionic gonadotropin and selective estrogen receptor modulators such as clomiphene citrate have been used to empirically hasten recovery of testicular function, the efficacy and durability of such therapeutic interventions have not been evaluated rigorously. Furthermore, integration of cognitive and behavioral interventions into a holistic treatment plan to address the body image disorder and the psychosocial contributors that render men susceptible to AAS abuse is necessary to prevent relapse. Integrated nationwide efforts to raise public awareness of the serious health consequences of AASs are urgently needed. Finally, it is time to review a whole range of national and international laws governing the manufacturing, distribution, and sales of these compounds on the Internet and through other black-market avenues, to stem this looming threat to public health.

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Correspondence and Reprint Requests: Anna L. Goldman, MD, Research Program in Men's Health: Aging and Metabolism, Brigham and Women's Hospital, 221 Longwood Avenue, Boston, Massachusetts 02115. E-mail: Algoldman1@bwh.harvard.edu.

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