LEADING ARTICLE

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Anabolic Steroids
A Review for the Clinician

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Abstract

The number of athletes self-administering ergogenic pharmacological agents to increase their competitive edge continues to be a problem. Most athletes using anabolic steroids (AS) have acquired a crude pharmacological database regarding these drugs. Their opinions regarding steroids have been derived from their subjective experiences and anecdotal information. For this reason, traditional warnings regarding the lack of efficacy and potential dangers of steroid misuse are disregarded. A common widely held opinion among bodybuilders is that the anabolic steroid experts are the athletic gurus who for years have utilised themselves as the experimental participants and then dispensed their empirical findings. This review will address the common anabolic steroid misconceptions held by many of today's athletes by providing an evaluation of the scientific literature related to AS in athletic performance.

As athletic competition continues to intensify, athletes strive for higher levels of performance to achieve success. Many of these athletes, as well as their coaches, believe that one must do whatever is required to win. If this formula requires the use of performance enhancing substances, such as anabolic steroids (AS), this is an acceptable gamble. Thus, the number of athletes administering performance enhancing pharmacological agents to achieve their goals is no longer limited to elite athletes, but to all categories of athletes.[1]

Being actively involved with the bodybuilding population, through various regional and national bodybuilding competitions as well as interviewing bodybuilders around the Midwest, the authors are aware of the use of various types of performance enhancing agents. These athletes have varying attitudes on the effects, mechanism of action, and adverse effects that are related to the use of these substances. AS are the most prevalent agents being used among this population. AS are also the most studied of all the performance enhancing agents. Although there are many AS studies, there is no consensus among researchers regarding their effectiveness as ergogenic agents. In contrast, bodybuilders eagerly postulate numerous potential mechanisms of action and endorse AS efficacy because of their first-hand experience.[2]

The AS using athletes of today have a 'sophisticated' steroid pharmacological knowledge, based on both their subjective experiences and anecdotal information, which in their minds surpasses the majority of healthcare providers.[1,3] For this reason, traditional warnings from healthcare providers regarding the lack of efficacy and potential dangers of steroid misuse are largely disregarded.[1] Today,

it appears that the AS experts in athletic competition are not medical clinicians, but athletes and former athletes who dispense their anecdotal AS experience as dogma to anyone willing to listen. Healthcare professionals caring for these athletes need to have a more thorough understanding of the AS ergogenic literature to have legitimate dialogue with these patients when caring for them. Clinicians run the risk of losing their credibility with patients because they are under-informed as to the efficacy and toxicity of the AS.[1]

Unfortunately, based on the pattern of AS usage currently being practised in the US, past efficacy and toxicology studies are of limited value in delineating the benefits and hazards of these drugs in the common dosages used by today's athletes. Due to the limitations among current studies on the effects of AS, and the lack of literature in athletic performance, understanding the beliefs of the user by the general practitioner may be difficult. The goal of this article is to provide an unbiased summary of the relevant literature relating to AS use, including epidemiology, pharmacology, efficacy, adverse effects and misconceptions common among bodybuilders. This review will also incorporate the anecdotal theories of bodybuilders relating to safety and efficacy and the relevant literature that rebuts or strengthens their arguments. The uses of nutritional AS, such as androstenedione, are not included in this review.

1. Epidemiology

The prevalence of AS use has been reported in several populations, but data on the exact prevalence are limited to surveys of students and athletes who may be reluctant to admit actual usage of these controlled substances. There have been estimates of more than 1 to 3 million current or former AS users in the US. Many of these may be young adults.[4,5] The most recent estimates report that 4 to 12% of US high school boys have used AS at sometime in their life.[6] A recent survey conducted by Blue Cross and Blue Shield Association[7] reported that AS were the second most common substances known to be used for athletic performance among 12- to 17-year-old people, second only to creatine (31 *vs* 57%, respectively). Sullivan et al.[8] reported that 65 to 84% of adolescent AS users were participants in organised athletics.[8] On the other hand, other reports showed that 3.2% of Modesto, California 7th grade girls and 2.8% of Massachusetts 6th and 7th grade girls have reported using AS, respectively.[9,10] These reports of AS use may be confounded by false positive reports, consisting of over the counter AS supplements or failure to accurately answer survey questions correctly. Nonetheless, these numbers are worrisome, especially when considering the adverse growth suppressing effects of AS in young adults.[11] A recent National Collegiate Athletic Association survey[12] found that only 1.1% of college athletes surveyed reported AS use, and Yesalis et al.[13] reported 29.3% of college football players and 20.6% of male track-and-field athletes reported AS use. Some of the highest estimates have come from Yesalis and Bahrke,[10] reporting that 78% of track-and-field athletes in 1972 had prior steroid use.

After Olympic athletes, the second most prevalent group believed to misuse AS is the bodybuilding and/or weightlifting population. Yesalis et al.[14] reported that 55% of elite power lifters admit to AS usage. Tricker et al.[15] reported the same percentage among amateur competitive bodybuilders. These high numbers relate to the fact that many bodybuilding competitions do not actually test for AS usage among competitors. Many of the 'natural bodybuilding' organisations provide the option of polygraph or urinalysis tests if a competitor stands out as an AS user. Most 'major' competitions such as those held by the National Physique Committee, state that athletes must be 'drug free' but do not test the competitors. Additionally, athletes have found systems to work around the rules of competing 'drug free' and have actually challenged the credibility of drug testing in athletic competition.[16]

Although these reports of AS usage seem high, our experience in surveying bodybuilders suggests that these numbers may be under estimated. Indeed, current methods of self-reporting and/or surveying AS usage may yield inaccurate estimates in this population. We have observed that since AS were

categorised by the US Congress as Schedule III (non-narcotic) class drugs of misuse in 1990,[10] AS users have become far less forthcoming about their use of these drugs. This makes identification of AS using athletes by the primary care practitioner as well as in epidemiology studies problematic.

2. Physiology

In general, the physiological mechanisms of AS are commonly misunderstood and overstated in the bodybuilding population. Many beliefs are anecdotal at best, and not supported by the medical literature.

The two most common AS questions posed by bodybuilders to physicians are, 'How exactly do AS cause muscle growth,' and 'Is this a dose-dependent effect?' AS have numerous proposed mechanisms of action related to athletic performance. These include: increased skeletal muscle protein synthesis and skeletal muscle hypertrophy;[17,18] a decrease in the rate of protein breakdown;[11] an increase in the number of mononuclei;[19] activation of satellite cells;[19] and an increase in the number of androgen receptors containing mononuclei.[19] However, the exact mechanism is not understood. Misconceptions among athletes regarding the effects of AS on physiology often occur, and may account for the increase in serious adverse effects seen in this population.

The physiological function of satellite cells in muscle growth is a source of considerable confusion. The effects of AS on the satellite cells are commonly misunderstood by bodybuilders. During muscle growth, myoblasts (young muscle cells) proliferate to eventually form mononuclei (mature muscle cells) in skeletal muscle. There are a number of myoblasts that do not mature into mononuclei; these cells are labelled as satellite cells.[19] After injury, such as that related to athletic training, satellite cells are recruited as the primary vehicle in muscle repair. These cells are eventually incorporated into muscle fibres as mononuclei during the repair and growth process.[19] Strength training increases the number of satellite cells, thereby causing muscle growth.[19] When the stress from exercise or training does not induce muscle injury there does not seem to be growth in the muscle. The number of satellite cells available for recruitment in AS users versus non-users does not differ.[19] Thus, AS do not affect muscular hypertrophy by increasing the number of satellite cells in the muscle after injury. Instead, training appears to be the dynamic parameter that governs satellite cell number. This finding contradicts the notion of most bodybuilders that AS increase muscle recovery after intense training. The misconception of faster recovery during heavy training may be psychological and related to the AS-induced euphoria athletes experience during training. This issue will be discussed in more detail in section 4.4.[20]

Some bodybuilders have reported that AS will precipitate muscle growth without intense strength training. Thus, AS are hoped to be an antidote for the 'ancient wisdom' of 'no pain no gain'. However, the available data suggest the opposite. Bhasin et al.[21] provided evidence that testosterone administration could increase muscle strength and size in males, but only in the presence of weight-training. Use of AS and exercising theoretically increases the number of mononuclei in the muscle that can be used to increase protein synthesis and hence repair injured muscle and increase muscle size and strength.[19] For muscle growth to occur, stress on the muscle is required. Thus, the idea of using AS without increased weight-training to increase muscle size and strength is erroneous.

Most bodybuilders believe that a high protein diet enhances muscle growth during training. This observation is true since athletic training causes the catabolic effects of the glucocorticoids to generate a negative nitrogen balance. The body responds to this negative nitrogen balance by utilising the protein stores of the body to revert to a positive balance.[20] AS are extremely anticatabolic and convert a negative nitrogen balance to a positive balance by improving the utilisation of dietary protein and increasing protein synthesis.[17,20] AS use in normal and catabolic (training) individuals precipitates protein synthesis within the muscle cell, which in

turn results in a positive nitrogen balance. Since normal individuals are not in a negative nitrogen balance (catabolic state), the effects of AS will only be short-lived.[20] This fact explains why AS users report that the more they train and ingest protein while using AS, the more they 'grow'.

AS oppose the effects of glucocorticoids, not only through a positive nitrogen balance, but also through competition for glucocorticoid binding sites.[18,22] This effect decreases the amount of cortisol and other glucocorticoids available in the body. Studies[22] show that testosterone and other AS compete with cortisol, dexamethasone and triamcinolone for glucocorticoid binding sites. This competition may help reverse the negative nitrogen balance induced by training. Hence, the belief of some athletes that AS have an anticatabolic effect that results in a positive nitrogen balance is correct.

Most bodybuilders assume that there is a dose-dependent effect of AS on androgen receptor formation and muscle mass increase (unpublished observations). This notion is not absolutely correct in the absence of strength training. Kadi[19] showed that androgen-receptor–containing muscle fibres or mononuclei are highly selective. Androgen receptor content of the muscle fibres is a function of the type of muscle. There can either be a receptor up-regulation (increase in receptors) or a down-regulation (decrease in receptors) depending on the type of skeletal muscle involved. This could explain the distinguishing features of most bodybuilders, such as large trapezius and deltoid muscles, which may result from greater AS receptor up-regulation in these two areas.[19]

The significance of the AS-androgen receptor complex interaction is commonly misunderstood. When an androgen binds to the androgen receptor on the nucleus of a muscle cell, a receptor-androgen complex is formed that is then transferred into the nucleus of the muscle cell. Once in the nucleus, this complex binds to complementary regions on DNA to activate the transport-RNA and produce messenger RNA that encode a variety of enzymes and proteins.[17,23] The action that eventually occurs is the up- or down-regulation of the androgen receptors, increased protein synthesis and possibly an increase in the number of mononuclei in a muscle fibre.[17,23] Hence, the effect of AS on muscle fibre androgen receptors is dependent on the muscle type and number of receptors present.

Muscle fibres replicate after strenuous activity, which in turn increases the total number of androgen receptors in that muscle group. An increased number of androgen receptors provide additional functional binding sites for androgens, which in turn leads to an enlargement of that muscle group.[17] An opinion that transcends all the AS medical literature is that AS do not provide much benefit in the absence of strength training.[19,24-26] This opposes bodybuilders' anecdotal observations that higher doses of AS are more effective for muscle growth in the absence of increased strength training. The only means by which excessive supraphysiological doses of AS can benefit an athlete is by there being a surplus of uninnervated AS receptors. However, the only means to achieve a surplus of AS receptors is by heavy training.[19]

The final performance-enhancing effect of AS, which is less commonly known among bodybuilders, but well known by runners, is the resultant increase in erythropoietin synthesis. This increase in erythropoietin subsequently increases hematocrit and blood oxygen carrying capacity.[24] Because of these effects, AS have been used in the treatment of anaemia.[27] However, this indication has been largely forgotten after recombinant human erythropoietin (epoetin alfa) became commercially available. Although the increase in oxygen carrying capacity would be expected to increase athletic performance, it is partially offset by sodium retention and blood volume increase. This can result in potentially fatal sludging of blood should the hematocrit increase too much.[24] These haemodynamic alterations may contribute to some of the bodyweight gain observed by AS users.[24] Currently erythropoietin has replaced the use of AS for 'blood doping' where athletes transfused themselves with blood having a greater than normal content of red blood cells.

3. Efficacy

Reviews of the effect of AS on athletic performance suggest that there is only limited evidence to support the efficacy of these drugs in athletic performance.[10] Many studies[21,25,26,28] contain significant methodological flaws in dosage and administration strategies when compared with real-world use. Athletes 'stack' AS. The drugs are administered in cycles of gradually increasing doses and increasing numbers of agents combined together (stacked). The cycles used are generally between 7 to 14 weeks in length and involve a combination of oral agents and long-acting injectable agents.[29] In contrast, for ethical reasons, clinical investigations have been restricted to single agent regimens. Athletes tend to use oral agents in doses that are similar to those of clinical studies, but typically use injectable steroids at doses 3 to 8 times those utilised in clinical trials.[29] Disconcerting to us are anecdotal reports of supraphysiological doses of the more hepatotoxic C-17 alkylated agents being used (table I). Because higher dosages of AS tend to be used by athletes, it is difficult to compare anecdotal reports of efficacy with findings of clinical trials evaluating AS as single agents administered at lower dosages.

Table I. Commonly used anabolic steroids

Oral agents: drug
C-17 alkylated agents
Ethylesterenol
Fluvoxymesterone
Fluvoxymesterone
Methyltestosterone
Metandienone
Oxymetholone
Oxandrolone
Stanozolol
Injectable agents: drug
Testosterone salts: cypionate, ecanoate, enanthate, propionate, phenpropionate, isocaparoate, testosterone propionate, phenpropionate, isocaproate, decanoate
Nortestosterone
Nandrolone decanoate
Nandrolone phenpropionate
Boldenone undecylenate
Methenolone enanthate

Currently available data suggest that AS cannot produce a significant effect on muscle strength unless they are combined with weight training. The most recent demonstration of AS ergogenic potential was documented by Bhasin et al.[21] Forty-three men were randomised into four groups: placebo and no exercise, testosterone and no exercise, placebo plus exercise, and testosterone plus exercise. Testosterone was administered as testosterone enanthate (TE) 600 mg/wk, defined as a supraphysiological AS dosage. The mean bodyweight in all participants who received TE increased significantly ($p < 0.001$) greater than that noted in the placebo group. The TE and exercise group increased the most, with an average bodyweight gain of 6.1kg. Additionally, both TE groups had significant increases ($p < 0.001$) in cross-sectional areas of the triceps and the quadriceps verses the placebo group, with the largest increase once again occurring in the TE plus exercise group. The greatest increases in bench press were observed in the TE plus exercise group ($p < 0.001$), although the placebo and exercise group did increase to a lesser degree ($p = 0.005$). There were no significant muscle increases observed in the placebo and no exercise group.[21]

Two additional studies[26,30] also observed increased strength with metandienone administration plus exercise over placebo groups, which supports the Bhasin et al.[21] findings. Hervey et al.[31] noted that high dosages (25 mg/day) did not produce obvious differences in strength over low dosages (10 mg/day). Thus, these data suggest that AS augment exercise to produce muscle growth. Additionally, the larger dosages used did not produce obvious muscle gains over the lower dosages. Unfortunately, no conclusions can be drawn regarding the mega-doses commonly utilised by today's AS users, because of a lack of controlled clinical studies.

There are many anecdotal and case reports of large muscle and strength gains by the use of supraphysiological doses of AS. Perry et al.[29] reported bodyweight gains of an average of 19.9kg after AS

use, and an increase in the mean maximal bench press of 47% ($p < 0.0001$). The authors hypothesised that the obvious individual benefits of the AS makes these drugs psychologically addictive in many users. Additionally, the expected doses used may not actually be the actual doses, because of the diluting of the AS by black-market retailers. This black-market quality control problem emphasises the importance of obtaining serum testosterone profiles (total, free and weakly bound serum testosterone concentrations) in determining the effects of mega-doses of AS.

Contrary to beliefs of athletes using AS, some investigators believe that AS induce their beneficial effects as a result of psychological rather than physiologic effects. Ariel and Saville[25] showed that an athlete's expectation of strength gains from AS could cause muscle growth, independent of AS use. Fifteen male participants were informed that some of them would be selected to receive AS; instead, all participants received placebo. The apparent psychological effects of AS on strength were observed in several participants who experienced significant strength gains due to the belief that they were receiving AS. This study emphasised the psychological aspect of human performance, and the potential benefits of placebo supplementation on psychological enhancement. This motivational effect may help athletes produce significant athletic improvements even in the absence of AS administration.

In light of the quality of AS literature, there remain a number of issues that need to be resolved to completely discern the efficacy of AS. All of the studies reviewed used single agents, contrary to the commonly used 'stacks' among athletes. Typically the doses administered were much lower than the mega-doses used by present day athletes. Despite the unknown efficacy of stacking, many researchers have suggested that stacking is a non-issue for muscle growth.[19,24] This is logical because regardless of the number of AS being used, the endpoint is still the same, that is an increase in the free, weakly bound, and total testosterone concentrations in the body. Thus, all future studies of AS ought to have in common these three clinical chemistry parameters. Additionally, if these parameters are routinely measured, clinical correlations between AS dose and strength gain, muscle mass increases and adverse effects can be made. This monitoring strategy is beneficial to the athlete in that it will probably result in the use of smaller doses of AS. It also benefits the healthcare practitioners who are attempting to monitor and treat these athletes as patients. Lack of a patient-physician relationship has lead athletes to following guidelines in lay publications such as those contained in the Underground Steroid handbook.[1,32]

4. Adverse Effects

The adverse drug effects of AS can be divided into 5 general categories: hepatic, cardiovascular, reproductive/endocrine, dermatological and psychiatric (table II).

4.1 Hepatic Effects

The association between liver function tests (LFT) elevations and AS has been documented in the literature.[20,28,33] Bodybuilders are well versed and quite concerned about this adverse drug effect. Elevations in aspartate transaminase, alanine transaminase, lactate dehydrogenase and alkaline phosphatase have been reported with AS use.[20] Although weightlifting alone can elevate LFT, individuals using AS are at a greater risk of having elevated LFT.[20] However, hepatic enzymes usually return to normal once AS are discontinued. The reversible course of the LFT elevations explains why athletes administer AS in a cyclic pattern.[34] Consequently, if AS are administered continually for at least 1 month, but generally for greater than 2 to 5 months at supraphysiological doses, dose-dependent jaundice and hepatic dysfunction are likely to develop.[34] Death caused by AS hepatotoxicity is extremely rare.[34]

Of the AS, the C-17 alkylated AS are more often associated with liver toxicity.[34] The most common C-17 alkylated AS used by athletes are the oral agents such as methyltestosterone, metandienone, oxymetholone, oxandrolone and stanozolol. Non-alkylated intramuscular agents such as testosterone and nortestosterone are much less likely to produce

Table II. Most common adverse effects of anabolic steroids

Hepatic
LFT elevations (hepatotoxicity)
Liver cancer
Cardiovascular
Decreased HDL
Increased LDL
Increased total cholesterol
Decreased triglycerides
Fluid retention (elevated blood pressure)
Cardiac hypertrophy
Reproductive and endocrine
Decreased LH
Decreased FSH
Decreased thyroid functioning
Adverse effects in males
decreased spermatogenesis
abnormal sperm morphology
feminisation in males
decreased size of testes
Adverse effects in females
hirsuitism
voice deepening
clitoral hypertrophy
decreased breast mass
amenorrhoea
male pattern baldness
Dermatologic
Oily hair
Oily skin
Alopecia
Sebaceous cysts
Increased incidence of acne
Psychiatric
Mood changes
Possible aggression
Possible hostility
Dependence and/or addiction

FSH = follicle-stimulating hormone; **HDL** = high-density lipoprotein; **LDL** = low-density lipoprotein; **LFT** = liver function tests; **LH** = luteinising hormone.

liver problems.[20,34] However, many AS users misuse other substances including alcohol, which could possibly compound hepatic adverse drug effects. There have been cases of carcinoma of the liver associated with either high dose AS, long periods of administration of AS or in AS users with predisposing medical conditions.[20,34] Cyclic administration of AS reverses the risk of liver toxicity.[3] Additionally, avoiding C-17 alkylated agents (oral agents) is another practice that decreases hepatotoxicity. The ultimate means of preventing liver toxicity are AS abstention and the avoidance of other potentially hepatotoxic agents, such as alcohol. Although accepting of these facts, athletes are not usually concerned since the benefits of increased muscle mass and strength overshadow the known risks.

4.2 Cardiovascular Effects

Use of AS can lead to detrimental changes in serum lipid profiles. Potential changes include increases in low-density lipoprotein (LDL) and decreases in high-density lipoprotein (HDL).[27,33,35] Bodybuilders are generally of the opinion that since steroids are chemically similar to cholesterol, they will affect lipids in the same way as eating too much cholesterol. For bodybuilders this effect is not harmful since many of them are on ketogenic diets, which emphasises moderate to high fat, and low to moderate complex carbohydrate foods, while consuming extremely high amounts of protein.[32] Lipid changes are typically unpredictable and are unrelated to dosage and agents administered. A meta-analysis[35] conducted in 1991 reported decreases in HDL of 39 to 70% (mean 52%). These changes generally occur within the first week of administration and normalise within 3 to 5 weeks after AS discontinuation. Conversely, reports of LDL elevations between 11 to 100% have been reported (mean 36%).[35] Since HDL levels decrease and LDL levels increase, total cholesterol levels generally do not reflect these changes and the atherogenic potential of AS can often be overlooked.[35]

Unfortunately, many bodybuilders seem to believe that cholesterol monitoring is all that it required to monitor their lipid status. Triglyceride levels are also decreased by the exogenous androgen administration.[3] The long-term impact on morbidity and mortality of labile lipid profiles is unknown. However, an increase in LDL levels might directly contribute to arteriosclerosis especially if

these agents are used over long periods of time.[8] With an increased risk of cholesterol plaques in the coronary vessels, a subsequent thrombus may occur in athletes using AS.[8] AS also stimulate platelet aggregation, increase coagulation enzyme activity, and cause coronary artery vasospasm.[8] Thus, AS have the potential to predispose users to thrombus formation by reductions of HDL, increases in LDL, increased platelet aggregation, coronary artery vasospasm and enhanced coagulation enzyme activity.

Elevations in blood pressure in AS users have been reported and most likely result from blood volume increases and fluid retention.[8,27] This effect has not been well studied in humans, although is well-documented in animal studies.[8,27] Anecdotally, bodybuilders will complain of feeling an increase of pressure in their head and body resulting from what they believe is elevated blood pressure. AS also increase heart rate, which may lead to hypertrophy of the left ventricle.[8,36] Case studies of AS users at autopsies have found cardiac hypertrophy in these patients.[8] The consequences of cardiac hypertrophy can lead to decreased maximal oxygen uptake, remodelling of the heart, myocardial ischaemia and cardiomyopathy.[8] These effects are serious and can lead to sudden cardiac arrest, and will persist well after cessation of AS.[8] Unfortunately, it is difficult to ascertain whether the effects of AS on the heart are independent of the other agents present in the polypharmacy regimens of many AS users such as amphetamines as weight loss agents, as well as alcohol and tobacco cigarettes.

4.3 Reproductive/Endocrine Effects

In men, AS administration produces a predictable, dose-dependent depression of luteinising hormone (LH), and follicle-stimulating hormone (FSH) via the negative feedback loop of the hypothalamic-pituitary-gonadal (HPG) axis.[30,37,38] As both LH and FSH are required for spermatogenesis, AS administration can lead to hypogonadotropic hypogonadism. The resulting effects of these physiologic changes include declines in sperm density and sperm count, decreased sperm motility, abnormal sperm morphology, testicular atrophy, and no change in libido.[10,27,39,40] However, the observed effect on libido was based on testosterone doses not exceeding 500 mg/wk. These effects generally worsen with increased use of AS, and severe oligospermia can lead to infertility.[41] Bodybuilders are usually aware of these effects and often use agents such as chorionic gonadotropin (hCG) to stimulate LH production and testicular testosterone production.[32] Turek et al.[41] described a case report of an AS user who was administered hCG 2000 to 3000 units three times a week. Following 3 months of treatment, the patient's wife became pregnant, reportedly due to LH and sperm normalisation. FSH activity is required for completion of spermatogenesis. However, FSH activity is not precipitated by hCG. This leads to the belief that sperm counts are increased by hCG, but they may not be 100% viable. Many athletes who discontinue AS have their sperm morphology normalise within 4 months. However, this is not necessarily always the case since normalisation is a function of both the magnitude and duration of AS exposure.[38] Some individuals required up to 1 year for normalisation of morphology and motility.[37,38]

AS can also lead to feminisation in males from the conversion of testosterone to estrogen metabolites (aromatisation).[27] As a result, many AS users report increased voice pitch and gynaecomastia, although these effects are unpredictable. Our experience notes that many users of AS self-administer the antiestrogenic agent tamoxifen to antagonise these effects. Unsurprisingly, the efficacy and safety of this practice remains to be confirmed. Our experiences with AS-using bodybuilders indicate that hair loss is minimal with testosterone ester doses of less than 600mg/wk. The adverse effect is reversible on discontinuation of the AS.

AS use in women can lead to hirsutism, acne, deepening of the voice, clitoral hypertrophy, decreased breast mass, decreased menstruation or amenorrhoea, increased appetite and male pattern baldness. Even after discontinuation of the causative agents, these effects are sometimes irreversible.[42]

The willingness to tolerate any physical and/or reproductive adverse drug effect to achieve an athletic goal is unique among AS administrating athletes.

Other endocrine effects include decreased thyroid function and decreased serum T-4 binding globulin concentrations.[3]AS is known to cause acne and other skin changes including, but not limited to, oily hair and skin, alopecia, sebaceous cysts and hypertrophy of sebacious glands. High doses of AS increase the amounts of *Propionibacteria acnes,* free fatty acids and cholesterol in the skin, which lead to these dermatological changes.[3]

4.4 Psychiatric Effects

Aggressive behaviour and mood changes have been linked to use of AS in case reports, animal studies and controlled clinical trials.[43,44] Although these reports describe increases in aggression and violent behaviour with AS use, there are relatively few controlled studies relating aggressive behaviour and mood changes to AS use among a bodybuilding and/or weightlifting population. Despite the nature of various reports on mood changes with AS administration, many bodybuilders report that they feel AS elicit an antidepressant-like feeling. This observation was recently challenged when Seidman et al.[45] reported no antidepressant effects of testosterone replacement in men with major depressive disorder. Conclusions of this study are limited and future studies of AS use in depression are needed.

Six randomised controlled studies have administered supraphysiologic doses of testosterone to healthy male participants and observed them for changes in their mental status.[40,46-50] In general, these studies indicate little risk of mood changes or aggressive behaviour with doses of up to 300 mg/week. However, with larger doses, changes in various mood and aggression subscales have been observed.

Pope et al.[48] described significant increases in the Point Subtraction Aggression Paradigm (PSAP), and the Young Mania Rating Scale (YMRS) among recipients of higher testosterone doses (600 mg/wk) compared with placebo.[48] While between-group differences were observed, the distribution of individual scores was also important. On average, the endpoint YMRS scores were 3 points higher in recipients of testosterone. However, this difference does not indicate that all participants had a 3-point increase, but rather that most participants experienced no change, while a few individuals experienced marked changes. While Pope et al.[48] was able to demonstrate significant alterations in aggression and mood endpoints, the majority of controlled studies have not. This may be because psychiatric adverse drug effects are dose-dependent and all of the negative studies did not expose the participants to large enough doses to induce a change in the participants' mental status. Additionally, the negative studies indicate that individuals with a positive psychiatric history including personality disorder may be more susceptible to changes in mood and aggression.[40,46,47,49,50]

Although AS use promotes aggression and mood changes, there are several limitations to the data. First, many of the studies did not enrol bodybuilders and/or weightlifters as participants.[40,46,47,49,50] The inclusion of healthy male participants does not represent individuals who are likely to use AS such as weightlifters, bodybuilders and other athletes. The second limitation is the exclusion of individuals with psychiatric disorders, particularly personality disorders. Such individuals may be more susceptible to AS-induced psychiatric changes than normal control participants. Finally, AS regimens were limited to a single agent administered weekly at doses less than 600 mg/week.[40,46-50] These regimens do not represent the multidrug combinations (stacks) and/or mega-doses of AS used by bodybuilders. Furthermore, the maximum dose given in clinical trials was 600 mg/week for 2 weeks, which is far below the doses commonly used by bodybuilders.[46,48]

Data regarding AS use in bodybuilders and/or weightlifters and associated psychiatric changes are limited. Yates et al.[6] compared weightlifters that were either AS users (n = 20) or non-AS users (n = 20) to alcoholics (n = 20) and non-weightlifting community controls (n = 20). Personality disorders were assessed using the Diagnostic and Statistical

Manual of Mental Disorders (3rd edition, revised) [DSM-III-R] criteria for cluster A, B and C personality traits, and the self-report personality diagnostic questionnaire. Forty-five percent of AS users demonstrated antisocial personality traits compared with 0% of community controls ($p < 0.001$).[6] In a later study, Yates et al.[51] examined the Buss-Durkee Hostility Inventory (BDHI) scores for eight AS users, four previous AS users to 25 non-AS using weightlifters. There were no significant differences among AS users, non-AS users and previous users on overall BDHI scores, but there were significant elevations on the BDHI subscores of assault, indirect aggression and verbal aggression among AS users.[51]

A more recent study by Pope and Katz[52] conducted interviews with weightlifters using AS ($n = 88$) and non-users ($n = 68$). DSM-III-R criteria were applied to identify psychiatric syndromes. Twenty-three percent of AS users experienced major mood changes of mania, hypomania or major depression. In contrast, the rate of major mood changes was only 6% among non-AS users ($p < 0.07$). Aggressive behaviour, including fights, domestic disrupts, assaults and arrests, was common among AS users. All participants denied previous behaviour of this type before AS use.[52]

Our experiences with AS users indicate that psychiatric effects are unique to each individual and overall conclusions are difficult to make. However, there are data suggesting that AS administration may be addictive. In interviews with 49 AS users, at least one DSM-III-R symptom of dependence was reported by 94% of the sample, while three or more symptoms were reported by 57% of the sample.[53] Three symptoms are required for a diagnosis of drug dependence. A recent article[54] reported that 23% of AS using participants met DSM-IV criteria dependence, while 25% met DSM-IV criteria for abuse. The authors concluded that AS were addictive and suggested that dissatisfaction with body size might lead to dependent patterns of use.[33] Our experience with many athletes using AS suggests that dissatisfaction with their body size and increases in strength and size obtained from AS are the primary stimuli for continued usage of these agents. Although these observations may be related to an underlying body dysmorphic disorder diagnosis, and unrelated to AS usage, no studies have been conducted addressing this issue in this population. Clinicians should not discount the addictive potential of these agents, as competitive athletes are often willing to use any substance to obtain their goals.

5. Conclusion

Understanding how AS are used in the bodybuilding community merits more study. The desire among competitive athletes to succeed is a powerful stimulus and using legal substances for illegal purposes to obtain these goals has become an increasingly large concern for healthcare professionals. Healthcare professionals should be able to educate their patients regarding the risks of using these agents. A clinician's warnings will gain credibility if they have a sound understanding of the issues related to AS use so that they can have an informed conversation with the patient/user. Clinicians should impress upon their patients that, despite the cavalier use of AS among athletes, the long-term effects are not well established and they ought to be cautious. This requires the clinician to obtain as much knowledge about AS as possible by reviewing not only the medical literature, but mass-media literature as well. Physicians must warn their patients who use AS that the effects of these agents on overall health have not been extensively studied, and encourage them to avoid these agents to prevent any future health risks.

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