

FIRST NORDIC CONFERENCE ON ABUSE OF ANABOLIC ANDROGENIC STEROIDS AND ANTI-DOPING WORK
September 20-21, 2007, Uppsala (Sweden)

The conference was presented with the following words: "Society's efforts to combat the abuse of anabolic androgenic steroids (AAS) have increased, particularly in the last year due to some tragic events, in which abusers of these agents were involved. In Sweden there are a small number of groups working with general counseling and care of individuals with these abuse problems, and with different kind of symptoms. Some of these groups are engaged in research and development in the field. The aim is then partly to improve the possibilities to detect abusers of anabolic androgenic steroids and other hormonal drugs among patients that seek help for a variety of symptoms. The work is also aimed to map the abuse and its dimension, where it takes place, and how to introduce preventive measures.

The aim of the present conference was to update the knowledge about the abuse of anabolic steroids, and communicate this information to those who are directly or indirectly concerned by the problem: schools, governmental agencies, the health care system, politicians, etc.

The conference was arranged by the Swedish network for work against anabolic steroid abuse." The organising committee consisted of Mathias Hallberg, David Hoff, Tommy Moberg, Anders Rane, Kurt Skårberg, and Rolf Trulsson.

Opening addresses

In a Google search there were 3720000 hits on "testosterone" and "doping" gave 19 900 000 hits.

Historical remarks

From an historical point of view the start of the more specific search for the substance forming boys into men was when in 1889 the Harvard professor Charles-Edouard Brown-Séquard (1817-1894) self-injected subcutaneously a "rejuvenating elixir" consisting of an extract of dog and guinea pig testicle. He reported in the Lancet that his vigor and feeling of wellbeing were markedly restored but, predictably, the effects were transient. In 1927, Koch and his student, Lemuel McGee, derived 20 mg of a substance from a supply of 40 pounds of bull testicles that, when given to castrated roosters, pigs and rats, remasculinized them.

The Organon group in the Netherlands was the first to isolate and identify the hormone. In 1935 the paper "On crystalline male hormone from testicles (testosterone)" by KG David, E Dingemans, J Freud and E Laqueur appeared. The chemical synthesis of testosterone was first reported in 1935 by A Butenandt and G Hanisch. Only a week later, the Ciba group in Zürich, Leopold Ruzicka (1887-1976) and A Wettstein, announced a patent application. These independent partial syntheses of testosterone from a cholesterol base earned both Butenandt and Ruzicka the joint 1939 Nobel Prize.

In World War II German soldiers were treated with anabolic steroids. In 1950s there was a

spread medical use of anabolic androgenic steroids and an increasing use of AAS in sports.

Arne Ljungqvist, so well known that all brackets after his name are superfluous, gave his view on "Sports, anabolic steroids, and society". First he gave some landmarks regarding the use of anabolic steroids and the actions taken against them:

- 1960s AAS came into sport
- 1967 IOC Medical Commission
- 1974 First tests in sport for AAS
- 1983 Creation of CAS
- 1988 Ben Johnson caught in Seoul
- 1989 East-West relations improve
- 1991 IAAF starts out of competition testing for AAS
- 1990s Several court cases
- 1999 Creation of WADA
- 2004 Sports adopt WADA Code
- 2005 UNESCO Convention

The present fight against doping

WADA (World Agency against Doping) is created by a fifty-fifty partnership by the Olympic movement and public authorities. Its present budget is 25 million US dollars per year, with 25 percent planned for anti-doping research. The WADA Code sets the standards for:

- substances and methods prohibited in sport
- how sampling should be conducted
- how samples should be analyzed and results reported
- how TUEs should be granted
- what penalties should be imposed in case of Anti-Doping rule violation

According to the published figures from WADA from 2006 there were world-wide 198143 doping test performed, and of those were 4332 positive for doping (2.2 %):

- anabolic androgenic steroids 45 %
- beta-2-agonists 15 %
- cannabinoids 13 %
- stimulants 11 %
- diuretics and masking agents 7 %
- glucocorticosteroids 7 %

In Sweden the doping cases per category 1981-2005 has been:

- hormones 62 %
- refusals 23 %
- stimulants 7 %
- narcotics 5 %
- others 3 %

Since 1998 there has less than 0.6 percent positive cases in Sweden, even though there has been up to about 3500-4000 test a year.

Swedish law against certain doping substances (NB not according to the definitions in sports) was passed in 1991 and has been repeatedly amended, last time 2005. Banned under Swedish law is trafficking, possession, and intake. The penalty for breaking this law depends on the severity: from fine to ½ to 4 years imprisonment. The law concerns:

1. synthetic anabolic androgen steroids
 2. testosterone and its derivatives
 3. human growth hormone
 4. substances that enhance the production and release of 2 and 3 above (including aromatase inhibitors and anti-estrogenes)
- The customs has made important – and in a continuously increased number – seizures the last years, even though there has been little dedicated search for doping substances (most has been done together with seizures of narcotics and alcohol):

year number of seizures tablets ampoules

1997	49 000
1998	72 000
1999	336 236 300 23 430
2000	440 145 200 33 980
2001	565 417 400 35 630
2002	796 510 000 34 000
2003	982 619 300 55 950
2004	1043 398 550 28 160
2005	1217 172 071 12 689

There are also reports on the number of doping crimes in Sweden.

year reports prosecuted

1995	288 196
1996	320 196
1997	340 183
1998	273 291
1999	416 198
2000	438 238
2001	482 313
2002	640 343
2003	634 402
2004	925 362

The UNESCO Convention on doping is an important step against doping as it harmonizes first the thinking – and then hopefully – the actions to fight doping:

”Enables governments to align their domestic legislation with the WADA Code thereby harmonizing the sport and public legislation in the fight against doping in sport.”

Today there are legislations at least in Denmark, France, Germany (under way), Italy, Norway, Spain, and Sweden.

The American experiences of anabolic androgens in the society

Harrison G Pope (psychiatrist, Harvard Medical School) discussed “Abuse of anabolic androgenic steroids in the society: a problem underrecognized by the medical profession”. There are three main ingredients from a social point of view of the misuse, i.e. not medically indicated use, of anabolic androgen drugs:

- highly effective drugs
- supportive social climate
- individuals with body-image concerns

He reported on his studies on adult male physical self-images, and found that a large part of men think that they have too little muscle – irrespectively how much muscle they actually have – and wants to have more muscles. If the men then work on getting more muscles there is no tendency that they think they get enough; rather these individuals still think that they are “too small” and want and need more. This means that there is no saturation limit for these persons. The researchers also had investigated if the men could describe their body in an accurate way, and found that the men at least described that they had less muscles and were more fat than they really were. There are also indications that they thought that they were less sexual attractive than they ought to be due to too little muscle. On the other hand, when ordinary women were asked what body images they were attracted by they usually described perfectly normal looking men. This means that there is an obvious discrepancy between how much muscles adult man have, how much they think they have, how much they think they should have, and how much they think women like them to have [Kanayama K, Barry S, Hudson JI, Pope HG. Body image and attitudes toward male roles in anabolic-androgenic steroid users. *Am J Psychiatry* 2006; 163: 697-703].

Pope’s group had also interviewed 89 male weightlifters [Kanayama et al. *Am J Psychiatry*, 2006]; 41 non-users of AAS and 48 users of AAS, of the latter group 24 “experimenters” and 24 “heavy users”. The preoccupied thought how these groups evaluated themselves as too small and needed to get bigger were 65, 85, and 95 percent, respectively. To the question “Have you refused to take your shirt off in public?” the answer was yes in 10, 35, and 45 percent, respectively, and to the question “Have you given up enjoyable activities because of this preoccupation (e.g. going swimming)?” the answer was yes in 7, 17, and 38 percent, respectively. These answers further underline that the users of anabolic androgenic steroids have – or get – a weird way of looking at their bodies; an unhappy and unfair way.

There are obvious social and traditional differences between different countries. Examples of this are that in China up to now there has been little interest in getting a body with a lot of muscles (on the other hand, old age is much respected). Also in large part of the Latin world there is little interest for muscular bodies, whereas the “Californian life-style” exaggerates big muscles, youth and sun tan in men (and big breast is women). This means that there are different drives for use in different parts of the world.

To the question on how many users of anabolic steroids there are in the US, Pope responded that false positive response to questionnaires is an important problem. It is common that American persons think that they have used anabolic steroids even though they have only used corticosteroids or nutritional supplements boasting of anabolic effects. However, a good

guess is that there is about 1 million US adult males using AAS, i.e. 1 percent of the population, whereas about a tenth of that is found in a female population.

Take together Pope advocated that:

High effective drugs + supportive social climate + individuals with body-image concerns → steroid abuse.

Raging hormones

Pope then went on with a second part of his talk, named “Anabolic steroids, mood disorders, and violence” and gave examples of “raging hormones” effect on normal young men. He had written on maniac or hypomanic episodes in steroid users [Pope et al, Arch Gen Psychiatry, 1994]. He gave figures of significant mood changes reported by individuals taking low doses of AAS in 7 percent, on medium doses in 10 percent, and high doses in 28 percent. The medium dose was then defined as 300-1000 mg testosterone per week, which might be compared with 50-70 mg testosterone per week produced by a normal male.

He also highlighted the Scandinavian work on manner of deaths in users of AAS [Pettersson et al, Drug Alcohol Depend, 2006]. The percentages of deceased users were 44 percent of all intentional deaths in steroid users, about 5 percent in amphetamine users, and 9 percent in heroin users. Twenty-two percent of the homicides were steroid users, whereas no of amphetamine and heroin users were in the homicide group. In the suicide group the corresponding figures were 25, 5, and 10 percent, respectively.

In one study regarding last three years criminal offences in 25 percent of violent criminals the individual was AAS-positive, whereas 12 percent in AAS-negative were convicted by violent crime; weapons 12 to 2 percent, respectively, fraud 8 and 18 percent, and crimes against property 18 versus 40 percent [Klötz et al, Forensic Sci Int, 2007].

Pope described in detail the effects of supraphysiologic doses of testosterone on mood and aggression in normal man [Pope GH, Kouri EM, Hudson JI. Effects of supraphysiologic doses of testosterone on mood and aggression in normal man; a randomized controlled study. Arch Gen Psychiatry 2000; 57: 133-40]. He had performed a randomized controlled trial in 52 men. Of them 26 had no gym experience or AAS, 13 had gym experience but denied AAS use, and 13 had gym experience and AAS use. It was a cross-over study with testosterone in increasing doses (200 mg → 600 mg) versus placebo with two wash-out periods, altogether six weeks times four. The subjects were evaluated with, among other tests, with “young manic rating scale”. The rating was 1 with placebo, 2.5 with 300 mg testosterone and 4 with 600 mg testosterone. However, the response was marked uneven between the subjects. Actually, most had only minimal hypomanic symptoms (85 %), whereas 11 percent had a moderate change of mood, and only 4 percent of the individuals had a marked response, i.e. two persons. During this relatively short time-period there were no signs of increased muscle mass, and there were no correlation between blood levels of testosterone and changes of mood measured. In a computer-game with a possible aggressive behavior the subjects on testosterone were found to act with a dose-response aggressiveness. It was not possible to predict the aggressive behavior in advance.

It is a wide spread belief among the not medical educated users of AAS that nandrolan gives less mood changes than other anabolic androgenic steroids. However, this has not been

scientifically tested.

What should raise the suspicion?

There are certain psychiatric clues to possible use of anabolic-androgen steroids in men:

- uncharacteristically aggressive behavior
- uncharacteristic hypomanic symptoms
 - o grandiosity
 - o decreased sleep
 - o hypersexuality
 - o recklessness
- uncharacteristic depressive symptoms
 - o sudden depression onset
 - o anhedonia
 - o hypersomnia

In the US and UK an ominous development is the tendency of AAS users to also use opiates [McBride AJ, Williamson K, Petersen T. Three cases of nalbuphine hydrochloride dependence associated with anabolic steroid use. *Br J Sports Med* 1996; 30: 69-70; Arvary D, Pope HG. Anabolic steroids: a possible gateway to opioid dependence. *N Eng J Med* 2000; 342: 1532; Kanayama G, Cohan G, Weiss RD, Pope HG. Past anabolic-androgenic steroid use among men admitted for substance abuse treatment: an unrecognized problem? *J Clin Psychiatry* 2003; 64: 156-60].

Endocrine expression of androgen abuse

Egil Haug (Hormone Laboratory at Akers University Hospital in Oslo) spoke on "Endocrine expression of androgen abuse". He started by giving some epidemiological data from Norway:

Wichstrøm & Pedersen 2001 (n=8877), age 15-22 years 0.8 % positive
males/females = 2/1
Pedersen et al 2001 (n=10828), age 14-17 years 1.8 %
males/females = 2/1
The Heltet study 2003 (n=9500), age 13-18 years 3.0 %
males/females = 2/1
Pallesen et al 2006 (n=1351), age 16-18 years 3,6 %
males/females = 6/1

He then gave an overview of the human physiology of testosterone. Testosterone induces spermatogenesis, increase of muscular mass, stimulation of sexual activities, inhibition of breast development, stimulation of protein synthesis and bone marrow red cell production, and reduction of plasma lipids. Dihydrotestosterone differentiates the external genitalia, differentiates prostate growth, stimulation of hair follicles and sebaceous glands, affects LH negative feedback, and possibly also influences spermatogenesis. Estradiol works through a negative feedback on LH, causes epiphyseal fusion, and develops the breasts.

There are several endocrine side effects in males:

- supraphysiological doses of AAS ® suppressed anterior pituitary function
- LH⁻ ® reduced testosterone production
- FSH⁻ ® reduced sperm production, reduced fertility, and reduced testicular volume
- changes in libido
- using AAS ® increased sexual activity
- between cycles ® decreased sexual activity
- reduced ejaculate volume
- water retention
- breast enlargement (gynecomastia)
- the enzyme aromatase converts testosterone to estradiol, which stimulates breast growth, "bitch tits"
- prostate enlargement?
- increased prostate volume has been measured in AAS abusers, but no significant increase in cancer of the prostate
- reduced hormone binding proteins
- reduced serum concentration might have hepatic effect
- reduced total hormone concentration might have no change in the free, biological active concentration

In females the most important side effects are:

- supraphysiological doses of AAS ® suppressed anterior pituitary function
- menstrual disturbances with oligo- or amenorrhea
- reduced fertility
- changes in libido
- reduced size of mammary glands
- water retention
- virilizing effects on the foetus??
- there are also obvious virilizing effects
 - o growth of sebaceous glands ® acne and oiliness of the skin in the head, face and chest
 - o increased body hair (hirsutism)
 - o deepening of the voice
 - o enlargement of the clitoris
- hair loss like in males ® male-pattern baldness

The side effects in women are more or less irreversible.

Also in children are there documented side effects:

- premature virilizing in both sexes
- premature closure of growth plates ® reduced final height
(used in medicine to treat boys predisposed to excessive height)
(misused in sport to optimize the height of gymnasts)
- suppression of pituitary LH/FSH-secretion ® reduction in testicular size
- gonadal function is usually normalized when AAS use is stopped

For all there are documented haematological side effects:

- testosterone increases the production of red blood cells ® increased haemoglobin

concentration

- stimulates erythropoietin (EPO) production in the kidneys
- stimulates erythropoietic stem cells in the bone marrow @ increased number of EPO-responsive cells

From a medical point of view this means that there is an increased risk of having thrombo-embolic complications like stroke. However, this has not been documented as a true effect in epidemiological studies (yet?).

Haug concluded that abuse of anabolic-androgenic steroids are known to produce a wide range of endocrine side effects , but the prevalence of permanent endocrine side effects is not known. Usually normal endocrine function is restored when the abuse is stopped

Anabolic steroids and the brain

Professor Fred Nyberg (Uppsala) had been given the task to discuss “Anabolic steroids and the brain.” Regarding how the brain is affected by anabolic steroids there were in PubMed less than 10 publications in 1995, but in 2007 it is found 176 publications. If the MeSH is “testosterone AND brain” there were on the day of the conference 8445 publications available. However, regarding the effects of doping it is still problematic as the doping population always use steroids at superphysiological doses. Another problem is that the doping individuals not seldom also take other drugs, and there is a fluctuation – or maybe an increase – over the years. In one comparative study of AAS in high school students there was in the survey of 1575 students from their 1st yr at high school in 1995 a use of anabolic androgenic steroids in 2.7 percent of the boys and 0.4 percent of the girls. In a similar study (n=636) in 2002 4.6 percent of the boys had uses AAS and 0.4 percent of the girls. However, most troublesome was that it was concluded that use of AAS often was combined with use of narcotic drugs and involvement in violence.

The reported effects of AAS related to brain are:

- euphoria
- increased energy
- increased self esteem
- increased sexual activity

- aggression
- impulsivity
- irritability
- acts of violence

- anxiety
- psychosis
- depression
- eating disorders
- decreased cognitive capability

Since the first noted influence of anabolic androgenic on the brain it has been discussed if the AASs can change the personality. From a psychobiological perspective it may then be postulated that temperament is dependent on genetics, whereas character is dependent on environmental factors. If that is true it should be most rewarding to study the character after giving AASs. In rats it can be studied for example anxiety (“fleeing” and “freezing”), impulsivity (spontaneous locomotion), rewards (free alcohol consumption), and aggression (defensive aggression). It has then been shown that pretreatment with AAS increases alcohol intake [Johansson et al, Brain Res Bull 2000].

Opioid peptides balance the activity of dopamine in the brain reward system, with dynorphin as inhibitor and enkephalin/beta-endorphin as stimulator of dopamine – it is well known where in the brain these effects take place. It seems as if AAS induce an imbalance between endorphins controlling the dopamine activity in the brain reward system. AAS also induces an imbalance in the dopamine system [Kindlundh et al. Europ J Neurosci 2001; 13: 291-6]. Self-administration of testosterone is blocked by dopamine receptor antagonists. It is shown that AAS affect the effect of morphine in experimental mice: AAS reduces tolerance to morphine and increases the reaction to opioid withdrawal [Celerier E, Yazdi MT, Castane A, Ghozland S, Nyberg F, Maldonado R. Effects of nandrolone on acute morphine responses, tolerance and dependence in mice. Eur J Pharmacol 2003; 465: 69-81]. In other rat experiments AAS increase defensive aggression which is significantly worse together with amphetamine. AAS induce dominant behavior and increase neuronal activity (c-fos) in central amygdala (a brain area involved in aggression) [Johansson-Steensland et al. Eur J Neurosci 2002; 15: 539-44]. In conclusion, it is shown in rat experiments that:

- AAS increase defensive aggression
- AAS increase dominant behavior and decrease anxiety
- AAS increase free intake of alcohol
- AAS increase sensitivity for other drugs of abuse (amphetamine and cocaine)
- AAS potentiate opiate abstinence

Nyberg finished by advocating that there are many questions yet unsolved regarding the mechanism of action of the anabolic androgen steroids. Examples of these are:

- by which mechanism do AAS affect the brain?
- do they interact with steroid receptors?
- are AAS receptors present in the brain?
- how do AAS interact with neuropeptides, dopamine, serotonin, and other brain transmitter systems?

Crime and premature death

The Uppsala-Stockholm research around anabolic androgenic steroids, crime and premature death, i.e. a medico-legal perspective, was discussed by Ingemar Thiblin. He defined several different groups of users/misusers of anabolic steroids:

- elite athletes (a small group)
- “non-competing athletes”, well-adjusted individuals with esthetic motives (the largest group)
- competing body builders or fitness athletes
- young men (and women) with a propensity for drug misuse and criminality
- established drug addicts
- professional criminals

The number of individuals documented to use anabolic androgen steroids Thiblin characterized as a tip of an iceberg. Less than one third (approximately 1500 cases) of the 5500 deaths per year subjected to medico-legal autopsy in Sweden is tested for illicit drugs. Approximately 30 cases (i.e. 0.5 %) are tested for AAS. For example, in a cohort study, only 50 percent of the AAS users that died were tested for anabolic steroids. Only three of those were positive in connection with the autopsy. During the latest 10-year period 30 percent of all AAS positive cases were disclosed by 3 of approximately 30 active forensic pathologists. The police often demands analyses for illicit drugs and benzodiazepines, but only exceptionally anabolic androgen steroids, on apprehended violent perpetrators at custody. However, there seems to be an improvement the latest years.

As a screening, one might look for signs like

- striae
- typical muscular physiomy
- gynecomastia
- testicular atrophy

Also there might be information of AAS possession, tip from relatives etc. Frequent findings at autopsy are:

- cardiac hypertrophy (concentric left ventricle type)
- testicular atrophy
- adrenal atrophy
- atheromas (fatty streaks)
- sparse visceral fat
- microscopic cardiac changes

In a study of succumbed under the age of 30 there were 7 percent in those not using anabolic steroids and 34 in the group that had been on anabolic steroids; a highly significant difference. Regarding cardiac hypertrophy the corresponding figures were 14 and 36 percent, respectively. For coronary sclerosis the comparison was 1 percent versus 13 percent.

In an autopsy study of 68 individuals that had been on anabolic steroids when they died, 43 percent died in an accident, 21 by suicide and 19 of homicide, 7 percent indeterminate, and only 10 percent of "natural causes". In the 19 that had been user of AASs earlier the corresponding figures were 32, 42, 0, 5, and 21 percent, respectively. Of those who used anabolic steroids 92 percent died by shooting and 8 percent by knives or alike.

It is clinically important to differ between the "steroid rage" and "strategic crime violence".

The steroid rage is characterized by:

- long term use of AAS
- current use (on-phase)
- impulsive
- negligible provocation
- uncontrolled violent rage with severely injured victims
- both domestic violence (including child abuse) and violence towards strangers
- offenders often, but not always, loaded with a personality disorder or other psychiatric disturbance, e.g. ADHD

- acute alcohol or benzodiazepine intoxication common triggering factor

Regarding strategic violence it might be discussed if this is just be that using AAS is part of a narcissistic criminal life style with fast cars, startling girl friends, heavy golden neck chains, muscles etc.

Testing of AAS

Mats Garle from the Karolinska University Hospital at Huddinge, “Dopinglaboratoriet”, discussed the AAS problem from a doping laboratory point of view. He stated that there are few laboratories analyse AAS today outside the sports testing. His department at the Karolinska at Huddinge started 1990 to analyse anabolic androgenic steroids on request from school nurses. Up till today the laboratory has analysed about 26 000 urine samples for AAS outside sports testing. These samples are coming from public medical service, workplace drug testing, forensic laboratory (police), prisons, and institutional care.

The basis for the testing today is the Gas Chromatography Mass Spectrometry (GCMS) analysis. The urine sample is then worked up with a extraction and derivatizing step. The urine sample is after that analyzed by using a gaschromatograph-massspectrometer instrument that gives a sample analysis time is 20 minutes with a printed report (10 pages) of chromatogram. Some of the anabolic steroids could also be analyzed with Ultra performance Liquod Chromatography – Tandem Mass Spectrometry (Quattro Premiere).

The outcome of testing is quite different with regard to from where the samples are taken. As an example of this the test from 2004 may be taken:

total tests positive (%)

workplace drug testing 964 24 (3)

patients 412 86 (21)

prison and others 351 74 (21)

The positive test then concerned nandrolone (n=126), testosterone (54), metandienone (22), stanozolole (14), methyltestosterone (9), boldenone (7), trenbolone (3), drostanolone (2), oxymetholone (2), metenolone (1), and mesterolone (1). There was one substances found in 105 samples, two substances in 37 samples, three substances in 15 samples, four substances in 3 samples, and five substances in one sample. In the first half of 2007 the figures are about the same:

total positive (%)

patients 258 48 (19)

workplace drug testing 993 16 (2)

prisoners 704 72 (10)

forensic laboratory 519 154 (30)

Doping as a social practice

Inge Kryger Pedersen (Department of Sociology, University of Copenhagen, Denmark) gave

a lecture on “Bulked-up bodies and education. Doping as a social practice”. Her starting point was to find out which social factors that initiate potentially dangerous taking of anabolic steroids to become bigger within the gym culture.

A relatively high percentage, 7.8 percent, of men training in Danish gyms has reported, that they have taken anabolic-androgenic steroids to enhancing their achievements or to modifying the appearance of their bodies [Pedersen, Benjaminsen, 2006]. The frequencies of doping are, however, very much dependent on how the population is selected:

0.6 % [0.3 %; 0.9 %]: a random sample of the Danish population of age 15-50 years (n=2003)

1.6 % [0.8 %; 2.4 %]: athletes in national elite teams of 14 selected sports federations (n=995)

4.7 % [3.4 %; 6.0 %]: members from 15 gyms and fitness centres (n=1035)

1.8 % [0.3 %; 3.3 %]: gymnasts on geographically representative teams of local athletic associations (n=325)

1.3 % [0.7 %; 1.9 %]: runners in the Copenhagen Marathon 1999 (n=1621)

9.4 % [7.6 %; 11.2 %]: licensed competitive racing cyclists (n=1060)

A Danish doping study now tried to identify the social characteristics of those who use drugs to analyse the relative importance of social indicators. There were 7040 responses collected in different physical exercise and sports communities. There was a straight correlation between education and use of drugs; those with lower education used more – except for bikers, where the well educated tended to use more drugs. Regard legal drugs that might increase athletic performance (e.g. caffeine tablets, sedatives, painkillers, diuretics, diet cures, asthma and locally anaesthetising drugs, extra proteins, creatine, ginseng, or schizandra) 43 percent of gym members have tried it. Of the men with low education and high training frequency (> 5 times a week) 82 percent had tried the legal drugs.

Taken together the study showed social differences in modifying the body with chemicals. It is then interesting to note that educational differences play such a big role in the gym study but a rather limited role among elite sports athletes on the national level. The distinction between the use of AAS for esthetic reasons and for purposes of improved athletic performance in a more functional sense may be important when seeking to identify factors associated with steroid use [Backhouse et al, 2007]. However, one must than question if this visual or esthetic appraisal is only a question of individual taste or not. This may be seen against a backdrop shown by Pedersen and Benjaminsen [2006], where 90 percent of the gym respondents with doping experiences agreed that the use of doping substances may be damaging for their health. Nevertheless, they were using these substances.

Pedersen concluded after empirical findings that:

- the reported use of doping substances varies significantly according to variables such as gender, age, education, training frequency, but also type of sports activity
- young men with lower education, who train frequently in gyms, seem more willing to experiment with pharmaceutical substances than others in the respondent categories
- it is remarkable that educational differences play such a significant role in the use of, dealings with, and attitudes towards doping substances among gym members
- in contrast, educational differences play a rather limited role in the rest of the sports milieus surveyed, particularly among elite sports athletes on the national level.

These findings make her convinced that doping should be looked upon as a social and cultural phenomenon and not only as an individual choice. Therefore future doping studies should be qualified with a perspective of body image instead of focusing on a rational choice perspective.

Psychosocial aspects on abuse of anabolic steroids

Tommy Moberg (Faculty of Social Sciences, Gothenburg) discussed the circumstances in society of doping. His gateway to the doping was through caring of abusers of narcotics, where it was found a substantial co-abuse of anabolic steroids.

When dealing with the victims of anabolic androgenic steroids Moberg repeatedly found that jealousy was the norm, and beating the nearest relatives (mother, father, girl-friend, younger brothers etc) was not uncommon – something that is seldom planned, but is something that happens by chance (i.e. the abuser cannot explain why it happens, and from a logical point of view it is not possible to understand).

Besides the aggressiveness caused by the anabolic androgenic steroids it is found problems with sleeping, monodepressiveness with much faster mood changes than in “ordinary” bipolar diseases, high frequency of suicide (after the use of the drugs), psychoses, and psychological dependency (as after amphetamine abuse). It is “normal” with a denial of the abuse. Of course all these effects of steroids use influence the society, both on an individual level and on a larger scale.

Moberg has for a long term been the coach and trainer for a successful junior handball team. He declared that his players are not allowed to attend gyms – he does not trust them – and they are not allowed to use dietary supplements – Moberg does not trust them either. Overall he declared his view on modern sports:

- the joy of sports is partly replaced by money and business
- winning can be done at any prize
- the physical capacity is overestimated regarding self-esteem and quality of life
- there is a tendency to look for shortcuts to the prize of losing more longstanding achievements
- money and success are evaluated higher than success
- drugs are accepted as short-cuts to success
- winning is equivalent with economical benefits

Medical management of abusers of anabolic steroids

Kurt Skårberg (Psychiatric Research Centre, Örebro) reported on his work in an outpatient clinic for drug abusers, with special effort on anabolic-androgenic steroids. He repeated that he often saw patients using not only anabolic steroids and other illegal drugs. His patients usually explain that they feel real fine when they are on anabolics, and find it difficult to stop as they then feel worse. They are also during drug intake sexually “wild” which to a certain point may be positive also for a partner, but in the long run may be disastrous. The aim of the treatment in these cases is a total abstinence from all drugs, including alcohol, to increase the

long-term social, mental, and somatic well-being. In the follow-up of their clients they usually take urinary and blood tests.

Skårberg has recently described the criminality part of the anabolic misuse [Skårberg K, Engström I. Troubled social background of male anabolic-androgenic steroid abusers in treatment. *Subst Abuse Treat Prev Policy* 2007; 2: 20]. He strongly underlined that individuals using anabolic steroids almost always use several illegal and not-illegal substances, such as: hormones, narcotics, alcohol, legal pharmaceutical substances, and dietary supplements.

In the clinic in Örebro it is done a psychiatric evaluation not until the patient has been off drugs for at least a month, and a psychologic evaluation not until after two months freedom from illegal drugs. Then it is performed a neuropsychiatric evaluation and test on the personality (Symptom Checklist 90, SCL-90; Personality Disorder Questionnaire, DIP Q; Temperament and Character Inventory, TCI). It is then also made a somatic evaluation. In Örebro they have also treated a few patients in-hospital.

Clinical management

Eva Edin (Psychiatrist from the Dependency Unit, Gothenburg) works on the oldest still working anti-narcotic out-patient clinic in Sweden. The clinic aims at users of illegal drugs with psychiatric problems. In Gothenburg amphetamine and cannabis was for a long time the only frequent drugs on the market, but during the 1990s heroin became frequent – but anabolic androgenic steroids were never discussed (even though they were probably there already then). Common for these patients are that they are open to discuss drugs overall, but they do not spontaneously report on anabolic androgenic drugs – one cannot be sure that they really look upon AAS as pharmaceutical substances, but more as a normal part of life.

Since 2005 all the patients are tested with ASI, Addiction Severity Index, and a primary evaluation shows that 80-90 percent of all new patients use AAS. Those patients that they feel better on anabolic androgenic steroids, have better sex, need it for bodybuilding but also for being able to perform the criminality they are hired for. There are also individuals that has started using anabolic steroids when in prison and treatment home as these drugs usually not have been tested for.

For a semistructured interview for a psychiatric diagnosis the unit in Gothenburg use:

- DSM-V, Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, 1994, American Psychiatric Association
- SCID I, diagnostics of psychiatric disease
- SCID II, diagnostics of abnormal personality

In a dependency unit, primarily attending due to narcotics, the individuals using AAS is a selected group that has a psychiatric bad situation, and most of the patients have already tried antidepressants. It seems that these patients as group are more vulnerable and have a more severe psychiatric prognosis. However, in Gothenburg there months is considered the time limit to make a secure psychiatric diagnosis.

In a follow-up of 24 patients with primarily abuse of anabolic steroids it was found that

some had disappeared to prison, and some was difficult to reach due to threats from criminal organizations of Hells Angel's type. On the other hand there were also a few that did not need more than a short time contact, and were not so interested to have new contacts with the psychiatric/anti-narcotic team. However, taken together, this tells something about the social situation of the AAS-users.

Of the remaining patients, all needing long term contacts, there were some characteristic factors:

- "heavy" personalities with slow affections
- cognitive dysfunctions
- depressivity
- social anxiety or fobia
- sexual dysfunction
- relation problem
- paranoia
- jealousy
- irritability

When comparing with other psychiatric patients, Edin's impression was that it takes longer time to establish a constructive relation. On the other hand, not until a trustful relation is established there is a possibility to detect the hidden paranoid component, but then it is almost impossible to hand over the patient to other part of the treatment team.

A small group of patients was characterized as "clean body-builders". They were

- well organized, well structured
- unproblematic childhood
- little criminality compared to the others
- 18-45 years
- seldom psychiatric problems before using AAS

Anabolic steroids among prisoners

Fia Klötz () described the finding from investigations from the Österåkeranstalten, a prison for about 150 prisoners in middle Sweden. Fifty-nine men were recruited and 56 percent of them admitted taking AAS before.

The AAS-users were younger; otherwise there were no demographic or somatic differences compared to those not admitting AAS-use. They all had the same history with respects to parents' health status, type of violence etc, and the abuse history was about the same. Not even crime including violence differed. This means that in this selected population AASs were of little importance – they might be quite different from those seen in the out-patient psychiatric care.

Of the AAS users the median age for the first use was 28 years. Of the users 81 percent had used injections, and 74 percent used injections as the first administration of the drug. For 27

percent anabolic androgen steroids were the first drug they used over all. They gave as the reason for taking the drug esthetics, curiosity, and longing for increased strength. The most common drugs used were decadurabolin, stanzolol, and methandienone (imported from Russia or Thailand). The users reported several symptoms and signs at use of AAS:

- 49 % irritated
- 27 % violent
- 30 % depressed
- 20 % dependent of the AASs
- 36 % drugs against side effects

Eight individuals estimated that AAS was the primary cause of crime (violence), five of them had taken AAS together with alcohol.

These findings indicated a more complex picture of misuse of androgenic anabolic steroids than what is usually reported from the sports federations and the police.

The Swedish illegal market of AAS

Gunnar Hermansson has for a long time worked in the central Swedish police authority with actions against smuggling of doping.

Sweden is probably the only country where also the use of anabolic steroids is illegal. The law is from 1991 (no 1969):

- synthetic anabolic steroids (39 named substances)
- testosterone (1 substance)
- growth hormone (1 substance)
- chemical substances that increase the synthesis or the blood levels of testosterone and growth hormone (3 substances)

An unofficial list of substances can be found on www.fhi.se (look for doping).

Hermansson described how and where AAS can be bought. Nowadays almost all of the drugs today are distributed over the internet; production countries seem to be primarily Thailand and China. Together with anabolic steroids it is most often sold growth hormone, Viagra®, HCG, thyroid hormones etc.

Trends for the 2000s seem to be:

- increased availability of drugs
- more seizures but also more that use AAS
- internet for information of AAS
- internet for marketing of AAS
- AAS from China
- larger bulks and higher strength
- increased shopping of AAS together with other drugs

Hermansson reported that in Sweden the police has used more time and force against doping the last years (the night during the two days of the conference there was a massive actions against Swedish AAS drug dealers all over Sweden, with large seizures).

AAS and other drugs

Nina Gårevik (,Anti Doping Hot-Line, Karolinska University Hospital) discussed the combined use of anabolic androgenic stereroids, AAS, narcotics and other drugs together. In a larger interview study (n=2617) it was found that those using both substances are younger than those using only AAS. GHB is used mainly in the Gothenburg area. It is obvious a larger problem in the two biggest towns with combined use of AAS and other drugs (in Stockholm it was found in 42 % of 200 individuals with abuse of AAS and narcotics, in Gothenburg 19 %, whereas it was substantially lower in the remaining investigated communities – however, selection bias may be a problem in such investigations). Of those using AAS it was, in the material of the Anti Doping Hot-Line (again with some selection biases), found (%):

stanozolol methan- oxymeth- nandrolone testosterone
dienone olone

Narcotics 18 14,5 4,5 30 34
unspecified

Amphetamine 12,5 10,5 4 22,5 20
cocaine

GHB 6 6,5 2 13 10

Marijuana 1,5 1 0 2 2

* 7,6 % (200 individ. 2002-2006) of 2617 callers to Anti Doping-Hotline with AAS-abuse

Most of the AAS/narcotic-users have no education after the first 9 years of school, and use of AAS is significantly lower among those that had been at university or the like. In a comparison of the users of only anabolic androgenic stereroids with those using both anabolic androgenic stereroids and narcotics it was found that nandrolone was the most used substance in both groups. The esthetic body-builders dominated in the first group, whereas in the second group it was more unclear why the abusers used AAS.

A co work between Nina Gårevik, Anti DopingHot-Line, Juvenile Drug Unit and Club Commission, two units in the police force of Stockholm was also described. An investigation of young men and women from Stockholm accused of narcotic crimes (mean 24 years) and individuals accused of more dangerous crimes (mean 31 years). It was then found that AAS in these groups is part of a use of multiple drugs, and often without connection to sports or gym. There are obviously several different types of misuse of anabolic androgenic stereroids, and all users of narcotics can also get hold of anabolic androgenic stereroids if they are interested.

Cardiac side effects of AAS

Paul Vanberg (Department of cardiology, Akers, Oslo) described the Oslo experiences of anabolic androgenic steroids effects on the heart. In a Finish study of weight-lifters in the elite 1977-82 the mortality at follow-up was 13 percent versus 3 in a control group. This means that the weight-lifters 20 years after their best active time had a 4.6 times increased risk of dying. The mortality was due to suicide, heart infarction, and liver coma. Also in the Thiblin forensic material 1/3 of the users of AAS had heart disease at autopsy.

There are several case reports, but no long-term follow-up on this matter. It is, however, known that an increased systolic blood pressure is found in AAS-users in a short time, but these results have been disputed (probably the possible of increased blood pressure is of limited effect from a health point of view).

There is regularly increased cholesterol and LDL cholesterol, but of greater importance is that there is a strong decrease of HDL-cholesterol (40-70 %), which might have a severe influence in the long run on the arteriosclerotic process of the heart.

The thrombocytes will have an increased stickiness and an increased number of unwanted receptors after administration of anabolic androgenic steroids.

With respect to reactivity of the vessels the effect of AAS may be characterized as an epinephrine effect. That means that the arteries are hyperreactive, and act with a vasospasm to in seldom cases might lead to a localized coronary ischemia.

There is also a direct toxic effect of anabolic steroids on the heart. The AASs are injuring the mitochondrias. In the long run it is found fibrotic areas, that might give disturbances of the rhythm and decreased power of each heart beat.

It is well known – since the start of last century – that testosterone and anabolic steroids increase the hemoglobin mass. The effect is partly due to an effect on the erythropoietin producing cells, partly due to a direct anabolic effect on the bone marrow.

At echocardiography it is regularly shown the users of AAS has a larger muscle mass in the left part of the heart, significantly enlarged compared to individuals training but without use of anabolic androgenic steroids. This is due to an increased muscle and not to an increased room for the blood (the actual ventricle). There are indications of a progressive diastolic dysfunction in these cases, but the clinical importance of this is not possible to predict yet. So far there are no good prospective studies, but it is well demonstrated that at least four months studies are needed. There has also been doubt that the method not is sensitive enough for this purpose.

In a recently published Italian study of 45 body builders on AAS it was shown that they had a decreased power of the heart contractility. The decrease was related to duration of use of AAS and the dosage. The performance of the athletes was also decreased.

In an American study of 24 long-term users of AAS (12 years) there was found calcifications in the coronary vessels of the heart in 14 patients instead of expected 3.

There are obvious large differences in individual sensitivity concerning side effects on the heart of AAS.

In a Norwegian study of 36 long-term users of AAS, 8 had premature (asymptomatic) heart disease detected with CT. Most of them had left ventricular heart muscle hypertrophy of varying severity together with an impaired muscle function. All had very low HDL, with a median of 0.3 (reference value 0.8-2.1).

It was also shown that dr Paul Vanberg has a good heart himself.

There was shown a good reversibility of the AAS-induced heart muscular mass increase after 4 months – just as the extremities muscle mass increase is reversed after stopping the AAS administration. However, it is less probable that the fibrosis is reversed and the calcification will never be reversed; i.e. after long-term use of AAS the heart is injured forever.

Anti Doping Hot-Line, Sweden

The Anti Doping Hot-Line, Sweden was presented by Annica Börjesson (Karolinska University Hospital at Huddinge). The Hot-Line was started 1993, and is national (2/3 of all contacts are from the Stockholm region). After being a “project” during many years it is nowadays part of the everyday care at the university hospital, though financed by a governmental body. There are, beside the professor in charge, one doctor PhD and 3½ nurses. All contacts taken are treated with the same professional secrecy as other medical care. However, all calls are anonymous.

The aim of the Hot-Line is not only to answer questions by telephone, but also to be active in research and education. During the last years the line has been more open to society, in order to find ways of prevention. It should make reviews from the literature to increase the collected knowledge in the society, which means that the knowledge shall also be presented to the public. Moreover, it is a goal to find new treatment options, with special reference to a holistic approach. The line should be able to inform the local health authorities on how to meet doping problems in the society.

Yearly there are about 2500 telephone calls and Internet questions – the latter part is increasing fast. Each telephone call is in median 13 minutes, which means that these figures represent a substantial work-load. The majority calls are to seek information on specified substances or questions about side effects of doping substances. Also young people that work on “projects” at school are frequent callers. Persons calling because of own abuse are young; usually they started with misuse of AAS at the age of 24, and they call 1½ year later. The most common side-effects leading to a telephone call are aggressiveness, anxiety, weight-gain, depression, and enlarged breasts.

In women, side effects of doping are the most common cause of calling the Hot-Line. However, even though the number of women calling because of own doping is increasing it is a small minority compared to men. The most common causes of calling for women are enlarged clitoris and lowering of the voice. Nandrolone, stanozolol, metenolone and

methandienone were the most commonly used AAS in women.

On the homepage www.dopingjouren.se or www.antidopinghotline.eu there were 71000 individual visits in 2006.

Norwegian aspects

Anders Solheim (Antidoping Norway) spoke on the Norwegian work outside sports. In Norway an active, systematic anti-doping plan has been present for 30 years. In sports the first doping testing was performed in 1977, and today about 3000 tests are done. This has resulted in few positive tests, which probably is due to that at least the top athletes are well aware that there is a very high risk of being tested – and found guilty if doped.

Antidoping Norway is a non-profit, non-governmental trust, that is not governed by the sports organizations either. It was founded by the Norwegian government, the Norwegian Sports Federation, and the Norwegian Olympic Committee, but is financed by the state (about 20 million € per year). The trust has 12 central administrators, 8 regional coordinators, and 45 persons who perform testings in the field.

The trust works, beside the testing, with spreading of knowledge. About 300 lectures and its like are given yearly. It is important to work together with the sports federations on all levels to satisfy their need. Besides that, the trust arrange special seminars for sports doctors and physiotherapists and their coworkers. An electronic new bulletin is regularly sent to 33 000 Norwegians with interest for anti-doping.

Of the 3000 yearly tests there are found about 10 cases of doping. Most of the tests are taken on elite athletes, and on sports where it is expected to gain most of doping. However, there are tests taken also on lower levels, but then primarily to show that testing can be done anywhere and anytime. Some of the research projects that are sponsored by Antidoping Norway may be mentioned:

- individual profiling on blood
- detection of corticosteroids in urine
- stimulating substances in not regulated pharmaceutical products ("nature medicines")
- what is efficient doping control? A worldwide investigation
- long-term effects of AAS on the heart evaluated with different methods

There is also documented international cooperation from the side of Antidoping Norway, e.g.

- Council of Europe antidoping convention
- UNESCO's antidoping convention
- 10-countries cooperation in IADA
- Nordic meetings with other antidoping agencies
- bilateral commitments (e.g. China)
- ANADO
- Special agreements with international sports federations (handball)
- WADA

Antidoping Norway has made a special program for gyms, as that has been found to be places with special problems. The program will work together with the gyms to make the latter healthy and safe places. It must then be underlined that the gyms can only take responsibility for their own activity and members. After two years (2007) there are more than 100 gyms that has adopted the program:

- education of the staff of the gyms
 - o establishing of routines at suspicion of doping and training in interviewing
 - o knowledge of effects and side effects of AAS
 - o knowledge of the law
 - o diet and diet supplements
 - o advice
- availability of printed information material
 - o printed material
 - o declarations for producers, distributors and salesmen of diet supplements
- doping testing
 - o possibility to state freedom from doping
 - o updated doping substance list
 - o rules for management of positive tests
- antidoping certificates

Antidoping Norway also wants to contribute to a discussion in depth of the basic values against doping together with local authorities, police etc:

- have the issues discussed locally
- education of employees in taxpaid organisations
- education of health personal (doctors, teachers in sports and social sciences)
- information to youngsters at special risk
- til unge i risikozonen
- discussions in small groups
- coordination of activities towards local sports (testing, lectures etc)
- coordination of activities towards gyms

The military forces have been identified as an important group to reach (military service is mandatory for young men in Norway). Also institutes for higher education in sports should be given special attention, as should the police schools, and the employees in youth care, prisons etc.

Antidoping Norway has also taken initiative to a national network against doping with the military, the customs, social- and medical authorities, department for education, department of justice and police, the governmental body for legal drugs, and the anti-doping hot-line. The network should:

- map the distribution channels for doping substances, with special reference to connection to criminality
- describe the economical incentives for doping drug-dealers
- describe the environments where doping is used, with special references to criminals and users of narcotics but also to gyms and sports
- coordinate actions against doping and work as a forum for discussion of single, local projects

Danish aspects

Finn Mikkelsen from Anti Doping Denmark, ADD, that is constituted as a self-governing independent institution based on “act of promotion of doping-free sport, 2005.” It has a secretariat with 7 employees and a budget of about 18 million €. It is stated that ADD shall perform doping tests, inform around doping, institute research and development against doping, participate in international cooperation directed against doping, and help other Danish authorities with knowledge in the field of anti-doping. It is also clarified that ADD has a responsibility to strengthen the basic values aiming at defeating doping both among the elite and the non-elite athletes, and arrange that Denmark are among the leading forces against international doping.

It has also been stated why the anti-doping mission is important also for the Danish government:

- it is a public health issue
- the drugs are often imported and sold illegally
- there is a risk and spreading drugs to all parts of organized sport

It has been clarified that doping is a problem far outside sports, and physical success seems to be necessary on many social arenas. There are in Denmark indications that a gradually increased number of youngsters have tried doping, and for all of Danes there are figures of 3-4 percent that has used AAS. However, among the elite athletes the use is less frequent, 1-2 percent. The availability of doping drugs is almost unlimited in Denmark, and the focus on doping in the media has both good and bad sides.

Anti Doping Denmark has taken the stand that the body shall cooperate with the media with assistance to research on doping, interviews on doping, sending out bulletins to the media and so forth.

There are estimation in Denmark that the business on doping substances is worth about 100 million DDK (14 million €). There are about 1600 tests taken yearly in Denmark for the Danish Sport Federation, and since 1993 the percentage of positive tests in this population has been 0.5-1.2. In 2006 there were 7 positive tests and weightlifting, one in karate, 1 in American football, and 2 in rollerblade hockey. To that should be added test taken on requests by other sports association, WADA, ANADOs etc. All together 2396 tests were therefore performed in 2006. The percentage of positive test has been considerably higher in fitness centers (around 10 %) and especially in commercial fitness centers (up to 20 %). One of Anti Doping Denmark’s important tasks since 2002 is to cooperate with the fitness centers to fight the use of doping. Users of gyms and fitness centers constitute today the largest proportion admitting intake of doping substances. Therefore ADD is introducing a “green card”. This means that all members in a fitness center with green cards are informed about mandatory doping controls, but also that anti-doping information is given – each center receive a certificate, posters, and information folders. To get the certificate the gym has to pay around 1700 €. It is interesting to note that the percentage of the population paying to tka part in gyms around 9 in all Nordic countries.

When dealing with problems of doping in fitness centers there are special challenges. One of

them is that there must be a reliable registry of the members. One must also think of the security of the testing crew, which might be different from the situation of organized sports with clearly defined coaches and trainers etc. Yet another problem might be the economy. If an active anti-doping policy is demanded the staff of the gym must be educated not only regarding testing but also the basic values of anti-doping. Probably there must be special care taken if there are strong suspicions of doping in a certain group or by an individual.

Anti Doping Denmark has instituted a 3-year project with the purposes:

- estimate the number of users of doping
- prevent that more young people use hormones
- inform about the risks of using anabolic steroids and other hormones
- increase the dialog with the users in fitness centers
- increase know-how
- develop support-functions for the users and their families

The target group is then primarily boys and young men (13-35 years of age). Secondary target group is older doping users and athletes from organized sport. A third target group is professionals and volunteers that work with young people. The budget for this project is for three years about 1 million USD.

Anti Doping Denmark is also engaged in sponsoring research. A sum of about 1 million DDK was available 2004-2007, but ADD has higher ambitions: to be the superior country in Europe with regard to research on doping. To reach there ADD is interested also in international projects. For 2006 it was handed out about 1 million DDK to traditional anti-doping projects, 3 million to social science research on doping, and 2.3 million for research on erythropoietin. To that may be added 1 million DKK for three consecutive years from WADA.

Summing-up

It was two full days for an enthusiastic audience. Most important were probably two aspects:

- we have in Scandinavia an enormous knowledge and experience in anti-doping
- even though all countries share the same basic values on anti-doping, the experiences are different, which can be used in a positive way
- the potential for Nordic co-operation is almost unlimited

Åke Andrén-Sandberg
Department of Surgery
Karolinska University Hospital at Huddinge
SE 141 86 Stockholm

ake.andren-sandberg@karolinska.se