



SWEDISH CLINICAL GUIDELINES ON

The Abuse of Anabolic Androgenic Steroids (AAS) and Other Hormonal Drugs

Dedicated to the Memory of Eva Edin

Our highly appreciated co-worker and co-author Eva Edin tragically passed away, while we were in the process of developing these guidelines. Her profound clinical experience and wide knowledge has been a prerequisite, and an essential cornerstone, in creating these guidelines. We miss her greatly and wish that she could have been part of our work to its completion.



PREFACE

The enhanced public awareness of *doping* in society over the past few years – including *doping* in sports – has made us more familiar with the concepts of doping, as well as increased our preparedness to prevent, detect and treat the abuse of doping substances. Strategies for anti-doping prevention and intervention in society at large may, among other things, include measures such as providing information, health care, research and legislation.

Individuals abusing doping substances, anabolic androgenic steroids (AAS) in particular, suffer from medical complications to a great extent. Since patients are often reluctant to disclose their drug abuse, the underlying cause for medical complaints may be difficult to identify in health care settings. This may partly be due to the fact that AAS are being used illicitly, and partly because the treating physician fails to disclose the abuse. The abuse of AAS is a fairly novel phenomenon, and knowledge among health care providers is still lacking about its prevalence and symptoms. Inadequate knowledge is also prevalent among actors from different sectors of society, involved in the fight against doping, such as administrative authorities, voluntary organizations, and athletic training facilities, as well as among those participating in the work at district and county council levels.

The document at hand has been produced by a working group consisting of clinical experts from different parts of Sweden who, in various ways, work with doping-related questions within health care and research. The purpose of this document is to summarize the current medical knowledge in the field of doping, especially concerning AAS,

in order to provide knowledge and practical guidance on diagnostics and therapy for those health care providers who encounter AAS-abusing patients.

Furthermore, the purpose is to provide a stimulus for increasing health care interventions, and also to serve as an incentive for research on doping regarding its causes, consequences, and treatment. This document does not in any sense claim to be complete, and could be considered as a living document that may evolve over time through continual updates. Information about updates will be posted on the Anti-Doping Hotline website, and may also be obtained through the authors (addresses and contact information is found at the end of this document).



SUMMARY

The abuse of anabolic androgenic steroids (AAS) is widespread, and it creates medical and psychological complaints, for which medical attention is sought in primary care and other clinics. In order to better understand individuals seeking treatment for these problems, and offer them adequate treatment, it is essential to detect the underlying abuse. This document offers some concrete examples of physical, mental, and laboratory-based indicators of an underlying abuse. Doping in society, outside the world of sports, occurs in various social settings, and for different purposes. A common denominator in abusers is a desire to change one's appearance, but also – to a certain extent – to affect mental functions. Not all effects attributed to AAS-abuse are based on scientific evidence. These perceptions frequently contribute to miscommunication in encounters between health care and the "doping society", where we, as health care professionals, may be perceived as ignorant.

In order to gain an increased understanding of the extent of doping-related health issues managed in health care, sharing a common view on diagnosis registration is essential. Establishing specific diagnostic criteria for AAS abuse and its consequences, might in turn facilitate in obtaining statistics on the consumption of health care due to AAS.

The therapy section covers investigation and therapy, psychosocial care, pharmacological treatment, and follow-up. We also suggest shared responsibility for health care between primary and specialized medical care.

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1. INTRODUCTION

1.1 Definitions

The term *dopning*, as set forth in the Swedish Doping Act (SFS 1991:1969), refers to the prohibition of certain doping substances. It is illegal to import, sell, possess, manufacture, dispense, purchase or use anabolic androgenic steroids. These substances are also mentioned in the Driver's License Act (VVFS 2008:166, 12 KAP, 1§), where they are equated with psychoactive substances that impair judgment and driving ability, and thus are forbidden by law. The term *doping* refers primarily to cheating in organized sports by using banned, performance-enhancing drugs or methods. The term *doping* onwards refers to doping encountered in health care, society and sports; while anabolic androgenic steroids will be referred to throughout as AAS.

"Use", "consumption", or "abuse" of doping substances – which is the most appropriate term to apply? Confidentiality is central to establishing and preserving trust in the physician-patient relationship, based on the rules of secrecy in public health care. What term to use in the clinical situation is thus determined by the circumstances. Utilizing words such as "use" or "consumption" of doping substances might give the impression of a permissive attitude toward doping. This may, however, be necessary at times in order to establish rapport with the patient. Using the word "abuse", on the other hand, may be necessary to make sure the patient fully understands the risks involved. The authors of these guidelines have chosen to use the term AAS abuse.

1.2 Prevalence

There are no reliable data to determine the prevalence of AAS abuse.

There are an estimated 10 000 active users of doping substances in society (Sweden), based on previous estimates (1). People involved in the anti-doping work agree with the notion that individuals who admit to ever having used doping substances add up to hundreds of thousands. Doping in society increases parallel to an increase in illegal imports of doping substances, as well as increased sales over the internet; and police and Customs statistics, which show that seizures have increased manifold over the last decade, can be considered a good measure for this.

1.3 Objectives and User Groups

Contrary to popular belief, the abuse of anabolic-androgenic steroid is not limited to doping in sports in order to enhance performance. Recent publicity surrounding famous athletes convicted of doping violations has been pronounced. Doping in society is a less familiar, but equally important, phenomenon. The reason why AAS abuse exists within the so-called gym culture, is to achieve improved physical appearance, and/or increased strength, as well as to strengthen self-esteem. AAS abuse also exists in a criminal context. Individuals abusing AAS can be characterized as either aesthetes (mainly gym members, body builders), *athletes*, or *violent offenders* (engaging in criminal activity) (2). Apart from these there are additional categories, such as those co-administering AAS and narcotics (3).

1.4 Patterns of Abuse

Doping substances are commonly abused in cycles lasting for several weeks, or even months, followed by a period of abstinence. Generally several substances of varying compositions are abused simultaneously. A majority of the abusers have experienced a number of positive effects from taking these substances, especially during the initial part of a cycle. However, a host of both serious and undesirable adverse side effects – physical and/or psychiatric in nature – can occur in all stages of the abuse. This indirectly affects people within the abuser's close circle of friends and family, as well as society at large, health care, and judicial

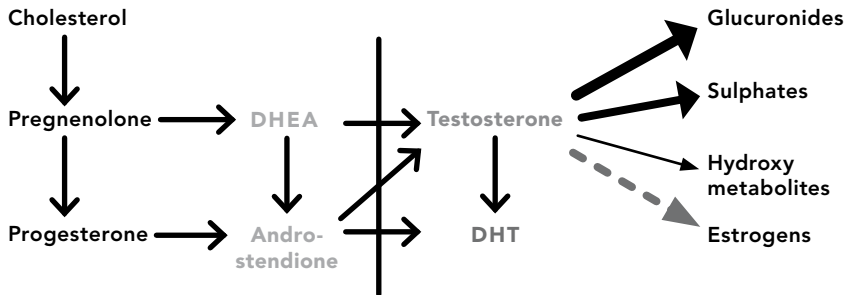
systems. Most people engaged in doping are young, the majority of whom are men. Since AAS abuse is illegal, there is reason to try and hide it from others. This might be one explanation as to why it is difficult to identify these individuals in health care, when a person seeks medical attention for symptoms associated with AAS abuse. Another explanation is that this type of abuse is a relatively novel phenomenon, and symptoms are still relatively unknown. There is a general conception that all AAS abusers exhibit aggressive behavior, which can be misleading.

1.5 Androgens och AAS

Androgens act through the androgen receptor, which exists in all organs in varying amounts. Certain androgenic effects are also mediated through estrogen receptors, since testosterone, in part, is converted to estrogen by the enzyme aromatase. Androgens play a pivotal role in the development and maturation of the gonads, prostate gland, sexual function, etc. Androgens also play important roles in non-reproductive organs, including bone, adipose tissue, skeletal muscle, brain, liver, and kidney. There is a correlation between androgens and the risk of developing certain diseases, for example, benign prostatic hypertrophy, prostate cancer, and polycystic ovarian syndrome.

Testosterone is the most important androgen. Men produce approximately 7 mg per day of testosterone, while women produce about 0.7 mg. Testosterone is converted into the even more potent dihydrotestosterone (DHT) in the body, while all other testosterone metabolites generally exhibit weaker androgenic activity. Certain testosterone precursors (e.g., dehydroepiandrosterone (DHEA) and androstenedione) have weak androgenic effects, and thus have a potential for abuse. The intake of AAS stimulates the growth of muscles, and thus augments muscle mass and strength, apart from the effects obtained through training. Intake also increases the number of cell nuclei per muscle fiber, a condition which may persist for many years after discontinuation of AAS (4). AAS reduce muscular recovery demands –

Figure 1. Testosterone and some of its precursors and metabolites.



Androgenic activity is marked in gray (the deeper the gray tone, the greater the androgenic activity). The thickness of the arrows indicates the significance of the metabolic pathways. The metabolic steps which primarily occur in the adrenal glands are shown to the left of the vertical line. The remaining reactions are catalyzed mainly in the testes, prostate and ovaries. The dashed line indicates conversion of testosterone into estrogen.

DHEA= dehydroepianrosterone, DHT= dihydrotestosterone

thereby enabling increased training frequency. AAS probably also mediate an anti-catabolic effect by binding to the cortisol receptor, as well as exert certain effects through the estrogen receptor.

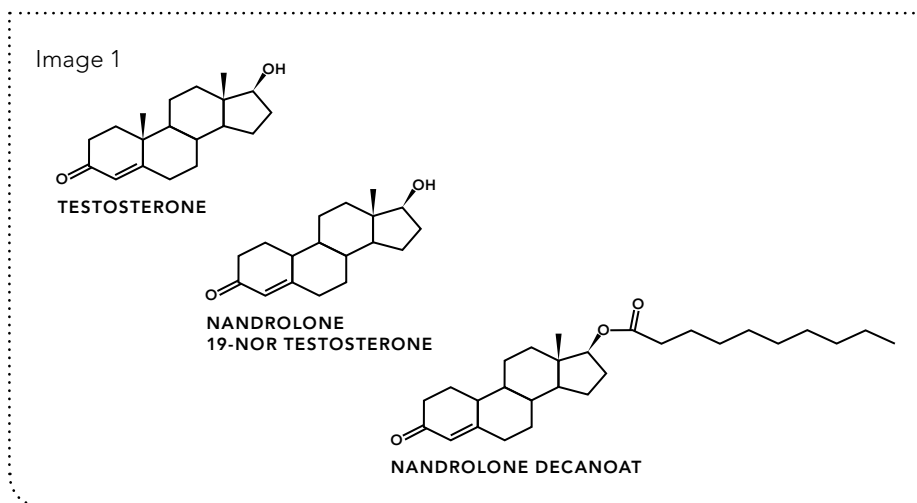
1.6 Doping in Sports

The use of doping substances in competition and during training has been banned for many years by the Swedish Sports Movement. "The World Anti-Doping Code" provides the framework for international harmonization in the fight against doping in sports. A doping list of prohibited substances and methods – issued by the World Anti-Doping Agency (WADA) – is a cornerstone of the World Anti-Doping Code. Apart from AAS, this list also covers a range of drugs and substances, both legal and illegal, that are either performance enhancing, or that mask the use of such drugs. This List provides a definition of doping in sports, which can be found on the Swedish Sports Confederation's website. This site also provides regulations governing anti-doping in sports, with associated guidelines concerning, among other things, doping controls and therapeutic use exemptions.

2. SUBSTANCES

2.1 Anabolic Androgenic Steroids

Approximately twenty different types of AAS-substances are encountered on the illegal drug market. The “ideal” doping substance would be one that has good anabolic effects, with only minimal androgenic effects. It is next to impossible to separate these two characteristic properties from each other thus, the term AAS. AAS are either physiologic (endogenous) or synthetic (exogenous), with similar chemical structures. The most commonly used substances are testosterone and nandrolone (5). Both have a similar chemical structure, and similar effects (see image 1).



A list of prohibited doping substances can be found on the Swedish National Institute of Public Health website (see Internet address at the end of the document).

Table 1 **Commonly Abused Substances**

ORAL SUBSTANCES		INTRAMUSCULAR SUBSTANCES	
Active substance	Brand name	Active substance	Brand name
Methandienone	Dianabol	Testosterone	Sustanon Testo depot Nebido
Stanozolol	Winstrol	Nandrolone	Deca-Durabolin
Oxandrolone	Anavar	Boldenone	Equipoise
Oxymetholone	Anadrol	Trenbolone	Parabolan

2.2 Other Substances of Abuse

AAS are most commonly used in combination with other substances and drugs, in order to achieve augmented effects and minimize adverse effects during AAS abuse.

Alcohol

The combined use of alcohol and AAS exists. This combination has been shown to cause increased levels of aggression, and lead to impaired impulse control.

Antiestrogens and Aromatase Inhibitors

These substances are abused with the intention to reduce the risk of gynecomastia, to maintain testicular volume, and to promote the endogenous production of testosterone after completing a cycle. Considered separately from other doping substances, these substances have less potential for abuse, since the testosterone concentrations acquired rarely reach high levels. Estrogens provide feedback inhibition on the

hypothalamic-pituitary system, and modulate the gonadotropin (LH, FSH) secretion. Administration of anti-estrogen or aromatase inhibitors blocks the production, as well as effects, of estrogen, and hereby testosterone production by the testes is increased.

Clenbuterol

Clenbuterol, is a β_2 -adrenergic receptor agonist, originally used to treat asthma, but is currently approved only for veterinary use. The drug is known to increase muscle mass and reduce body fat. Development of tolerance to Clenbuterol at the receptor level is known among users.

Ephedrine

Ephedrine is abused primarily by those who wish to increase body fat loss. In 2005 ephedrine was classified as a prescription drug due to its high content in dietary supplements.

Gonadotropins

hCG (Pregnyl) stimulates the Leydig cells within the testes to produce increased quantities of testosterone, and thus acts in the same way as LH.

IGF-1 (Insulin-like Growth Factor-1)

Is taken to increase muscle mass. However, the effects of IGF-1 have not yet been fully elucidated.

Insulin

Insulin is being abused because it facilitates glucose uptake from the blood by the body's muscle and adipose tissues and, at the same time, inhibits the breakdown of proteins. It is usually abused in combination with growth hormone.

Dietary Supplements

The use of dietary supplements is common among individuals who exercise, as a complement to their regular diets, in order to gain mus-

cle mass and reduce body fat. To date, however, there are no official controls on dietary supplements, and studies have shown that the declaration of contents often corresponds poorly with the actual contents of a product, or the product may contain banned substances. Dietary supplements may serve as a gateway to AAS abuse (6).

Prescription Drugs

Are commonly abused to minimize adverse effects, or to enhance effects of AAS. Examples include: hypnotics, sedatives, analgesics, anti-inflammatory drugs, potency enhancing drugs, antidepressants, antianxiety drugs, and diuretics.

Narcotics

Co-abuse of AAS and narcotics is common. Amphetamine and cocaine are abused in order to lose or maintain weight, while cannabis helps abusers to wind down and relax after a tough training session, and finally heroin is used for pain relief.

Prohormones

Prohormones are precursors to the sex hormones estrogen, testosterone, and nortestosterone (nandrolone) – thus they are converted to active hormones. Examples are androstenedione and DHEA.

Thyroid Hormone

Thyroid hormone is abused to increase metabolism, and thereby weight reduction.

Synephrine

A centrally stimulating substance – structurally similar to ephedrine – commonly used to achieve weight-loss.

Growth Hormone

Growth hormone (GH) is mainly abused because of its anabolic and

lipolytic properties. Growth hormone is perceived to have a positive effect on muscle and tendon ruptures. As of yet, there is a lack of evidence that supraphysiological mega doses of growth hormone (GH) alone, has any effect on muscle strength, beyond the effects acquired through a strict regimen of exercise and diet. GH appears to have synergistic effects if combined with AAS, and GH alone can stimulate collagen synthesis (7). Growth hormone – classified as both a prescription drug and as a banned substance within sports – is prohibited according to the Doping Act.



3. SYMPTOMS, SIGNS, AND ADVERSE EFFECTS

3.1 When to Suspect AAS Abuse

AAS abuse is quantitatively the greatest problem in doping. The typical patient is a male, between the ages of 17 and 30 years, engaged in weight-training, and using one or more AAS substances, who might, at some point, have tried growth hormone.

Table 2 shows a list of signs that should evoke suspicion of AAS abuse, as well as adverse effects that may require further investigation. Women abusing AAS experience the same adverse effects as men. Masculinization of features in women are common, and many of these adverse effects may be irreversible.

3.2 Somatic Adverse Effects

It can be difficult to establish a direct correlation between AAS substances and adverse effects, because of interactions between multiple co-existing factors in each individual.

Symptoms may vary between different substances, depending on the cumulative dosage, the duration of the doping cycle, the possible combination with other doping substances, as well as the intake of other illicit or prescription drugs, and alcohol. Furthermore, there seems to be an individual variation in the sensitivity to effects and adverse effects.

The short-term somatic effects of AAS abuse, to date, are relatively well documented, and there are even scattered reports of long-term effects.

Table 2 **Physical Signs and Adverse Effects of AAS Abuse**

- Rapid and significant weight gain (approximately 10 kg in 2-3 months)
- Muscular physique
- Disproportionate muscle growth, mainly around the chest, neck and shoulders
- Edema
- Severe acne, mainly on back, shoulders, and chest
- Striae (stretch marks) usually between the biceps and pectoral muscles, but may also occur on the back and thighs
- Excess body hair
- Gynecomastia (mammary enlargement)
- Altered sex drive, initially increased, then decreased, may cease after stopping cycle of abuser
- Potency problems
- Androgenic alopecia
- Cardiac problems (high blood pressure, lipid pattern abnormalities, palpitations, myocardial infarction)
- Liver abnormalities
- Local reactions at the injection site (swelling, redness, tenderness)
- Tendon and muscle tears
- Testicular atrophy (shrinking of the testicles)
- Fertility problems

Female-Specific Signs of AAS Abuse

- Abnormal menstruation
- Deepening of voice, irreversible
- Clitoral enlargement
- Increased growth of beard and body hair

3.3 Short-Term Adverse Effects

Hormonal

Supra physiological doses of AAS induce a hyperandrogenic state, in which the production of LH-FSH by the pituitary - and thus the

endogenous testosterone synthesis, and sperm production - is inhibited. Upon discontinuation of the AAS abuse, the reproductive capacity may recover, and is usually restored within a year.

There is a possible risk of permanent infertility, if laboratory and clinical evidence of hypogonadism persist for more than 2-3 years. Therefore, the negative impact of AAS abuse on male fertility must be taken into consideration in any infertility investigation.

Elevated serum levels of estrogen, androstendione, and dihydrotestosterone are seen in these patients during active abuse. AAS abuse is accompanied by a subsequent decrease in the levels of T₄, prolactin, and ACTH, without concomitant changes in cortisol serum levels. Since hormonal doping also exists among younger adolescents, AAS abuse can cause early onset of puberty, associated with the risk of premature closure of the skeletal growth plates and a subsequent shortening of the body length by 5-7 cm.

Cardiovascular

AAS abuse gives rise to an increased risk of lipid profile disturbances with decreased HDL and increased LDL, concomitant with a decrease in apo-A1, and an increase in apo-B (8). Total cholesterol and triglyceride concentrations do not appear to be affected to the same extent. The potential impact on the lipid pattern varies depending on the specific substance being used, and the total dosage, where orally administered AAS in the form of tablets in particular have negative effects.

Hepatic

Hepatic abnormalities are mainly associated with oral intake of AAS, in the form of tablets, where increased levels of transaminases, especially ASAT, have been noticed. Cholestasis and jaundice have also been encountered at times.

Mammary Glands – Skin – Muscles – Hair

One third to one half of individuals abusing AAS display gynecomastia – perceived as tender and aesthetically disturbing – often bilaterally symmetric. The gynecomastia is caused by the aromatization of testosterone to estrogen in the mammary glands. AAS abusers often try to reduce their discomfort through self-medication, which may offer a temporary relief, but no definite cure. Aggressive forms of acne may also be seen during an ongoing AAS abuse. AAS abuse probably causes hair loss, most evident in individuals with an inherited tendency to early baldness. Increased muscular volume, in combination with extensive training, increases the risk of acquiring typical skin lesions, with subsequent scarring, in the form of striae and streaks in the skin, mainly on the biceps and pectoral muscles. There is also an increased risk of muscle- and tendon ruptures.

Urogenital Adverse Effects

The testicular volume decreases during AAS abuse, due to inhibition of spermatogenesis.

3.4 Long-Term Somatic Adverse Effects

AAS inhibit LH and FSH secretion, resulting in reduced production of testosterone and sperm. In men the estrogen levels increase, sometimes to levels commonly seen in women. Long-term abuse of AAS causes a decrease in the (initially enhanced) sexual ability, followed by testicular atrophy and azoospermia. The infertility is presumed to be reversible, with full recovery of sperm production within a little over six months. Cases of permanent infertility have, however, been described with higher doses of parenteral AAS. In each infertility investigation, the male partner should therefore always be questioned about a possible AAS abuse.

In a Finnish study on a limited number of weightlifters, believed to have been abusing AAS, an increased mortality compared to controls was found at 12-year follow-up (9). Suicide and myocardial infarction

were found to be the most common causes of death. In a similar Swedish study, in which more than 1.000 former elite power sport athletes strongly suspected of having abused AAS were included, a 25 percent increased risk of mortality was found, during, and the years following, active career, with a normalization of mortality thereafter (10). Sudden cardiac death, acute myocardial infarction, stroke, and even pulmonary embolism, have been described among young men during AAS abuse in several case reports – although no cause-and-effect relationship has yet been established. In what way extremely strenuous training itself affects the risk of cardiovascular morbidity is as yet unknown. Long-term abusers likely have an increased risk of developing a condition where blood-filled cysts form in the liver (peliosis hepatis), and thereby face the risk of transfusion demanding hemorrhage.

3.5 Female-Specific Adverse Effects

Female AAS abusers usually present with a spectrum of clinical manifestations similar to that of androgen-producing tumors. Thus, hirsutism with virilization, i.e., significant increases in muscle mass, acne, hair loss along the hairline at the temples, and a tendency toward baldness is noted. Deepening of the voice and clitoromegaly are examples of irreversible adverse effects. Abuse of AAS may cause menstrual cycles to become irregular or completely absent. AAS abuse during pregnancy can cause severe virilization of female fetuses. Libido is increased initially.

3.6 Psychiatric Adverse Effects

The abuse of AAS is associated with a range of psychiatric effects and adverse reaction, which may manifest in different ways, depending on the duration of the abuse. Table 3 lists common psychiatric adverse effects of AAS abuse.

A classification of the psychiatric adverse effects has been suggested, with a division of these into three phases, where these effects generally tend to become more severe the longer the abuse goes on. Former AAS

Table 3 **Common Adverse Psychiatric Effects of AAS Abuse**

- Aggression
- Depressive symptoms (dysphoria, depression, suicidal thoughts, attempted suicide)
- Reduced impulse control
- Anxiety
- Panic disorder
- Affect instability
- Concern
- Psychosis
- Sleep disorders
- Megarexia
- Empathy disorder
- Reduced mentalizing capacity
- Jealousy
- Violence

abusers exhibit higher rates of psychiatric conditions, compared with nonusers, and individuals with an ongoing AAS abuse also show higher frequencies of depressive symptoms, aggressive behavior, and paranoid thinking than they did prior to their abuse. Other adverse effects include sleep disturbances, and delusional psychoses. Studies have found that administration of AAS to healthy individuals resulted in aggression, affective instability including manic episodes, personality changes, and in several cases breakthrough psychosis, as well as severe impulse control disorders (11). There appears to be an increased prevalence of threats, aggression, and violence against family members. Less fight or flight tendencies, as well as increased aggression in threatening situations, have been found in studies conducted among AAS abusers (12), as well as in neurobiological studies in rats. Although interindividual variations exist in terms of frequency and intensity of adverse psychiatric effects, all in all, three phases may be distinguished:

PHASE I: is a hypomanic-like state, subjectively perceived as positive by the patient, who experiences a feeling of increased self-confidence, and describes himself as being "strong and unbeatable". He also experiences increased energy, less fatigue, a decreased need for sleep, often an increase in sexual drive, and an ability to train through the pain.

PHASE II: is characterized by a loss of control and judgement, and difficulty setting boundaries. This typically manifests as new-onset mood swings, suspicion with jealousy, and sometimes aggressive behavior - both verbal and physical.

PHASE III: when the previous AAS-abuser is drug-free. The experienced positive effects from AAS - i.e., admiration from others and increased muscle mass - have vanished and are replaced by depression, anxiety, lack of energy, decreased self confidence, and impotency.

During phase II it is common for family members, such as girlfriends and parents, to raise their concerns, while the patient himself seeks help during the abstinence phase (phase III). During this phase it is important to be sensitive to signs of depression including a patient's complaints of a depressed mood with suicidal thoughts, and if so immediately offer psychiatric help.

Megarexia

Individuals abusing AAS often have a strong body image fixation, are obsessed with training and diet, and have an overall strive to become "big and beautiful". "Muscle dysmorphia" is a term used to describe a state in which even significantly muscular men perceive themselves as thin and muscularly underdeveloped. This is a specific type of body dysmorphic disorder, characterized by a distorted perception of what constitutes a 'normal' physical appearance. This can result in a significant eating disorder – a form of reverse anorexia – sometimes referred to as megarexia, or the Adonis Complex.



4. DIAGNOSIS

A diagnosis of AAS abuse is made on the basis of the gathered information obtained from the history, physical examination, and laboratory tests. Sensitivity and clinical observation are essential components of diagnostic evaluation. It is the authors' experience that patients rarely are questioned about doping, and that suspicion of an AAS abuse is seldom taken into account in the differential diagnosis. Since the effects and adverse effects are so multi-faceted, maintaining an index of suspicion to consider the diagnosis is needed.

In patients presenting with symptoms and clinical characteristics, history taking should include questions about AAS. The clinical suspicion must be verified by urine analysis for AAS substances.

Early diagnosis, through performing an adequate investigation, increases each patient's chance of receiving adequate treatment. Lack of knowledge about the abuse, means the clinical management, medical care, and nursing rest on unstable grounds. This section presents a proposal of what could be included in history taking and physical examination, and provides recommendations regarding laboratory analyses, when there is a reasonable suspicion of AAS abuse.

4.1 History and Physical Examination

Both psychiatric and somatic hypotheses are included in the patient history and physical examination. For further details about symptoms, characteristic features, and adverse effects commonly described, please see Chapter 3. Table 4 shows an example of recommended components of a medical history.

Table 4 **Medical History for Suspected or Verified AAS Abuse**

Social history	Medical/Psychiatric history
Educational level	Current complaints
Profession	Psychiatric history, including sleep
Occupation	Gynecological history for women
Spare-time activities	Previous diseases
Training experience/level	Current diseases
Networks	Current medications
Alcohol/drug use	Current dietary supplement use
Other types of abuse	Allergies/hypersensitivity
Criminality	

Characterization of AAS Abuse

In cases where it becomes evident that the patient has been abusing AAS, he or she should be questioned about what substances have been used, and to what extent.

Questions to Ask:

1. Age for AAS abuse debut
2. Duration of AAS abuse and duration of “cycles”
3. Which substances have been abused, and in what combination
4. Which pharmaceutical forms
5. Cumulative dosage for each substance

Physical Examination

The physical examination includes performing a general examination of the patient, together with an extended/targeted status, regarding specific organ systems which may be affected by an AAS abuse, as well as possible observed adverse effects. Table 5 gives an example of components of a physical examination.

Table 5 **Physical examination**

1. General appearance; Height, weight, and body mass index (BMI)
2. Heart (blood pressure, pulse, signs of heart failure, cardiac murmurs)
3. Lungs
4. Abdomen/rectal examination (hepatic enlargement, prostatic hypertrophy)
5. Urogenital (testicular atrophy)
6. Neurological examination
7. Chest (gynecomastia)
8. Skin/hair (acne, premature baldness, striae/stretch marks, especially axillary)
9. Musculoskeletal (muscular)
10. Specific to women: clitoral enlargement, deepening of voice, menstrual abnormalities, body hair

Analyses in Blood and Urine

Laboratory testing provides the basis for assessing both the nature of the abuse and the potential adverse effects. Apart from the basic laboratory tests (blood) and doping tests (urine), drug screening (urine) is recommended. An AAS abuse is considered to exist when analysis of the test, usually in urine, detects doping substances or their metabolites. Table 6 gives examples of basic laboratory tests that may be included as part of an investigation of AAS abuse.

Elevated Hb and EVF levels are observed during AAS abuse, and may reach very high levels. This can pose a certain risk of thrombus formation. Apart from being indicative of kidney damage, elevated creatinine levels may reflect an increased muscle mass as well as the rapid breakdown of excess muscle tissue.

The effect of AAS on cholesterol metabolism is often marked during an ongoing AAS abuse, resulting in high levels of LDL and low levels of HDL. Upon cessation of AAS abuse there will be a gradual reduc-

tion in LDL, and an increase in HDL.

Hepatic abnormalities may occur – especially with the use of synthetic or oral forms of AAS. During abuse of testosterone the blood levels can vary greatly, and may be completely normal at times, while LH, on the other hand, is always suppressed. The abuse of growth hormone (GH) causes an increase in IGF-1.

Table 6 **Basic Laboratory Testing for AAS Abuse**

1. Hb, EVF*
2. Electrolyte status (NA, K, Ca, Creatinine)
3. Glucose (plasma)
4. CRP
5. Liver status (GT, ASAT, ALAT, ALP, Bilirubin)*
6. Lipid status (HDL, LDL, Triglycerides)*
7. Hormones*
 - a. Testosterone (serum), SHBG (serum), LH (serum), FSH (serum)
 - b. IGF-1 (serum)
 - c. TSH, free T4
8. PSA (plasma) (men over age 45)
9. Urine samples tested for the detection of AAS and narcotics*

* Appropriate laboratory testing for assessing recovery following the discontinuation of AAS abuse.

Note that specimen collection instructions and normal value ranges may vary among different laboratories. Additional information can be obtained from each respective laboratory.

The specific doping test is performed by using a urine sample. When the doping test is carried out, a urine sample is collected from the patient under direct supervision – this in order to rule out urine specimen manipulation. AAS are classified as either water soluble or lipid soluble, which consequently makes it difficult to recommend one

particular technique for detecting the various substances. In general, positive findings are to be expected up until a few weeks after ingestion of oral steroids, whereas lipid soluble injectable forms can be detected in urine for up to several months after administration. An example of the latter is nandrolone (decanoate) – administered through injection – which can be detected long after injection, occasionally up to 12 months. Thus, in summary, the detection period can vary from a few weeks to several months after administration, depending on the substance used, as well as on its pharmaceutical form. The analysis provides the answer concerning the type of AAS that was abused – usually through detection of its metabolites. The lower reference range (cut-off) for each substance and metabolite is usually set at 10 ng/mL for a positive test.

It is not always possible to reliably distinguish between endogenous testosterone and exogenously administered substance. The testosterone/epitestosterone ratio can give indications of an abuse. This ratio is usually around 1. The normal ratio may vary between approximately 0.1-6.0, due to genetic variation. Ratios above 6.0 should raise suspicion of testosterone abuse. Nandrolone is another example where assessment may be complicated. In analysis, the substance or its metabolite (19-norandrosterone) should not exceed 10 ng/mL. Worth noting is that pregnant women can exceed this limit from pregnancy week 20, and that also oral contraceptive pills containing norethisterone, as well as ongoing menstrual periods can cause false positives tests.

For further information on analysis of doping substances, and to order these analyses, primarily contact the Department of Clinical Pharmacology at Karolinska University Hospital. Here analyses are performed on most substances, and the laboratory is accredited by Swedac. Analyses are also performed at Unilabs laboratory in Eskilstuna (the Mälars hospital).

It has become increasingly evident that combining AAS with other hor-

monal substances, prescription drugs, and/or narcotics is a common practice among AAS users. For this reason, routine testing for other drugs appears plausible.

4.2 Other Investigations

In those cases where adverse findings are suggestive of an ongoing AAS abuse, further investigation should be considered, in order to assess the extent of organ involvement or adverse effects. Investigations which may come under consideration are, for instance, ECG, 24 hour blood pressure monitoring, ECG stress test, and a Cardiac ultrasound (kidneys and liver possibly included).

4.3 Information on Laboratory Testing

Anabolic Androgenic Steroids

The analysis is performed at the Department of Clinical Pharmacology at Karolinska University Hospital, to mention one location. The test is usually not analyzed urgently, and answers are provided within a week.

Drug Screening

Analyses are performed at several Swedish laboratories, one of these being the Department of Clinical Pharmacology at Karolinska University Hospital. Laboratory tests are usually not analyzed urgently, but this can be performed upon request.

4.4 Classification and Diagnosis of AAS Abuse

ICD-10 Reporting

AAS abuse falls under the umbrella of mental health disorders, under the abuse of non-dependence-producing substances. In sub-groups of F55, steroids and hormones are mentioned as examples. Since one of the direct effects of AAS is permanent hypogonadism, short-term or long-term, this usually becomes a secondary diagnosis. Other con-

ditions that may come into question during the process of making a diagnosis, might be for example depression, psychiatric instability, violence, and paranoid tendencies. These should also be included when documenting the visit. Primary and secondary diagnosis may differ depending on the reason for seeking health care.

The following are suggested examples of diagnoses:

Primary diagnosis: In F55.9 abuse of non-dependence-producing substances (steroids, hormones) is classified.

Secondary diagnosis: E23.0E, classifies the decreased production of gonadotropins (the endocrine abnormality resulting from the abuse of anabolic androgenic steroids, leads to hypogonadism, when the deficit is not replaced with anabolic androgenic steroids).

4.5 Definition of Addiction According to DSM-IV

AAS are, as of yet, not classified as addictive substances, since scientific evidence for such a classification is lacking. According to the clinical criteria listed below, AAS abuse should be classified as an addiction in a psychiatric sense.

1. A need for markedly increased amount of the substance to achieve intoxicating effect
2. Withdrawal syndrome upon discontinuation of the abuse.
3. The substance is often taken in larger amounts or over a longer period than was intended.
4. A persistent desire, or unsuccessful efforts, to cut down substance use.
5. A substantial part of life is dedicated to obtaining, using, and recovering from the use of alcohol or narcotics.
6. Important social, vocational, or recreational activities are neglected.
7. Continued use despite somatic or psychiatric damages.



5. TREATMENT

5.1 Measures Taken at Initial Patient Contact

Upon initial contact with a patient who, directly or indirectly, seeks medical attention for an AAS abuse and/or AAS-related problems, the character and extent of the current problem is identified; through clinical, laboratory and psychosocial investigations, in accordance with the Diagnosis section. Suicidal thoughts associated with depression require immediate referral for psychiatric assessment. It is also valuable to, as early as possible, identify possible existing social problems (such as other forms of abuse, unemployment, and criminal behavior crime) which can lead to contact with Social Services.

5.2 Primary Care Treatment

If possible, treatment of occasional symptoms related to AAS abuse, should be provided through primary care. If the patient has a confirmed abuse, absence of severe symptoms, such as psychiatric disorders as well as a true desire to cease the abuse, a follow-up visit is booked within 2-3 months, for follow-up discussion, physical examination, and laboratory testing. By that time, regression of symptoms and pathological laboratory findings hopefully will be observed.

In case the patient presents with multiple symptoms, especially during an ongoing AAS abuse, referral to an addiction specialist should be made, since these patients can be resource consuming in terms of time and investigation. Referral to an addiction unit should be made in cases where a co-occurring addictions exists (i.e., opiates, GHB, benzodiazepines, amphetamines). Table 7 shows some examples of specific symptoms where referral to a specialist may be considered

Table 7 **Specific symptoms which may require specialist referral**

PSYCHIATRISTS: Suicidal thoughts/depression, signs of psychosis, aggression

CARDIOLOGIST: Heart failure, cardiac valve dysfunction, ischemia

PLASTIC SURGERY: Gynecomastia, which does not respond to medical therapy

ORTHOPEDIC SURGEON: Muscle/tendon ruptures

DERMATOLOGIST: Severe acne

UROLOGIST: Prostate symptoms, testicular atrophy

FERTILITY UNIT: Fertility problems

ENDOCRINOLOGIST/ANDROLOGIST: Hormonal imbalances (i.e., low testosterone levels), testicular atrophy, infertility

5.3 Specialist Level Treatment

The key players in management of the patient include the specialist physician – e.d., the endocrinologist or a specialist in internal medicine with a special interest in this field – joined by a psychiatrist, who is also especially interested, at an addiction clinic (staff included). The specialist physician identifies the patient's current complaints, based on former and ongoing AAS abuse, including co-existing abuse of other drugs.

Thereafter, further investigations are decided upon, based on the clinical picture and laboratory findings. Subspecialty referrals may also come into question. Laboratory testing at a specialist level is, to a great extent, identical to that at primary care level. This physician should preferably have the primary responsibility (GP) for the management of the patient, regardless of what referrals are being made.

5.4 Treatment at Psychiatric/Addiction Clinics

Addiction treatment is an important part of the initial therapy for an AAS abuse. Treatment is usually team-based, involving a physician, a nurse, a psychologist, a social worker, and a physical therapist, all wor-

king together to lay the groundwork for a realistic treatment plan. The aim of this may be abstinence from drug abuse, and treatment of current psychiatric and physical symptoms, which have resulted from the abuse, or existed prior to onset of the drug abuse. The general management does not differ from that of other abusing or psychiatric patients.

Psychiatric Investigation

After the patient has remained drug-free for approximately one month, the psychiatric investigation is initiated. Frequently encountered problems during an AAS abuse is also included in this investigation. During the psychiatric assessment the psychiatrist also decides on routine treatments for current conditions. Most common is depression – especially with suicidal thoughts and tendencies – various anxiety disorders, and sleeping problems. A psychological assessment, including a neuropsychological evaluation, and a personality assessment, is initiated after the patient has remained drug free for at least 3 months.

Specialist assessment tools include the Addiction Severity Index (ASI), the Alcohol and Drug Diagnosis Instrument (ADDIS), the Temperament and Character Inventory (TCI), and the Structured Clinical Interview for DSM (SCID).

5.5 Discontinuation of AAS

Initially, AAS abuse is often psychological in nature (with a wish to alter both one's body and personality), which later will turn into a psychological dependence. Discontinuation of long-term severe abuse results in hypogonadism-related symptoms, as well as a significant risk of developing other symptoms. The symptoms may manifest as increased cravings for AAS, dissatisfaction with one's body, depression, restlessness, sleeping disturbances, and fatigue (13).

5.6 Pharmacological Therapy

There may be a need for pharmacological therapy during ongoing, or discontinued, AAS abuse. Listed below are some suggestions of adequate treatment for different conditions.

Psychiatric Symptoms

The depressive symptomatology seen in individuals after discontinued abuse of AAS is often so extensive and agonizing that pharmacological antidepressant medication is necessary, in addition to counseling, and general supportive measures. Clinical observation suggests that these individuals often require longer periods of treatment, as well as a combination of antidepressant, and anti-anxiety medications. The combined use of SSRIs and SNRIs may be required in order to achieve full remission. Insufficient or premature cessation of therapy itself can pose an increase risk of both self-destructive actions and “self-medication” through relapse into an AAS abuse.

Table 8 presents therapy suggestions for psychiatric complaints, based on the experiences from one of our national addiction clinics.

Table 8 **Treatment proposal for psychiatric complaints**

DEPRESSION – mirtazapine 30–60 mg at night, or venlafaxine 75–150 mg/day.
May be combined when needed.

ANXIETY – If part of depression/GAD treat with venlafaxine 75–300 mg/day

PANIC DISORDER – sertraline 25–200 mg/day, or citalopram 10–30 mg/day

PSYCHOSIS (paranoia - mania) – risperidone 1–4 mg/day or olanzapine 10–15 mg
or aripiprazole 10–15 mg.

SLEEPING DISORDER – mirtazapine 15–30 mg at night, or quetiapine 25–50 mg.
Sedative-hypnotics are for temporary use only.

Endocrine Symptoms

Low serum testosterone levels (i.e. <12 nmol/L) can exacerbate pre-existing complaints – especially concerning depression, general physical and mental fatigue. An increase in serum testosterone levels to the normal range may be accompanied by improvement in mood. Complete abstinence from AAS is an absolute prerequisite for drugs to be prescribed, and a treatment contract should be established, and documented in the patient's medical record. Follow-up is performed using continuous analyses (AAS in urine, serum testosterone, serum LH)

Aromatase inhibitors are the treatment of choice in patients with residual, clinically symptomatic, and laboratory confirmed (serum testosterone <10 - 12 nmol/L), hypogonadism, 6 to 12 months after discontinuing the AAS abuse (this time period may be discussed), and when spontaneous normalization of the serum testosterone levels fails to occur. The aromatase inhibitors can increase serum testosterone to desirable levels of 15-20 nmol/L within a few months, with concomitant improvement in the patient's general condition, and without major adverse side effects

- Aromatase inhibitors (e.g., anastrozole at 1 mg/d)

Some patients fail to respond to aromatase inhibitors, which leave testosterone replacement therapy, or chorionic gonadotropins, as the only option for treatment. This type of therapy may be initiated after 4-6 weeks of treatment with aromatase inhibitors, if testosterone levels have not yet normalized. This type of therapy should be managed in endocrinology clinics/specialist centers.

- Testosterone gel (50-100 mg daily).
- Chorionic gonadotropin (1500 E subcutaneous injection, twice a week)

Treatment with testosterone gel formulas is preferable, because it is rapidly metabolized, and allows for assessment of an individual's endogenous production within a few weeks after the cessation of therapy.

Depot injections (Nebido) are less preferable, since these prevent adequate assessment of restoration of the endogenous production.

Acne

In mild cases, standard acne treatments are recommended. In severe cases, the patient should be referred to a dermatology clinic. It is important to acknowledge the existence of an AAS abuse, because isotretinoin combined with AAS may compromise liver function.

Gynecomastia

In cases of gynecomastia, medications can be used over a limited period of time (2 to 3 months) with the intention of inhibiting further growth of the mammary glands. If the gynecomastia does not regress, the patient should be referred to a surgical clinic for assessment. Correction of gynecomastia through plastic surgery is often required. Attitudes towards this type of surgery vary considerably between different surgical clinics, and patients often have to seek care from the private sector in order to have the surgery. Treatment of gynecomastia should be initiated as early as possible, for better effect. It is, however, important that this treatment does not become an integral part of a continued AAS abuse, which is why a treatment contract should be established in such cases as well.

- Aromatase inhibitors (e.g., anastrozole at 1 mg/day)
- Antiestrogen (e.g., Tamoxifen 20-40 mg/day).

5.7 Psychosocial Management

The patient referral path to a specialist may be of importance for future investigations. A self-referring patient, or a patient referred from primary care, or from another physician that the patient has seen, is often well aware of his abuse, and its associated risks, and thus motivated for therapy, which ultimately facilitates the management. On the other hand, patients who have come into care through the involvement of concerned family members, school personnel, or social authorities

(due to co-existing drug abuse), can often completely deny, or tone down their AAS abuse, which in turn might pose obstacles to further investigations and treatments. It is therefore important for treatment to be individualized for each patient, and for short and long term goals to be defined. A substantial portion of AAS abusing patients have a co-existing abuse of other drugs, and thus are inclined to have known social problems, such as poor academic/educational achievement, unemployment, and criminality (14). It is important to establish contacts between the patient, the specialist, and possibly social authorities, for support, cooperation and collaboration regarding occupation, and a life free of drugs, through testing, and driver's license endorsements. The patient's relationship with family members shows great variance, and can have a major impact on the outcome. Lending support to relatives by engaging them in dialogue, or by encouraging them to join at the follow-up visits might be valuable in some cases; and (even more so) may help motivate the patient to attend the initial, as well as, the follow-up visits.

Social Situation

People with an AAS abuse often feel that they gain support and recognition from others at the gym. Here they can socialize with like-minded, who are equally highly motivated to gain muscle mass, and become as well-trained as possible. With time, virtually no socializing occurs other than within the inner circle of the gym. The abuser's entire life usually revolves around diet, dietary supplements, doping substances, and weight training, which is all reflected in the use of social codes for topics of discussion and language usage within one's own subculture

AAS abusers often report having had a problem-filled childhood with social problems. Many abusers have struggled through hardships when growing up; some, for example, have experienced physical and mental domestic violence, while others report having been bullied, or having had concentration problems. Many abusers have low self-confidence

and self-esteem, which in turn may come to manifest itself in the urge to build a big and muscular physique, through the use of AAS.

An AAS abuse will not only affect the AAS user, but also the people present in his or her immediate surroundings. Family members often express that their lives are being negatively affected. They are also often in great need of support. The abuser goes through many physical, mental, and social changes. Those closely related to the abuser may become victims of aggressive attacks, jealousy, suspicion, and violence. Denial, excuses and lies are common among abusers since he/she fears the possible consequences of the abuse being revealed. A lot of AAS abusers perceive themselves as clean-living people, and strive to defend and sustain their lifestyle for as long as possible. The abuser is convinced that he/she is training, eating, sleeping, and abusing in the "correct" way, and seeks peer support for this in his/her subculture.

Counseling

No singular therapy is advocated after discontinuing AAS abuse. Several different types of counseling may come into question, and the discussions may have a positive outcome, no matter what the approach. Cognitive Behavioral Therapy (CBT) has been the suggested approach in the treatment of those suffering from dysmorphophobia and eating disorders. Others advocate a revised 12-step approach with an emphasis on body perception and self-image. Motivational Interviewing (MI) is a style of communication which has been proposed by a number of authors in various articles, as well as by people working with AAS abuse. Participating in counseling group therapy can offer an alternative option.

Supportive counseling serves to encourage the patient to become drug free, and to teach him to live without drugs. It also serves as guidance in the abstinence phase after discontinuing AAS abuse. Incorporating motivational strategies into the initial encounter with a patient is of primary importance

During the initial phase of therapy, it is important to establish rapport and trust with the patient. It appears to be preferable to run a quite structured conversation in the initial phase, where the positive as well as the negative effects of doping abuse are being addressed. Once the therapeutic relationship has been established the counselor can work on creating discrepancy, and support the patient by describing the negative effects of the abuse, as well as create a distinct structure in order to prevent relapse. Documenting this through the creation of a written relapse prevention plan may be preferable. The highest risk for self-destructive behavior and suicide exists during the period when the abuser has high levels of AAS in his body, and a few months following discontinued abuse. Note that an assessment of suicide risk should be a part of every clinical encounter (the provider should use a familiar and widely endorsed tool for an assessment of suicide risk).

5.8 Follow-up

Attending to mental health problems – such as depression and anxiety – through frequent clinical follow-ups, are of great importance. These problems can persist for a long time, and may last for several years in some cases. Offering regular check-ups regarding somatic complaints, with blood tests included, has proved valuable, as it can serve as motivation for the patient. Network meetings attended by professionals as well as people in the patient’s inner circle, can facilitate in developing a clearer picture of the patient’s needs and strengths. Patients who wish to continue training should be encouraged and supported to do so. Breaking old patterns by choosing to train at a different gym, is usually perceived as a positive part of treatment. Collaboration between physical therapists and personal trainers can lend support to patients who wish to learn how to train the “right” way while sparing the joints. Bear in mind that discontinued AAS use, results in an impaired muscle status – something that tends to be psychologically demanding for the patient. Some patients benefit from seeing a dietitian, who can provide advice and support.

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The Anti-Doping Hotline

Through information, education, development, and research, the Anti-Doping Hotline aims to decrease the abuse of doping substances as well as increase the level of knowledge, whilst raising awareness of the consequences of doping in society.

The Anti-Doping Hotline is located at Karolinska University Hospital, Dept of Clinical Pharmacology, and is staffed by nurses and physicians. The Hotline provides a nationwide service which has been in existence since 1993, and receives its funding from the Ministry of Culture, and the Ministry of Health and Social Affairs. The Hotline services are carried out in collaboration with various health care agencies, as well as other authorities and organizations.

A part of the Hotline activity is to provide consulting services to both private individuals and professionals having questions about doping. Hotline callers may choose to remain anonymous, and the confidentiality of callers is paramount, as is always the case in the healthcare system.

The Anti-Doping Hotline also provides an interactive website, offering the opportunity to ask written questions, receive facts on doping and doping related substances, as well as get information about our current work.

Phone: **020-546 987** for within Sweden

+ **46-8-585 811 90** for outside Sweden

Hours: Weekdays 10 am - 4 pm.

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