

UNIVERSITA DEGLI STUDI DI MILANO

ISTITUTO POLICLINICO SAN DONATO

CENTRO PER LO STUDIO E LA TERAPIA DELLE MALATTIE CARDIOVASCOLARI

"E. MALAN"



CARDIOSTIM

**RISK STRATIFICATION OF SUDDEN DEATH IN YOUNG
COMPETITIVE ATHLETES**

up to date 2006

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Arrhythmias in competitive athletes

Competitive athletes are considered by the public the epitome of health with a normal heart.

It is, however, not a rare finding to observe during a sport career several types of arrhythmias.

In some cases arrhythmias can be life-threatening and can lead to major events as an arrhythmic syncope, cardiac arrest and sudden death.

Sport activity and arrhythmias

There is also evidence to suggest that athletic activity can

- 1. have a trigger effect in the induction of pathological arrhythmias in athletes with silent underlying arrhythmogenic pathologies.**
- 2. Induce a clinical “acceleration” of many types of latent arrhythmogenic structural heart diseases, or of primary disorders**

Arrhythmias in competitive athletes

Since 1974 we have continuously evaluated competitive athletes performing different types of sports, and referred to us for arrhythmias. All these athletes underwent an individualized risk assessment by arrhythmologic investigation, with a study protocol including non-invasive and invasive diagnostic techniques.



Arrhythmogenic effects of illicit drugs in athletes

The current management of athletes with arrhythmias is complicated by the large use of “illicit drugs” taken, at any age, both by professional and non professional athletes.

Prefer the term “illicit drugs” rather than “doping”:

- a. **drugs taken as true “doping”, or “performance enhancing drugs (PEDs)”**,
- b. **“masking agents”, i.e. drugs taken to the aim of masking the presence of other specific drugs in tests for doping control.**
 - **“antagonists of side effects” (e.g. gonadotropins, agents with estrogenic activity, alfa reductase inhibitors (finasteride) etc.**



Arrhythmogenic effects of illicit drugs in athletes

- 1. Almost all the illicit drugs banned by the International Olympic Committee (IOC) and since 1999 yearly updated by the World Anti-Doping Agency (WADA), may cause cardiac collateral effects, through a direct or indirect cardiac effect, and may provoke arrhythmogenic effects (short, medium or long-term) and sudden death**

The 2006 IOC list of the “Prohibited classes of substances”
www.wada-ama.org - World Anti-Doping CODE
SUBSTANCES AND METHODS PROHIBITED AT ALL TIMES
(in-and out-of-competition). PROHIBITED SUBSTANCES.

S1. ANABOLIC AGENTS

1. Anabolic Androgenic Steroids (AAS)
 - a. Exogenous AAS
 - b. Endogenous AAS
2. Other Anabolic Agents, including but not limited to:
clenbuterol, zeranol, zilpaterol

S2 HORMONES AND RELATED SUBSTANCES

1. Erythropoietin (EPO);
2. Growth Hormone (hGH), Insulin like Growth Factor (IGF-1), Mechano Growth Factors (MGFs);
3. Gonadotrophins (LH, hCG);
4. Insulin;
5. Corticotrophins.

S3. BETA-2AGONISTS

S4. AGENTS WITH ANTI-ESTROGENIC ACTIVITY

S5. DIURETICS AND OTHER MASKING AGENTS

THE 2005 IOC LIST OF SUBSTANCES PROHIBITED IN COMPETITION

S6. STIMULANTS

S7. NARCOTICS

S8. CANNABINOIDS

S9. GLUCOCORTICOSTEROIDS

SUBSTANCES PROHIBITED IN PARTICULAR SPORTS

P1. Alcohol

P2. Beta-Blockers

www.wada-ama.org - World Anti-Doping CODE

Arrhythmogenic effects of anabolic androgenic steroids in athletes

The IOC (WADA) 2006 list of prohibited classes at all times (in and out competition) of Anabolic Androgenic Agents (AAS) is a complete update comprehending the more recent pharmaceutical products and contains also designer drugs in order to provide a complete spectrum for present and future antidoping controls.

Steroids may be used in oral, 17alpha-alkylated, or intramuscular, 17beta-esterified, preparations.

The 2006 prohibited list of Anabolic Androgenic Steroids (AAS) (S1)

a. Exogenous* AAS, including:

18alpha-homo-17beta-hydroxyestr-4-en-3-one; bolasterone;
boldenone; boldione; calusterone; clostebol; danazol;
dehydrochloromethyl- testosterone; delta1-androstene-3,17-
dione; delta1-androstenediol; delta1-dihydro-testosterone;
drostanolone; ethylestrenol; fluoxymesterone; formebolone;
furazabol; gestrinone;
4-hydroxytestosterone; 4-hydroxy-19-nortestosterone; mesta
nolone; mesterolone; metenolone; methandienone; methandriol;
methyldienolone; methyltrienolone; methyltestosterone;
mibolerone; nandrolone; 19-norandrostenediol; 19-
norandrostenedione; norbolethone; norclostebol;
norethandrolone; oxabolone; oxandrolone; oxymesterone;
oxymetholone; quinbolone; stanozolol; stenbolone;
tetrahydrogestrinone; trenbolone and other substances with a
similar chemical structure or similar biological effect(s).

The 2006 prohibited list of Anabolic Androgenic Steroids (AAS) (S1)

b. Endogenous ** AAS:

androstenediol (androst-5-ene-3beta,17beta-diol); androstenedione (androst-4-ene-3,17-dione); dehydroepiandrosterone (DHEA); dihydrotestosterone; testosterone. and the following metabolites and isomers:

5alpha-androstane-3alpha, 17alpha-diol; 5alpha-androstane-3alpha, 17beta-diol; 5alpha-androstane-3beta, 17alpha-diol; 5alpha-androstane-3beta, 17beta-diol; androst-4-ene-3alpha,17alpha-diol; androst-4-ene-3alpha, 17beta-diol; androst-4-ene-3beta, 17 alpha-diol; androst-5-ene-3alpha,17alpha-diol; androst-5-ene-3alpha,17beta-diol; androst-5-ene-3beta,17alpha-diol; 4-androstenediol (androst-4-ene-3beta,17beta-diol); 5-androstenedione (androst-5-ene-3, 17-dione); epi-dihydrotestosterone; 3alpha-hydroxy-5alpha-androstan-17-one; 3beta-hydroxy-5alpha-androstan-17-one; 19-norandrosterone; 19-noretiocholanolone.

2. Other Anabolic Agents, including but not limited to: Clenbuterol, tibolone, zeranol, zilpaterol.

For purposes of this section:

* "exogenous" refers to a substance which is not capable of being produced by the body naturally.

** "endogenous" refers to a substance which is capable of being produced by the body naturally.

Arrhythmogenic effects of anabolic androgenic steroids in athletes

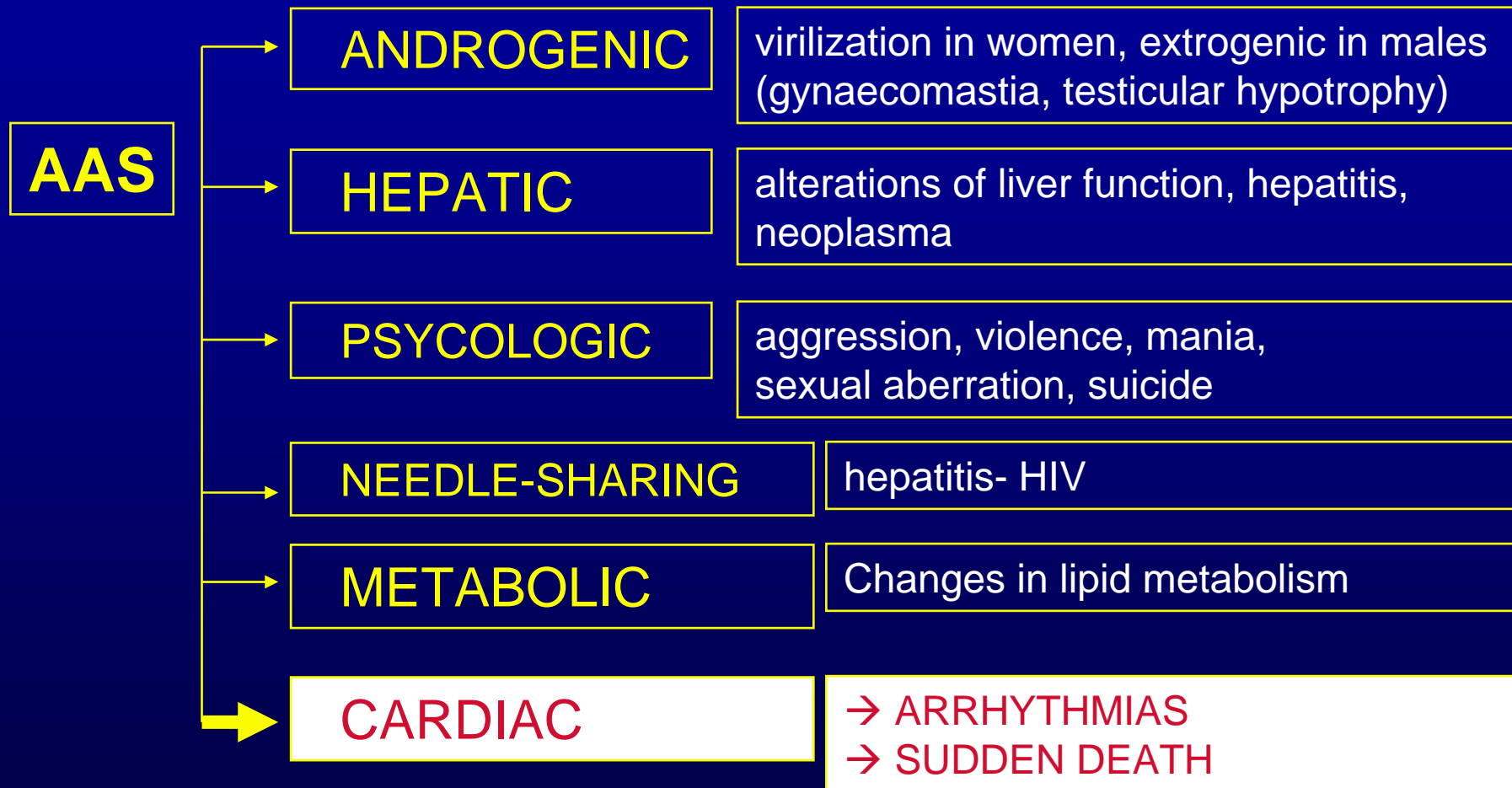
ANABOLIC ANDROGENIC STEROIDS (AAS) are derived from modified testosterone to enhance anabolic rather than androgenic action. They are taken as performance enhancing drug (PEDs) in order to increase protein synthesis, muscle mass, level of aggressiveness, and to obtain a rapid recovery after effort.

The first in the IOC/WADA List 2005 of prohibited classes - The most used illicit drugs and most frequently drugs discovered in anti-doping controls - Often taken by very young athletes.

IMPORTANT FACTS

1. Steroid users employ these agents at levels **10- to 100-fold in excess of therapeutic doses**
2. Use of multiple steroids simultaneously (**'stacking'**),
3. Often associated with **other substances with similar activity** or with **masking agents** for anti-doping controls or **to neutralize** hormonal side effects.

Side effects of Anabolic Androgenic Steroids (AAS)





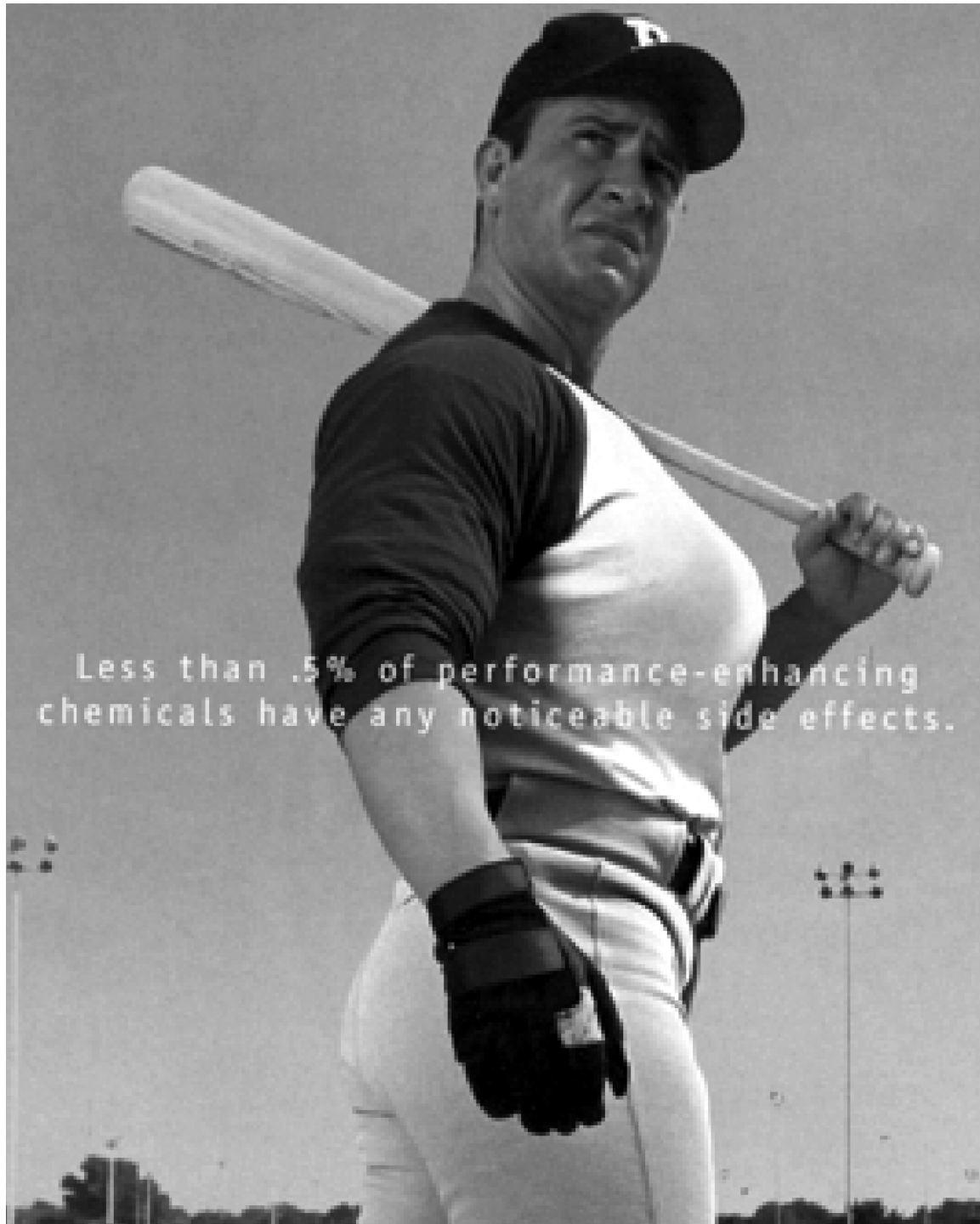
Doped East German athletes to receive compensation

Annette Tullis *Heidelberg*

Athletes from former East Germany who were given performance enhancing drugs for many years and who consequently experienced longstanding health problems will receive payments of several thousand euros, the German federal parliament decided on 13 June.



Former East German athletes Ute Krause (left) and Birgit Boese enter a Berlin courthouse for the trial of a former East German sports doctor accused of harming 142 sportswomen

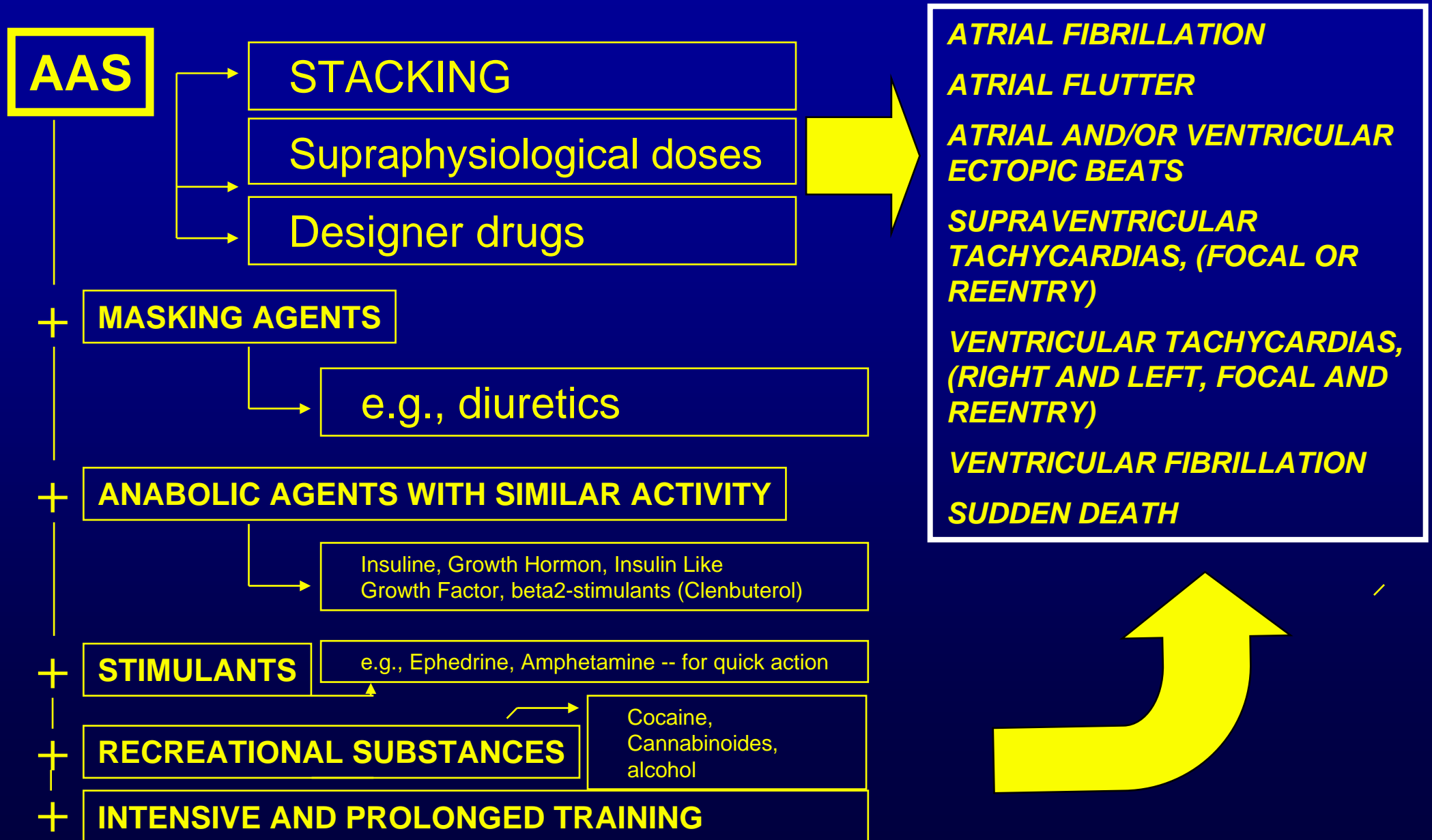


Less than .5% of performance-enhancing chemicals have any noticeable side effects.

Less than 5% of performance-enhancing chemicals have any noticeable side effects.


Arrhythmogenic effects of anabolic androgenic steroids in athletes

Combination of arrhythmogenic factors



Arrhythmogenic effects of androgenic steroids in athletes

Reported findings in 52 subjects with arrhythmic events/SD suspected to have used AAS

- Hypertrophic cardiomyopathy with necrosis, fibrosis, inflammatory changes,
 - Dilated cardiomyopathy (also myocarditis related)
 - Myocardial infarction with or without thrombotic occlusion
 - Systemic and cardiac thromboembolic events,
 - Myocarditis
 - Coronary atheroma, cardiac steatosis
 - Micropathology: 
 - Vasospasm in susceptible subjects
 - Sympathomimetic effect during physical activity,
Arrhythmias occur often during physical activity

- focal myocardial necrosis,
- regional myocardial fibrosis,
- contraction band necrosis,
- myocardial fibrosis,
- myocardial coagulation necrosis

Sources: Pub Med 1990-2005, 96 studies

- Trento-Milan cases 7 (0.2%) (1 SD, 1 CA, 5 AF) in 434 consecutive competitive arrhythmic athletes (387 males, mean age 23.5)



Arrhythmogenic effects of illicit drugs in athletes *Myocardial infarction, hyperkalaemia and ventricular tachycardia in a young male body-builder*

A 31-year-old body-builder taking **anabolic androgenic steroids, amphetamines, frumil (furosemide and amiloride), and potassium supplements** collapsed with a myocardial infarction. His serum potassium was 6.7 mmol/l and he had a run of ventricular tachycardia. He was unaware of the effects of the drugs on the heart...

Arrhythmogenic effects of anabolic androgenic steroids in athletes

Arrhythmogenic risk factors

In users of AAS

1. PREEXISTING LATENT ARRHYTHMOGENIC DISEASE

- a. Inherited forms genetic related (i.e. hypertrophy cardiomyopathy, dilated cardiomyopathy, long QT, arrhythmogenic right ventricular displasia)
- b. acquired forms (i.e. myocarditis, ischemic heart diseases)

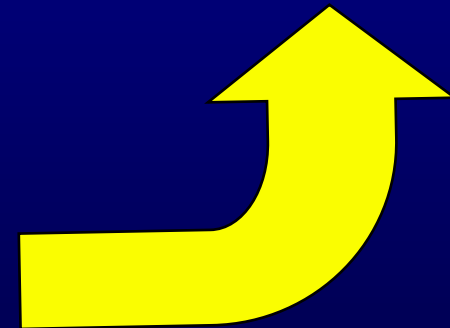
2. EX NOVO ARRHYTHMOGENIC HEART DISEASE

- a. Hypertrophyc/Dilated Cardiomyopathy, Ischemic/Trombo-embolic diseases, myocarditis

From supraphysiological doses, stacking, intensive prolong training particularly in strenght trained athletes such as weightlifters, bodybuilders, powerlifters and throwers

**SUPRA/VENTRICULAR
ARRHYTHMIAS**

**VENTRICULAR FIBRILLATION
SUDDEN DEATH**





Arrhythmogenic effects of illicit drugs in athletes ***Nutritional Supplements***

Pro-hormones and steroid hormones and stimulants (ephedra) may be present, even though they are not clearly specified in the content list, in some dietary supplements for athletes, who, therefore, are exposed both to a possible positive doping control and arrhythmogenic effects.

Such products do not require the same scrutiny as drugs that undergo the FDA approval process

(Current opinion in Pediatrics 2000,12,382-387)

Arrhythmogenic effects of androgenic anabolic steroids in athletes

CONCLUSIONS (I)

AAS are one of the most important illicit drugs prohibited at all times (in and out competition) in the 2005 IOC-WADA list, taken to “improve athletic performance”

AAS may induce a wide spectrum of arrhythmias frequently during physical effort:

- **focal or re-entry type, supra/ventricular, lethal or not**
- **through a direct or indirect arrhythmogenic effect**
- **in the short, medium or long term**

Arrhythmogenic effects of anabolic androgenic steroids in athletes

CONCLUSIONS (II)

1. In presence of an underlying latent arrhythmogenic heart disease (e.g inherited cardiomyopathies at risk for sudden cardiac death), **AAS may induce severe detrimental cardiac arrhythmic event** acting as revealing, unmasking or enhancing factors.
2. **Long-term administration of AAS**, can provoke arrhythmias due to **'ex-novo' arrhythmogenic heart diseases** (Hypertrophic/Dilated Cardiomyopathy, Ischemic/Thrombo-embolic diseases, myocarditis)

especially with

- **Supra physiological doses**
- **Simultaneous combinations with other illicit drugs**
- **Subjects with intensive prolonged training**