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Cause and Manner of Death Among Users of Anabolic Androgenic Steroids

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ABSTRACT: Medicolegally investigated deaths among 34 male users of anabolic androgenic steroids (AAS) are described. Nine persons were victims of homicide, 11 had committed suicide, 12 deaths were judged as accidental and 2 as indeterminate.

In two cases of accidental poisoning, the levels of pharmaceuticals and illicit drugs were considered too low to be the sole cause of death and AAS was considered part of the lethal polypharmacia.

Chronic cardiac changes were observed in 12 cases. In two cases of accidental poisonous deaths, these changes were regarded as contributory cause of death.

Homicides, suicides, and poisonings determined accidental or indeterminate in manner were related to impulsive, disinhibited behavior characterized by violent rages, mood swings, and/or uncontrolled drug intake.

The observations in the present study indicate an increased risk of violent death from impulsive, aggressive behavior, or depressive symptoms associated with use of AAS. There are also data to support earlier reports of possible lethal cardiovascular complications from use of AAS. Furthermore, a contributing role of AAS in lethal polypharmacia is suggested. Finally, the observations indicate that use of AAS may be the gateway of approach to abuse of other psychotropic drugs.

KEYWORDS: forensic science, anabolic androgenic steroids, cause of death, homicide, suicide, pathology, mixed substance abuse

The term anabolic androgenic steroids comprises endogenic testosterone, synthetic testosterone, and synthetic derivatives of testosterone (1). Since testosterone was isolated and synthesized in 1935, it has, along with its modified derivatives, been used clinically in a large number of conditions, e.g., hypogonadism, severe burns, anemia, and depression (1). However, due to side effects and the development of alternative methods of therapy, the only clinical applications today in Sweden are replacement therapy in hypogonadism and palliative therapy in terminal mammary cancer. From the early 1950s, AAS have been used by athletes in various strength-intensive sports (2) and during the 1980s, the use spread to groups other than elite athletes (3). During the last decades reports of severe somatic and mental complications of AAS use have emerged. Examples of somatic complications with a potential for lethal outcome are myocardial infarction and left ventricular hypertrophy (4–6). Some of the mental side effects may also be related to premature death. Thus, it has been suggested that depressive symptoms associated with use of AAS may convey an increased risk of suicide (7). Also other behavioral changes reported as frequently occurring during current use of AAS, e.g., increased aggressiveness, impulsiveness, and lack of inhibition (8–10) are associated with increased mortality (11).

In spite of the potentially lethal side effects of AAS use, such use has so far passed without much attention in medicolegal practice. The main reason for this is probably that there are no established acute toxic effects of AAS (12). The aim of the present study is to scrutinize cause and manner of death among medicolegally examined cases in which the use of AAS has been proven and to discuss hypothetical connections between the behavioral and somatic side effects of such use and premature death.

Methods

Inclusion Criteria

The material consists of two categories, viz., current users of AAS and subjects who had discontinued AAS use within six months. Cases lacking positive urine analysis as confirmation of AAS use were included in the presence of anamnestic data in which the informant stated specified compounds and/or an on/off pattern typical for use of AAS. Thus, statements of AAS use not otherwise specified with regard to compound or pattern of intake were disregarded.

Selection of Cases

According to Swedish law (SOSFS 1996:29), the police must be contacted in all cases of suspected unnatural death, i.e., when there is no known disease to explain the demise. This means that, in addition to primarily suspected unnatural deaths, i.e., homicide, suicide or accident, cases of sudden unexpected death including unexpected death among drug and alcohol abusers are investigated by forensic pathologists.

The study base ($n = 26$) consists of casualities subjected to medicolegal autopsy at the Departments of Forensic Medicine in Stockholm and Uppsala, during 1985–1998. The remaining eight subjects were identified at the other departments of forensic medicine in Sweden during 1994–1998. During the years 1995–1998, autopsy cases with conspicuous muscular hypertrophy or other signs of AAS use have commonly been tested for AAS at the departments in Stockholm and Uppsala. At these departments, 10 out of 100 analyzed cases were AAS positive during the years 1995–1998. In eight additional cases lacking positive urine analysis, current or recently discontinued use of AAS was confirmed by

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relatives. During this period (1995–1998), the total number of autopsies (Stockholm and Uppsala) on males aged 20–45 years was 1550. Before 1995, analysis of AAS was performed infrequently, usually to confirm previously recognized use of AAS. Eight subjects had been noticed before 1995 (1985–1994) at the Stockholm and Uppsala departments.

In the group of verified AAS users ($n = 34$), the primary suspicion of AAS use was based on external stigmata such as muscular hypertrophy ($n = 27$), striae ($n = 3$), and gynecomastia ($n = 1$) in 27 instances and testicular atrophy in one. In six cases lacking external or internal signs of AAS use, information in the forensic anamneses indicated such use. The use of AAS was confirmed by positive urine analysis in 21 cases. In cases with negative or inconclusive analytical results (10 cases) or when tests had not been performed (3 cases), information from the police (3 cases) or relatives/acquaintances/medical records (10 cases) confirmed current or recently discontinued use of AAS.

Data Collection

Data concerning basic medicolegal aspects of the AAS-cases were gathered from autopsy and police records (all cases), medical records (6 cases), and information given by relatives/acquaintances (forensic anamnesis) (16 cases).

Toxicological analyses concerning tranquilizers, sedatives, analgesics, illicit drugs, and alcohol were performed in 32 cases. In one case, illicit drugs were not included in the analysis, and in another case, toxicological analysis was not performed.

Analysis concerning AAS is only performed on urine. This implies that analyses with regard to presence of AAS in blood—when the urinary bladder is empty—could not be performed.

All analyses regarding pharmaceuticals, illicit drugs, and alcohol have been carried out at the Laboratory of Forensic Chemistry in Linköping using routine methodology. Before 1995, analyses concerning testosterone and all known synthetic AAS were performed at the Doping Laboratory, Huddinge Hospital by gas chromatography/mass spectrometry (13). From 1995, the AAS analyses have been carried out at the Department of Forensic Chemistry in Linköping by gas chromatography/mass spectrometry (14) covering testosterone and all known synthetic AAS but Formebolone. Testosterone is regarded positive when the ratio urinary testosterone/epitestosterone is >6 (15).

The study was approved by the ethical committee of Karolinska Institute.

Results

Thirty-four medicolegally examined deaths among Caucasian males aged 20 to 45 years with current or discontinued use of AAS were culled from a 14-year period (1985–1998). Two cases were recognized during the 1980s and 32 during the 1990s. Nine persons were victims of homicide (Table 1). Eleven cases were judged as suicide (Table 2). The remaining 14 were determined as accidental (12 cases) or indeterminate (two cases) (Table 3). The accident category comprises six deaths following collapse upon heroin intake, two cases of traffic accident and four cases related to combined drug intake and one to hypothermia from passing out in a cold environment during intoxication. Information concerning age, year of

TABLE 1—*Results of medicolegal investigation in nine cases of homicidal death.*

Case Age/Year of Death	Cause of Death	External Signs of AAS Use	Pathology	Phase of AAS Use	Urine Analysis AAS	Toxicology μg/mL Blood	Length/cm Weight kg
1. 24/1990	Shot in head	Muscular hypertrophy	–	Unclear	Not done	0.01 codeine B	178 cm 98 kg
2. 22/1994	Shot in trunk	Muscular hypertrophy Striac over m. pectoralis and m. biceps	Mild myocardial fibrosis Adrenal and testicular atrophy	Current	Nandrolone Stanozolol Testosterone	Negative	198 cm 115 kg
3. 20/1994	Shot in head	Muscular hypertrophy	–	Current	Testosterone	1300 ethyl alcohol	175 cm 91 kg
4. 34/1996	Stabbed in chest	Muscular hypertrophy	–	Current	Nandrolone Testosterone	2300 ethyl alcohol 0.04 amphetamine	174 cm 103 kg
5. 22/1997	Stabbed in neck and chest	Muscular hypertrophy	–	Unclear	No results due to analytical problems	110 ethyl alcohol 2.2 karbamazepin 0.1 amphetamine 0.2 ephedrine	180 cm 80 kg
6. 21/1997	Multiple shots in head and trunk	Muscular hypertrophy	–	Current	Nandrolone	Negative	170 cm
7. 27/1997	Stabbed in neck	Muscular hypertrophy	Mild myocardial hypertrophy (465 g) Moderate coronary atheromatosis	Current	Nandrolone Metonolone Testosterone	0.1 diazepam 0.1 nordazepam 40 gamma-hydroxy-buthyrate (GHB) 480 GHB (Urine) 0.5 amphetamine 0.2 ephedrine	177 cm
8. 45/1998	Shot in head	Muscular hypertrophy	Testicular atrophy	Current	Nandrolone	Negative	183 cm 110 kg
9. 24/1998	Shot in neck	Muscular hypertrophy Striae over pectorals	Adrenal and testicular atrophy	Current	Nandrolone	0.07 cocaine 0.5 benzoylecgonine	180 cm 98 kg

TABLE 2—*Results of medicolegal investigations of 11 suicides among users of AAS.*

Case Age/Year of Death	Cause of Death	External Signs of AAS Use	Pathology	Phase of AAS Use	Urine Analysis AAS	Toxicology μg/mL Blood	Length/cm Weight kg
10. 39/1985	Hanging	Muscular hypertrophy	Patchy myocardial fibrosis	Unclear	Not done	Not done	173 –
11. 26/1988	Poisoning	Muscular hypertrophy	Myocardial hypertrophy Advanced coronary atheromathosis and intramural arteriolosclerosis Testicular atrophy Adenomatous prostatic hyperplasia	Current	Nandrolone	0.17 7-amino-flunitrazepam 0.4 amitriptylin 0.1 nortryptilin	193 cm –
12. 25/1992	CO-poisoning	Muscular hypertrophy	Chronic active hepatitis	Current	Methandienone	Negative	164 cm 89 kg
13. 23/1994	Shot in head	Muscular hypertrophy	Reduced number of Leydig cells in testicles Focal testicular fibrosis	6 weeks since discontinuation	Negative	Negative	182 cm 86 kg
14. 25/1994	Hanging	Muscular hypertrophy	–	Current	Methandienone	130 ethyl alcohol 190 ethyl alcohol(Urine) 0.8 ephedrine	181 cm 85 kg
15. 36/1995	Poisoning	Muscular hypertrophy	Mild myocardial hypertrophy (510 g)	Current (methandienone)	Not done	3.6 dextropropoxi-phene 0.02 flunitrazepam 0.3 7-amino-flunitrazepam	196 cm 120 kg
16. 25/1997	Explosion	Muscular hypertrophy	–	Current	Methandienone	250 ethyl alcohol 0.2 citalopram 0.7 zopiklon 0.3 amphetamine	179 cm 95 kg
17. 21/1997	Poisoning by morphine pills	No	Testicular and adrenal atrophy	6 months since discontinuation	Negative	Ethyl alcohol neg 1100 ethyl alcohol(Urine) 2.2 morphine*	169 cm 62 kg
18. 33/1997	Poisoning	Muscular hypertrophy	Mild steatosis in heart and liver Testicular atrophy	Unclear	Inconclusive due to analytical problems	840 ethyl alcohol 100 paracetamol 6.7 dextropropoxi-phene 0.8 citalopram	179 cm 83 kg
19. 29/1998	Hanging	Muscular hypertrophy		Unclear	Negative	0.3 amphetamine 0.1 diazepam	174 cm 87 kg
20. 35/1998	Poisoning	–	Myocardial hypertrophy (505 g) Fatty liver	Current	Metenolone Nandrolone Testosterone	710 ethyl alcohol 28 paracetamol 1.8 dextropropoxi-phene 0.3 diazepam 0.2 nordazepam 0.7 codeine	185 cm 95 kg

* Morphine pills.

death, phase of AAS use, and basic forensic aspects is given for each case in Tables 1–3. Data regarding toxicology and observed violent behavior/psychological side effects are summarized for the categories manner of death (homicide, suicide, and accident/indeterminate) in Tables 4 and 5.

Circumstantial Data

Homicidal Deaths

Nine males aged 20–45 years (mean 26.5) were victims of homicide. All homicide victims were acquainted with the perpetrator. In two cases, the AAS users had been shot shortly after having battered the physically inferior perpetrator. One of these perpetrators was a sporadic user of AAS, but was not currently using AAS when committing the homicide. Two other victims, who both had a history of frequent involvement in physical violence, had been stabbed in fights initiated by themselves. Yet another victim, who also had a history of recurrent involvement in physical violence, was stabbed to death by a fellow bodybuilder during a quarrel concerning illicit GHB trading. Four homicides were execution-like shootings among criminals active in extremely violence-prone criminal constellations. These perpetrators were all bodybuilders.

TABLE 3—*Results of medicolegal investigations of 12 cases of accidental (case 21–32) and 2 cases of indeterminate (case 33 and 34) manner of death among users of AAS.*

Case Age/Year of Death	Cause of Death	External Signs of AAS Use	Pathology	Phase of AAS Use	Urine Analysis AAS	Toxicology µg/mL Blood	Length/cm Weight kg
21. 23/1991	Car crash Driver	Muscular hypertrophy	–	Current	Nandrolone Methandienone	Negative	171 cm 81 kg
22. 27/1991	Car crash, Passenger	Muscular hypertrophy	Adrenal atrophy	Unclear	Negative	0.1 benzoylecgonine	188 cm 96 kg
23. 21/1993	Death in connection to heroin intake	–	–	Current	Stanozolol	0.11 morphine 0.02 codeine 0.06 fenmetrazine 0.05 7-amino-flunitrazepam	174 cm 67 kg
24. 20/1995	Death in connection to heroin intake	–	Moderate left ventricular hypertrophy	Unclear	Negative	0.005 6-acetylmorphine 0.23 morphine 0.07 codeine 8 paracetamol	182 cm 76 kg
25. 31/1996	Heroin intoxication in combination with cardiac hypertrophy	Muscular hypertrophy	Mild left ventricular hypertrophy Testicular atrophy	Unclear	Negative	0.1 dextropropoxiphene 0.05 7-amino-flunitrazepam 0.07 morphine 0.01 codeine	192 cm 107 kg
26. 22/1996	Acute myocardial complication of combined drug effects	Muscular hypertrophy	Mild, diffuse myocardial fibrosis	Current	Nandrolone Metenolone Testosterone	0.1 methadone 0.05 7-amino-flunitrazepam	170 cm –
27. 32/1997	Death in connection to heroin intake	–	–	Current	Boldenone	1800 ethyl alcohol 0.1 diazepam 0.22 morphine 0.02 codeine	177 cm 75 kg
28. 23/1997	Myocardial infarction provoked by daily intake of amphetamines during a two-week period preceding death	Muscular hypertrophy Gynecomastia Striae over pectorals and biceps	Coagulation necrosis in posterior wall of left ventricle Advanced patchy myocardial fibrosis Moderate coronary atheromatosis	Approx 2 weeks since discontinuation	Negative	0.2 diazepam 0.2 nordazepam 0.7 amphetamine 0.4 metamphetamine 0.001 THC	188 cm 84 kg
29. 20/1998	Death in connection to heroin intake	Muscular hypertrophy	Testicular atrophy Peliosis hepatitis	Current	Testosterone	0.12 morphine 0.02 codeine 0.2 amphetamine 0.001 THC	184 cm 96 kg
30. 20/1998	Death in connection to heroin intake	–	–	?	Negative	100 ethyl alcohol 0.23 morphine 0.02 codeine 0.3 dextropropoxiphene	180 cm 72 kg
31. 23/1997	Myocardial ischemia provoked by combined drug effects	Muscular hypertrophy	Patchy coagulation necrosis in myocardium	Current	Testosterone	0.1 diazepam 0.1 nordazepam 0.08 morphine 0.04 metamphetamine 0.06 fenmetrazine	178 cm 80 kg
32. 39/1998	Hypothermia	Muscular hypertrophy	Endocardial fibrosis Fatty liver	Current	Nandrolone Testosterone	290 ethyl alcohol 23 karbamazepine	165 cm
33. 25/1990	Dextropropoxiphene poisoning	Muscular hypertrophy	Advanced myocardial hypertrophy (820 g)	Current	Metenolone Mesterolone Nandrolone Norethandrolone Oxandrolone Stanozolol Testosterone	8.8 dextropropoxiphene 3.4 paracetamol 0.1 diazepam 0.1 nordazepam 100 ethyl alcohol	190 cm 123 kg
34. 42/1998	Poisoning by morphine, dextropropoxiphene and alcohol	Muscular hypertrophy Striae over pectorals Severe acne vulgaris	Moderate coronary atherosclerosis Testicular atrophy	Current	Testosterone	0.2 dextropropoxiphene 1.3 morphine*	183 cm 91 kg

* Morphine pills.

TABLE 4—*Toxicological results in 34 medicolegally examined unnatural deaths among users of AAS.*

	Accident/Indeterminate $n=12$* $n=2$	Homicide $n=9$†	Suicide $n=11$‡
Alcohol	4	3	5
Central stimulants	5	4	3
Opiates	8+1§	0	1§
Dextropropoxiphene	4	0	3
Benzodiazepines	7	1	4
Antidepressants	0	0	3

* 1 case negative.
† 3 cases negative
‡ 2 cases negative, 1 not analyzed.
§ Morphine pills.

TABLE 5—*Observed violent behavior, psychiatric symptoms reported as associated to use of AAS, and phase of AAS use documented in 34 medicolegally examined unnatural deaths among AAS users.*

	Accident/ Indeterminate $n=12/2$	Homicide $n=9$	Suicide $n=11$
Violent behavior	2	5	8
Increased energy/ self-esteem	3	No information	7
Mood swings	3	No information	8
Impaired reality testing	0	No information	1
Irritability/ aggressivity	3	No information	10
Depression	3	No information	8
Phase of AAS use	current = 9 discontinued = 1 unclear = 4	current = 7 unclear = 2	current = 6 discontinued = 2 unclear = 3

Suicidal Deaths

Twelve males aged 21–39 years (mean 28.8) committed suicide. In each case, relatives had noticed psychiatric symptoms, mainly episodes with hypomania-like symptoms or depression, aggressive behavior, and lack of impulse control. In one case, episodes of impaired reality testing had developed about four months after the use of AAS was initiated. In four cases, mixed drug abuse had been established after the use of AAS had started and in two other cases, the intake of alcohol had been markedly increased during the previous year. Eight subjects had committed violent acts which caused problems in their relationship to close persons or in their occupational situation. In four cases, partner separations had occurred immediately prior to the suicide. Four subjects had written farewell letters. One subject had attempted suicide at a previous occasion.

Accidental Deaths

Eleven males aged 20–32 years (mean 24.2) were victims of accident. According to witnesses, the traffic accident was a result of remarkably reckless driving. The subject who died from hypothermia was found outdoors in the winter season. He had been using AAS intermittently during a 10-year period. During his early AAS career, he used no other drugs besides AAS. Gradually, he developed an abuse of alcohol and during the last years, he had suffered occasional seizures during abstinence. He used AAS almost continuously, also when not training, during the last years.

Five persons apparently had died in close connection to heroin administration with the syringes found besides the body. Another person died under similar circumstances. However, the toxicological analysis in that case showed relatively low levels of morphine and pharmaceuticals. For that reason, left ventricular hypertrophy was considered as a possible contributing factor. Two cases in which the cause of death was attributed to acute myocardial complications provoked by drug effects, were judged as related to mixed drug misuse, hence being considered as accidental in manner. Thus, an acute myocardial infarction in a 23-years-old person was judged as related to intense use of amphetamines, and recently discontinued use of AAS. Daily intake of amphetamines that had been going on without interruption during a two-week-period was provoked by a partner separation and the subject had communicated suicidal ideation. In the other case of drug-provoked acute myocardial ischemia, a period of excessive intake of AAS and various psychotropic substances accompanied by marked mental instability mainly constituted by mood swings, increased aggressiveness, and irritability, preceded death. The last subject in this category died under similar circumstances with a period of excessive intake of AAS and various psychotropic substances in connection to the fatality. In this case, the cause of death was regarded as a combination of drug effects (AAS, methadone and flunitrazepam) and diffuse myocardial fibrosis. Soon after the use of AAS was initiated, he exhibited profound mental changes with episodes of hypomania-like symptoms or depression and violent rages with battering of his girlfriend and damage of property.

Indeterminate Manner of Death

The two subjects in this category were successful athletes, 25- and 45-years-old, who had been using AAS for 7 and >20 years, respectively. The 25-year-old subject was treated for severe congestive heart failure during the last year. He had regular contact with a psychiatrist for various psychiatric problems during the last six months. Episodes of depression and anxiety were the dominating problems, but quick mood swings and violent rages were also documented. The other subject had a history of frequent involvement in physical conflicts when intoxicated. He was considered an alcoholic by fellow power lifters, but had never been subjected to medical or psychiatric care for his drinking problems. Both subjects developed abuse of analgesics with opioid features early in their athletic careers. There had not been any suicidal communication in either case.

Discussion

This series of fatalities among users of AAS represents selected medicolegal autopsy cases. Analysis of AAS is not part of the routine toxicological screening, and most forensic pathologists will only perform such analysis on subjects with extreme muscular hypertrophy and/or other stigmata of AAS use, such as gynecomastia or striae. At present, only urine can be used for analysis. Thus, when the bladder is empty or when urine analysis have turned out negative, there is need for anamnestic confirmation. Only a limited number of forensic pathologists with a special interest in drug-related pathology will engage in this time-consuming task. Moreover, in a large number of cases with stigmata highly suggestive for AAS use, the investigator has not been able to confirm such use by means of anamnestic information. Conversely, cases lacking stig-

mata of AAS use have come to the examiners' knowledge from spontaneous information by relatives, thus suggesting that there may have been other AAS positive cases where the use of AAS has not been suspected at all. Consequently, the identified cases are likely to represent a minimum rate of deaths among users of AAS rather than a comprehensive review of fatalities among the group. For these reasons, the data presented here are too limited and unsystematic to permit any firm conclusions. However, the consistency in the reported mental side effects and the strong temporal relationship between these symptoms and the use of AAS, should allow for cautious generalization about the mental effects observed.

The somatic complications described occur in a more sporadic pattern. In contrast to information on behavior that can be gathered retrospectively from different sources, the data concerning pathoanatomical changes are restricted to the autopsy protocol. Since the cause of death has been obviously unnatural in most cases, the forensic pathologist has not always sampled tissues for microscopic examination. Microscopic examination of the testes, the organ probably most consequently affected by AAS use, was only performed in ten cases. Thus, testicular changes as well as less conspicuous pathological changes in other internal organs, e.g., diffuse interstitial myocardial fibrosis or atrophy of the adrenal cortex, may have been missed in a number of cases.

Relation Between Use of AAS and Cause and Manner of Death

The death of an individual can be related to substance abuse in different ways: A. There may be a direct relationship, where the acute effects of the drug triggers lethal pathophysiological/pharmacological mechanisms. This relationship is frequent in deaths due to heroin intake, but other drugs, for example, amphetamine alone or in combination with prescribed medicinal drugs or alcohol, may also cause sudden and unexpected death (16). B. There may be an indirect relationship where premature death is a result of organic lesions or disease caused by substance misuse. Examples of such relationships are hepatic failure as a result of alcohol-related disorders or viral hepatitis, myocardial lesions of long-standing amphetamine abuse (17), or AIDS (18). C. The life-style and social situation of drug addicts often involve exposition for violence and other psychosocial stress. Reports from the USA emphasize the importance of such a relationship in cases of homicide and suicide among subjects using cocaine (19–21). D. Acute mental influence or persistent behavioral changes due to the drug may lead to increased risk-taking or self-destructive/suicidal behavior (21–24).

Since AAS have no known acute toxic effects, death directly attributable to pharmacological actions is usually not sought for by the forensic pathologist. However, in two cases in which the casualty was explained by combined effects of relatively low doses of diazepam, morphine, metamphetamine and fenmetrazine (case 31), and methadone and 7-aminoflunitrazepam (case 26), there was a history of intense intake of AAS during several weeks prior to the fatalities, which suggests that AAS may render the organism more susceptible to the actions of other drugs. However, to our knowledge, there are no data in the literature of such interactions, which underlines the need for further research into this issue.

Myocardial hypertrophy or other chronic myocardial lesions, i.e., diffuse or patchy myocardial fibrosis, and myocardial steatosis, were noticed in 12 of 25 microscopically investigated cases. One subject who had a seven-year history of advanced use of AAS had shown symptoms of severe cardiac failure and at postmortem examination extreme myocardial hypertrophy (heart weight 820 g) was found. Although there are reports of cardiac pathology, e.g., myocardial infarction, left ventricular hypertrophy, and coronary atherosclerosis (4–6,25–29) among young AAS users, a causal relationship has not been adequately tested in large-scale epidemiological studies. However, the relation between use of AAS and increase of certain risk factors for atherosclerotic cardiovascular disease and altered lipid metabolism, is more firm (25). The typical changes are an increase in the low density lipoprotein (LDL), corresponding decrease in the high density lipoprotein (HDL) by 30 to 50%, and a fall in apoprotein A1 (Apo A1) level (30–33). This lipid profile, which has been shown to persist for up to 5 months after discontinuation of AAS use (30) is associated with an increased risk of chronic coronary artery disease (34,35). Furthermore, cholesterol is known to potentiate the coronary artery response to norepinephrine in dogs (36,37) and increase platelet aggregation (38). Additionally, experimental data indicate that AAS exert direct toxic influence on the myocardium (39,40), some of which predisposing for arrhythmic events (41). From the above, it follows that use of AAS may put the user at increased risk of both acute vascular occlusion and arrhythmic sudden death. The fact that the two persons with ischemic heart events as terminal cause of death in the present study both were under acute influence of amphetamines, which leads to increased sympathetic stimulation as well as increased levels of circulating catecholamines, suggests that these deaths may have been due to combined effects of AAS and amphetamines. In this context, it should be remembered that despite the vast number of individuals who have taken amphetamines during the last five decades, the number of reported fatal cardiac events attributed to isolated use of amphetamines is low (17). Obviously, further knowledge concerning acute and chronic pathological and pathophysiological processes related to the use of AAS would not only be of medicolegal but also of clinical/preventional interest.

In most cases (heroin intoxication excepted), there seemed to be a relation between the fatal outcome and aggressive/violent behavior, lack of impulse control, and in the cases of suicide, also depressive symptoms. The circumstantial evidence regarding the homicidal deaths indicate high levels of aggression in each homicide victim belonging to this group. One may speculate that AAS-associated aggressive behavior of the coming-to-be victim may have been the triggering factor of the violence in the majority of these events. In 12 out of 16 cases belonging to the suicide, accidental or indeterminate categories in which a detailed background history was obtained, relatives or physicians had noticed a definite relationship in time between the use of AAS and impulsive violent behavior or depressive symptoms. Keeping in mind that the behavioral patterns as related to the use of AAS observed in the present study closely correspond to those earlier described (8,42–45), it seems reasonable to assume that the use of AAS may indirectly have contributed to the death of these individuals by causing or aggravating psychiatric symptoms to a degree amounting to suicidal or life-threatening behavior.

In only six cases were analyses regarding alcohol, pharmaceuticals, and illicit drugs negative. In the other cases, various drugs, e.g., benzodiazepines, dextropoxiphene, central stimulants, and heroin were detected either isolated or in combinations. In most cases of accidental death and the cases of indeterminate manner, combined overdose of several drugs was the cause of death. A similar pattern of drug misuse was present in eight suicides. Since in eight cases, the use of illicit drugs had been established after the use of AAS was started, the use of AAS may have been the first step in

the career of drug abuse, and thereby indirectly related to some of the deaths from uncontrolled substance misuse.

Heroin Related Deaths

As earlier pointed out, mixed drug abuse has been secondary to the use of AAS in some cases. However, in four instances of heroin-related death, the use of AAS seemed to be moderate and/or sporadic judging from the lack of stigmata of AAS use. Moreover, the past history indicated that these persons were primarily heroin addicts. The reason for heroin addicts to use AAS is unclear. Perhaps, they consider AAS as corroborates or a short-cut in gaining improved appearance in an effort to conceal the misuse of heroin. Another possibility is that AAS are used in order to improve sexual performance since abuse of opiates often results in impaired sexual function by lowering the concentration of plasma testosterone (46). Yet another possible explanation might be that AAS are used for their psychotropic properties, i.e., effects on the reward regions of the brain (47,48). A similar pattern of mixed abuse of AAS and cocaine or alcohol has earlier been observed (43).

In each case, the concentration of morphine was below 0.30 μg/mL which has been described as the lower limit of life-threatening concentration (49).

Pathology/External Stigmata

In addition to the cardiac alterations discussed above, the adrenals, and the testes showed pathological alterations in some cases. Testicular atrophy is a well-known consequence of feedback inhibition of pituitary hormones due to excess of circulating steroid hormones but the reversibility of the atrophic changes is not known.

The prevalence of external stigmata (gynecomastia, striae, and severe acne vulgaris) was low. Thus, the absence of such findings should be disregarded when possible use of AAS is pondered.

Conclusion

Although AAS, in contrast to many other psychoactive substances, have no known acute toxic effects on the organism, data from the present series indicate that use of AAS may contribute to premature death in various manners.

Fatalities due to relatively moderate overdoses of illicit drugs and pharmaceuticals among subjects with a history of current self administration of AAS indicate a possible contributory role of AAS in lethal polypharmacia.

Psychiatric complications of AAS use, in particular disinhibitive, aggressive and depressive behavior seem to constitute an increased risk for violent death principally by homicide, suicide, or uncontrolled intake of psychoactive drugs.

Observations of aggravation or initiation of misuse of other illicit drugs and/or alcohol after the use of AAS was started suggest that use of AAS may have an extension in misuse of other psychoactive substances, which subsequently may be lethal due to uncontrolled combined drug intake.

Chronic cardiac lesions were present in 12 cases. In two cases of fatal intoxication such pathologic changes were regarded as a contributory cause of death. Two subjects, who were under acute influence of central stimulants, died from acute myocardial ischemia. Considering the low incidence of lethal acute myocardial ischemia associated with isolated use of central stimulants together with experimental evidence of increased cardiovascular susceptibility to catecholamines associated with use of AAS, these cases suggest a synergism for central stimulants and AAS in causing myocardial ischemia.

In conclusion, the present observations support the notion that cardiovascular lesions from AAS use may take lethal proportions. However, the case series indicates that other possible complications to AAS use, i.e., synergism in lethal polypharmacia, violent death related to impulsive aggressive or self-injurious behavior, and the development of mixed substance abuse may also involve an increased risk of premature death.

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