

LEAPING FORW>RD

LISBON INTERNATIONAL CLINICAL CONGRESS
ESPÍRITO SANTO SAÚDE

1ST
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FEB 2014

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LEAPING FORW>RD

LISBON INTERNATIONAL CLINICAL CONGRESS
ESPÍRITO SANTO SAÚDE

17 FEB

SUDDEN DEATH
IN ATHLETES:
ONE STEP BEYOND

PEDRO GRANATE
NUNO CARDIM

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LEAPING FORW>RD

LISBON INTERNATIONAL CLINICAL CONGRESS



NUNO CARDIM

ESPIRITO SANTO SAÚDE

ARISTOTLE UNIVERSITY OF THESSALONIKI, GREECE



SPORTS MEDICINE LABORATORY

DIRECTOR: PROF. A. DELIGIANNIS



**ASTERIOS DELIGIANNIS
PROF. OF SPORTS MEDICINE
CARDIOLOGIST**

A dramatic, high-contrast photograph set against a dark, moody background. A woman with blonde hair, wearing a red, flowing dress, is captured in mid-dance. Her right arm is extended, and her hand is held by a skeletal hand. The skeleton, wearing a black hooded cloak, is partially visible on the left. The scene is lit from behind, creating a bright, glowing effect through what appears to be a window or a series of lights, which illuminates the woman's face and the edge of her dress. The overall atmosphere is mysterious and dramatic.

**Dancing with Doping
...to Cardiac Death !!!**

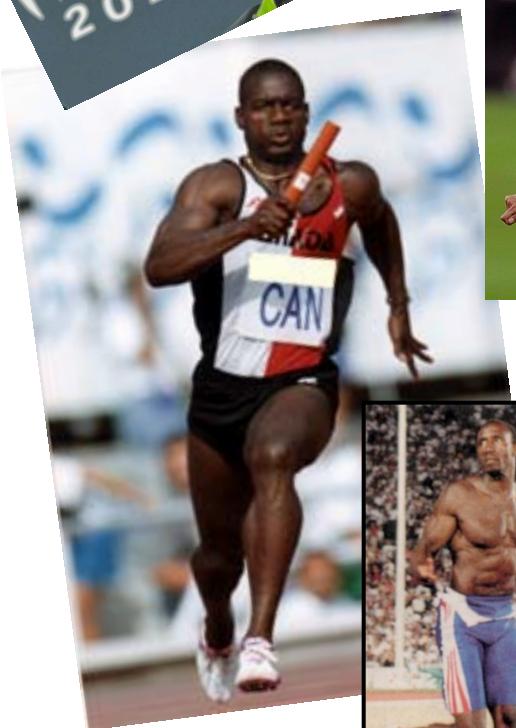
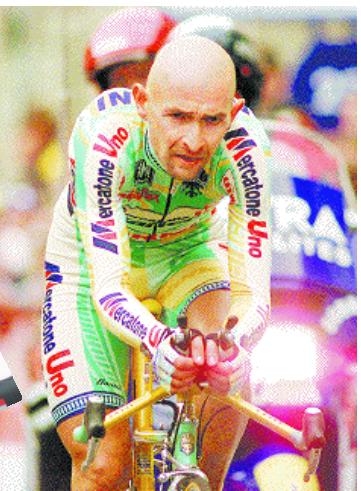
The New York Times

Opinion

WORLD U.S. N.Y. / REGION BUSINESS TECHNOLOGY SCIENCE HEALTH SPORTS

Doping in sport : To the athletes dying young





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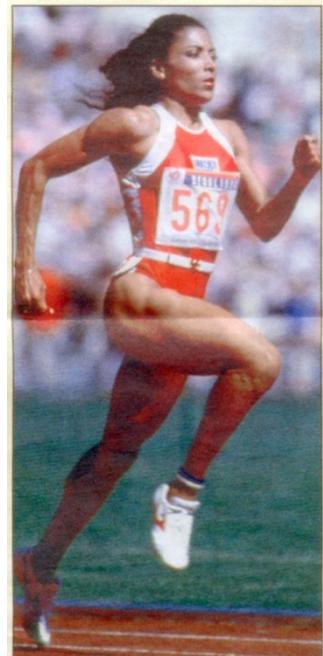
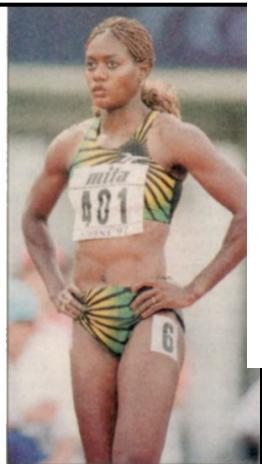
[Sport](#) > [Drugs in sport](#)

Athletics fights on after Tyson Gay and Asafa Powell doping scandal

Reeling from recent failed tests, athletics and the anti-doping agencies consider new options in the fight against drug cheats



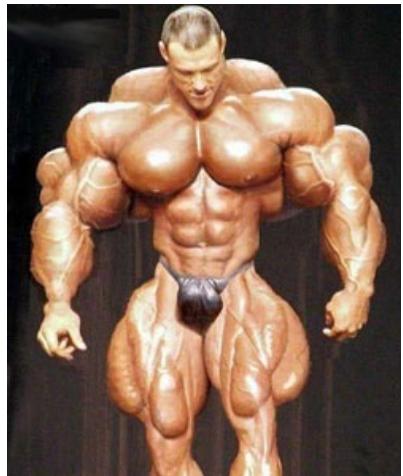
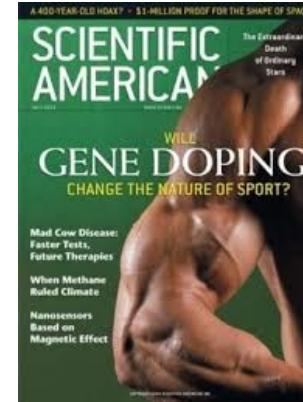
Sean Ingle
The Observer, Saturday 20 July 2013 19.59 BST



Cases during 2013

- On 31 January, Michael Rasmussen held a press conference where he admitted the use of doping for much of his pro career. He stated that he had used EPO, growth hormone, testosterone, DHEA, insulin, IGF-1, cortisone and did blood transfusions.^[458]
- On 6 March, Michael Boogerd held a press conference for Dutch news broadcaster NOS where he admitted to have used doping at the peak of his career (from 1997 until 2007). He stated that he had used EPO, cortisone and was subject of blood transfusions.^[459]
- On 18 March, Rolf Sørensen admitted using EPO and Cortisone during the 1990s.^[460]
- On 15 May, Sylvain Georges tested positive for heptaminol.
- On 24 May, Danilo Di Luca was positive on doping test.
- On 3 June, Mauro Santambrogio was positive on doping test.
- On 15 July, it was announced that 2013 Tour of Turkey winner Mustafa Sayar (Torku Şeker Spor) was provisionally suspended following the news that he tested positive for EPO during the Tour d'Algérie in March.^[461]
- On 24 July, a French Senatorial commission released a list containing the names of cyclists who, in a retroactive analysis, tested positive for EPO while competing in the 1998 Tour de France which includes: Manuel Beltran, Jeroen Blijlevens, Mario Cipollini, Laurent Desbiens, Jacky Durand, Bo Hamburger, Jens Heppner, Laurent Jalabert, Kevin Livingston, Eddy Mazzoleni, Nicola Minali, Abraham Olano, Marco Pantani, Fabio Sacchi, Marcos Serrano, Andrea Tafi, Jan Ullrich, and Erik Zabel. The same list also contained the names of cyclists who produced suspicious test results which includes: Stephane Barthe, Ermanno Brignoli, Giuseppe Calcaterra, Pascal Chanteur, Bobby Julich, Eddy Mazzoleni, Roland Meier, Axel Merckx, Frederic Moncassin, Stuart O'Grady, Alain Turicchia, and Stefano Zanini. Hamburger and Livingston were again named for producing positive results for doping tests during the 1999 Tour de France.^{[462][463]}

HISTORY OF DOPING



DEFINITION

**DOPING IS DEFINED AS THE PRESENCE OF A PROHIBITED
SUBSTANCE OR ITS METABOLITES OR MARKERS IN AN
ATHLETE'S BODILY SPECIMEN AND THE USE OR
ATTEMPTED USE OF A PROHIBITED SUBSTANCE OR A
PROHIBITED METHOD TO INCREASE ATHLETIC
PERFORMANCE.**

IOC, 2006

2014 PROHIBITED LIST OF WADA

Substances and methods prohibited at all times (in and out of competition)

Substances

- **Anabolic Agents**
- **Hormones and Related Substances**
- **Beta-2 Agonists**
- **Hormone Antagonists and Modulators**
- **Diuretics and other Substances and Methods Prohibited in-competition**
Masking Agents
- **Stimulants**
- **Narcotics**
- **Cannabinoids**
- **Glucocorticosteroids**

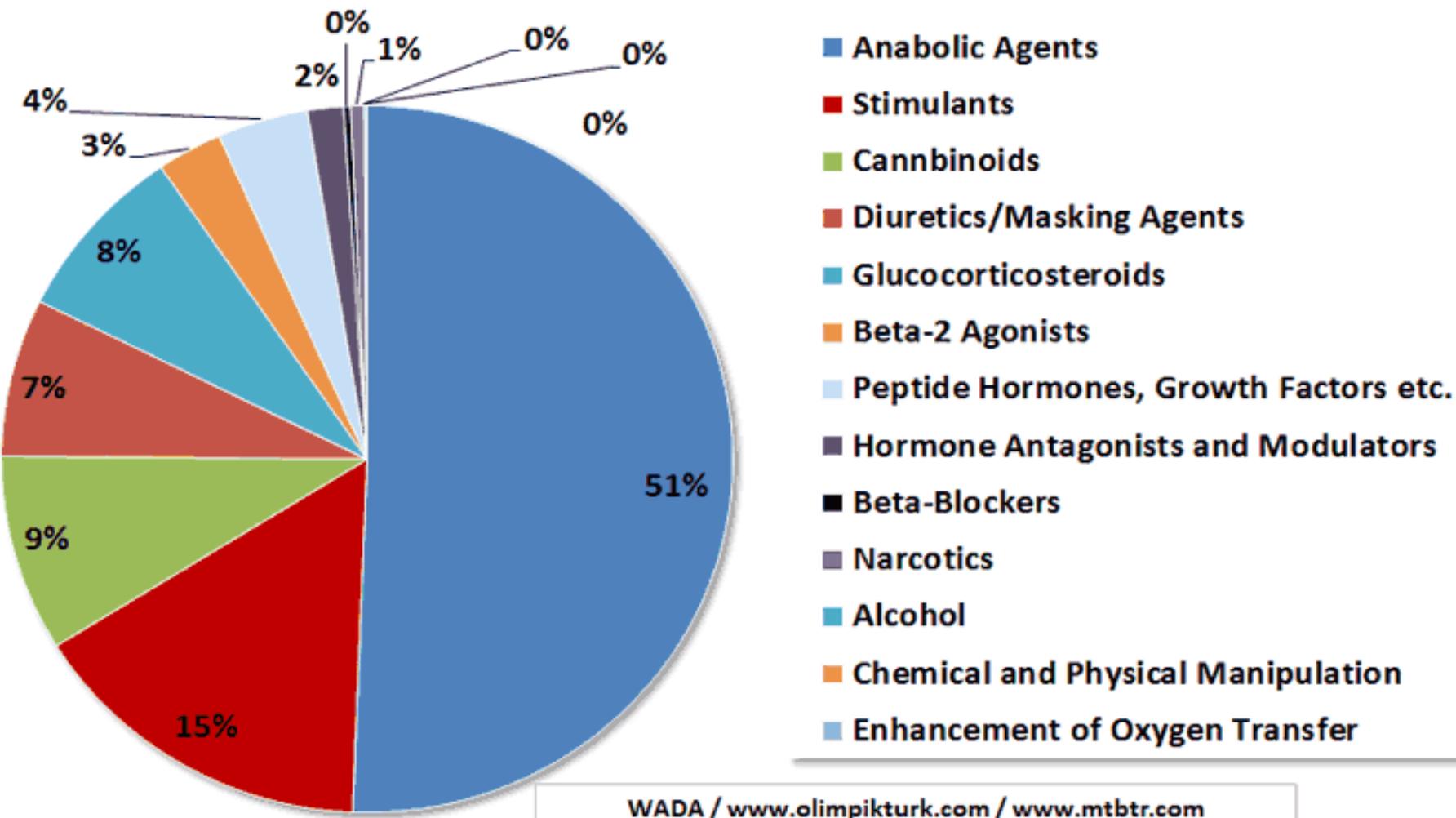
Methods

- **Enhancement of Oxygen Transfer**
- **Chemical and Physical Manipulation**
- **Gene Doping**

Substances Prohibited in Particular Sports

- **Alcohol**
- **Beta-Blockers**

Prohibited Substances Identified - 2012





Lippincott
Williams & Wilkins
a Wolters Kluwer business



EUROPEAN
SOCIETY OF
CARDIOLOGY®

Position Paper

ESC Study Group of Sports Cardiology Position Paper on adverse cardiovascular effects of doping in athletes

Asterios Deligiannis^a, Hans Björnstad^b, Francois Carre^c, Hein Heidbüchel^d,
Evangelia Kouidi^a, Nicole M. Panhuyzen-Goedkoop^e, Fabio Pigozzi^f,
Wilhelm Schänzer^g and Luc Vanhees^h on behalf of the ESC Study Group
of Sports Cardiology

AMONG BIOMEDICAL SIDE EFFECTS OF DOPING,

**THE CARDIOVASCULAR ONES ARE THE MOST
DELETERIOUS, WITH THE POTENTIAL TO LEAD TO**

INCREASED MORBIDITY AND MORTALITY.

European Journal of Cardiovascular Prevention and Rehabilitation 2006, 13:687–694

LIST OF DEAD ATHLETES FROM DOPING

- Denis Zanette (Italy) cycling – died January 2003, age 32. **Heart attack**
- Steve Bechler (U.S.) baseball – died February 2003, age 23. **Multi-organ failure**
 - Marco Ceriani (Italy) cycling – died May 2003, age 16. **Heart attack**
 - Fabrice Salanson (France) cycling – died June 2003, age 23. **Heart attack**
 - Marc-Vivien Foe (Cameroon) soccer – died June 2003, age 28. **Heart attack**
 - Marco Rusconi (Italy) cycling – died November 2003, age 23. **Heart attack**
 - Jose Maria Jimenez (Spain) cycling – died December 2003, age 32. **Heart attack**
 - Michel Zanolli (Netherlands) cycling – died December 2003, age 35. **Heart attack**
 - Johan Sermon (Belgium) cycling – died February 2004, age 21. **Heart attack**
 - Marco Pantani (Italy) cycling – died February 2004, age 34. **Heart attack**
 - Miklos Feher (Hungary) soccer – died April 2004, age 24. **Heart attack**
 - Alessio Galetti (Italy) cycling – died June 2004, age 34. **Heart attack**
 - David Di Tomasso (France) soccer – died November 2005, age 26 **Heart attack**

- **THE CARDIOVASCULAR SIDE EFFECTS OF DOPING DEPEND ON THE TYPE OF THE CONSUMED DRUG, AS WELL AS THE AMOUNT AND DURATION OF INTAKE.**
- **ATHLETES OFTEN USE A COMBINATION OF SEVERAL DRUGS IN HIGH DOSAGES LEADING TO INTERACTIONS AND COUNTERACTIONS.**

Deligiannis et al, EJCPR, 2006;13:687

10-9 weeks before the competition

daily:

**Ephederine, AN 1, Catagon, Aspirine,
Valium, Clenbuterol**

8-6 weeks before the competition daily:

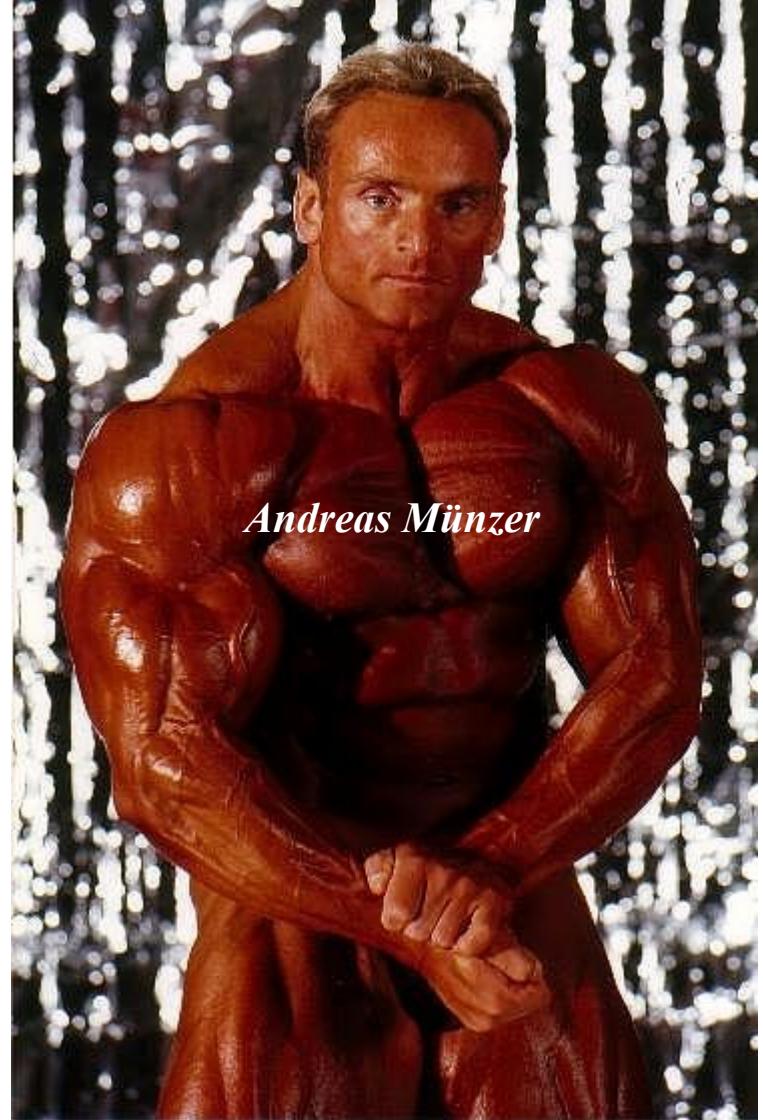
**2 inject. Testoviron a 250mg, 1 inject
Parabolan, 30 tabletts Halotestin, 30
tabletts Metandienon, 20IE* STH, 20IE*
Insuline,**

5-3 weeks before the competition daily:

**2 inject. Parabolan, 2 inject. 24IE*
Stromba, 30 tabletts Halotestin, 50
tabletts Stromba,**

2-1 weeks before the competition daily:

**2 inject. Masteron, 2 inject. Stromba,
40 inject. Halotestin, 80 tabletts
Stromba, 24 IE* STH, Insuline, IGF**



Birgit Dressel died due to a anaphylactic shock in 1987:

- **102 different substances were detected in her body**



CARDIAC SIDE EFFECTS OF PROHIBITED SUBSTANCES

	hypertension	arrhythmias	LVH	CAD	MI	HF	SCD
AAS	+	+	+	+	+	+	+
hGH		+	+			+	+
EPO	+					+	
Beta 2-Agonists		+			+	+	+
Diuretics		+					
Amphetamines	+	+			+	+	+
Cocaine	+	+		+	+	+	+
Ephedrine	+	+		+	+		+
Narcotics							+
Cannabinoids		+			+		+
Glucocorticosteroids	+			+			
Alcohol	+	+			+	+	+

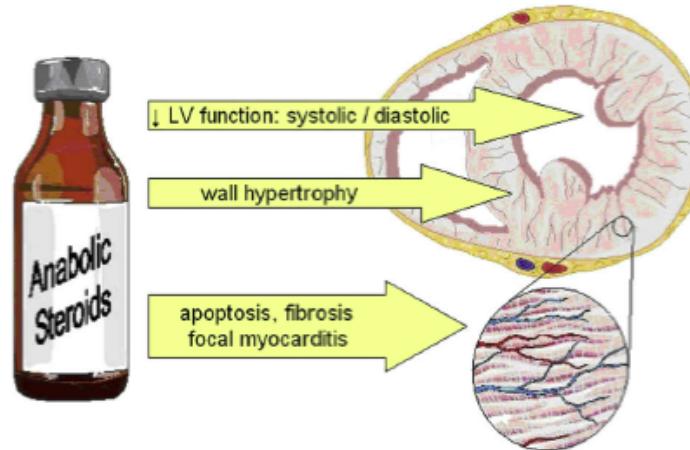
Deligiannis et al, EJCP, 2006;13:687

Editorial

Anabolic-Androgenic Steroids Worse for the Heart Than We Knew?

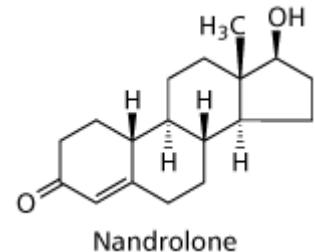
Matthew W. Parker, MD; Paul D. Thompson, MD

Circ Heart Fail. 2010;3:470-471

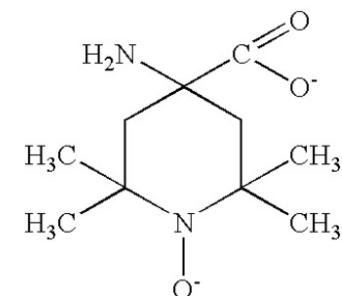


ANABOLIC AGENTS

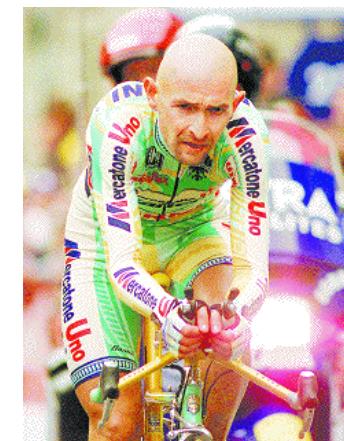
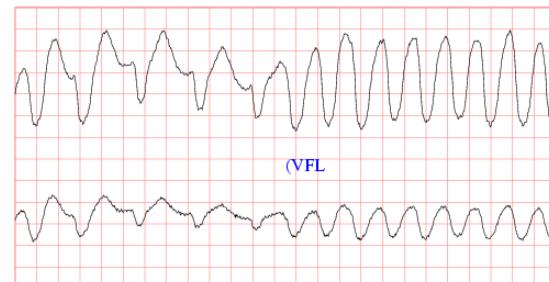
1. Anabolic steroids (AAS)
(e.g. nandrolone, testosterone)



2. B_2 – agonists
(e.g. salbutamol, fenoterol)



Sudden Cardiac Death
THE MOST TRAGIC
EFFECT !!!



SUDDEN CARDIAC DEATH IN ANABOLIC USERS

Sudden Cardiac Death in a 20-year-old Bodybuilder Using Anabolic Steroids
Cardiovasc Toxicol 2001;15:86:172
Dinkerman et. al.

Anabolic Steroid Abuse and Cardiac Death
Med J Aust 1993;158:346
Kennedy et al.



Case report

Anabolic androgenic steroids abuse and cardiac death in athletes: Morphological and toxicological findings in four fatal cases

Massimo Montisci^{a,*}, Rafi El Mazloum^a, Giovanni Cecchetto^a, Claudio Terranova^a, Santo Davide Ferrara^a, Gaetano Thiene^b, Cristina Bassi^b

^aDepartment of Environmental Medicine and Public Health, Section of Legal Medicine, University of Padua Medical School, Via G. Balleppi 50, 35121 Padova, Italy

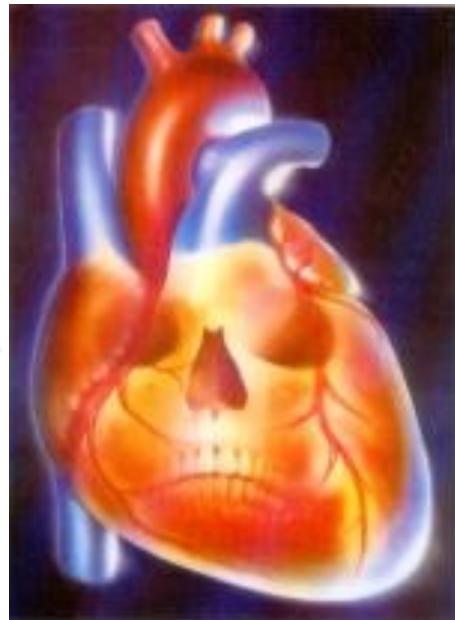
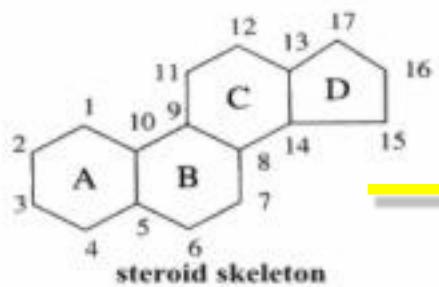
^bDepartment of Medical Diagnostic Sciences and Special Therapies, University of Padua Medical School, Via A. Gabelli 67, 35121 Padova, Italy

Anabolic Steroid Abuse and Cardiac Sudden Death:
A Pathologic Study

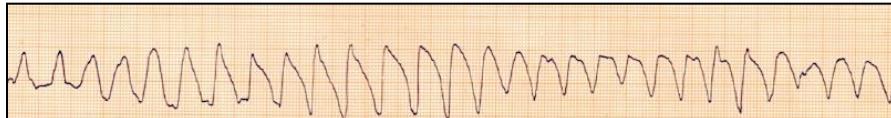
Fineschi et al.
Arch. Pathol Lab Med
2001;125:253

Sudden Cardiac Death During Exercise in a Weight - Lifter Using Anabolic Androgenic Steroids.
J. Forensic Sci 1991;35:1441
Luke et al.

CARDIAC SIDE EFFECTS

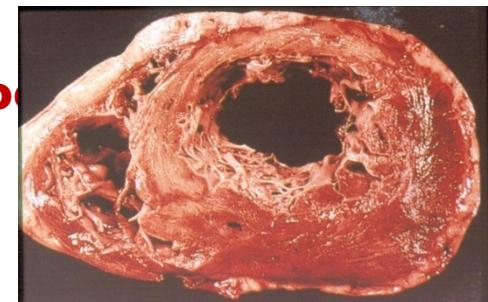


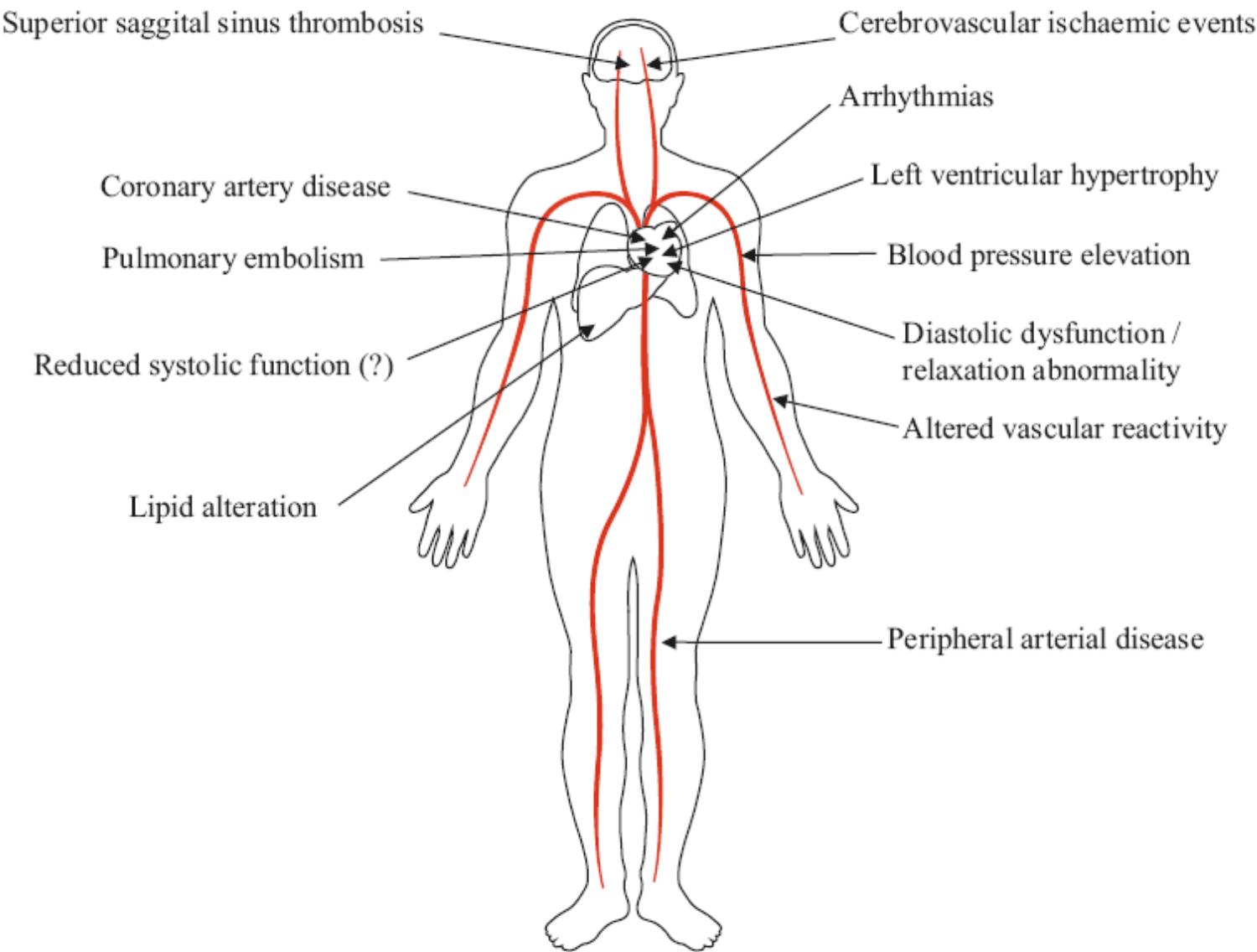
Sudden Cardiac Death



- Alterations of cardiac adaptations to exercise training**
- Cardiomyopathy**
- Myocarditis**
- Arterial hypertension**
- Coronary atherosclerosis**
- Cardiac arrhythmias**
- Ventricular dysfunction**

Myo

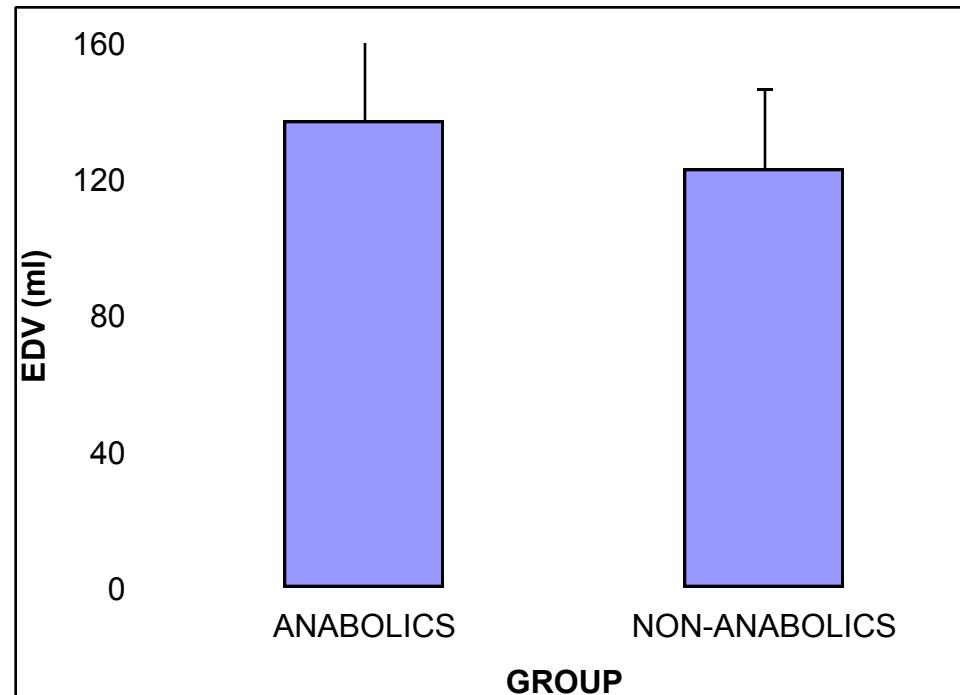
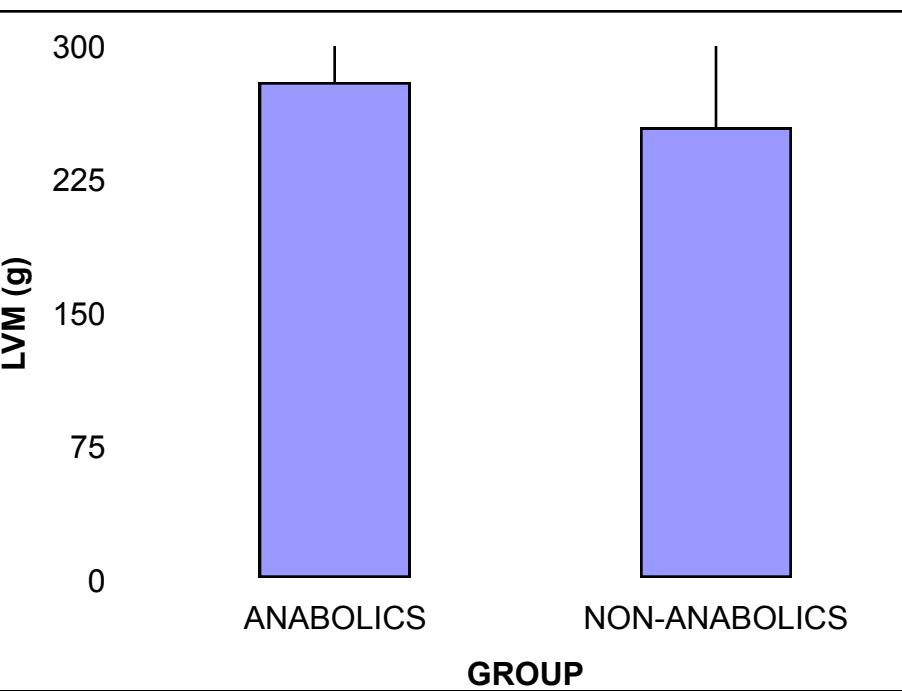




ANATOMICAL AND FUNCTIONAL EFFECTS OF ANABOLICS

- **INCREASE IN SIZE AND MASS OF MYOCARDIUM**
- **DILATATION OF CARDIAC CHAMBERS**
- **SYSTOLIC DYSFUNCTION**
- **INCREASE IN DIASTOLIC STIFFNESS**
- **IMPAIRMENT OF DIASTOLIC PROPERTIES**
- **THE EFFECTS ARE NOT REVERSIBLE AFTER DISCONTINUATION OF AAS (?)**

ECHOCARDIOGRAPHIC STUDY IN WEIGHT LIFTERS AND BODY BUILDERS



Deligiannis et al, Int J Cardiology 12:36,1998

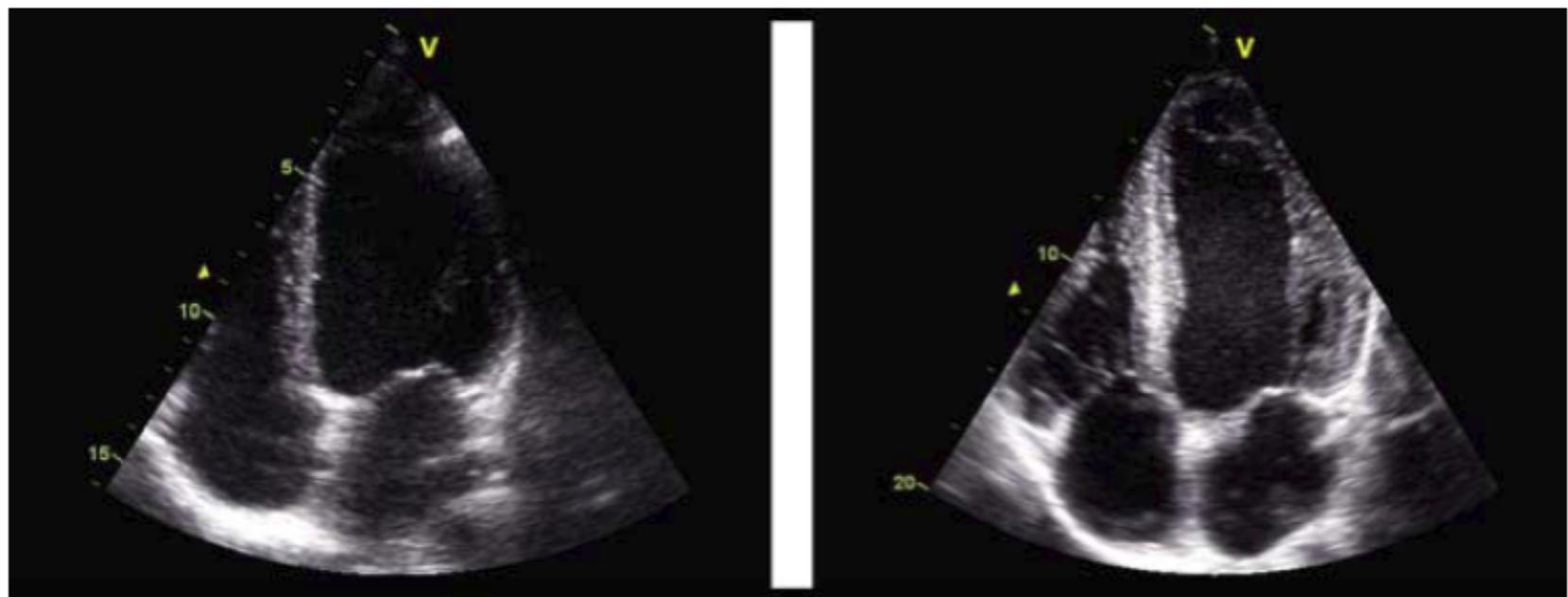


Fig. 3 Echocardiographic image of a drug-free 25-year-old powerlifter (*left*) with normal left ventricular wall thickness and of an AAS-using 37-year-old bodybuilder (*right*) with concentric left ventricular hypertrophy

MYOCARDIAL ANATOMICAL EFFECTS OF ANABOLICS

Study	Abused Agent	Dosage (mg/week)	Subjects, Age (years) Users Ex-Users Controls	Ventricular dimensions (cm)			PW (mm)		
				Users	Ex-Users	Controls	Users	Ex-Users	Controls
D'Andrea et al ^{61,‡}	—	525 (91)	20, 35 (3) — 25, 34 (3)	12.3 (1.3)	—	11.2 (2.1)	11.8 (1.4)	—	10.4 (2.1)
De Piccoli et al ⁶²	—	—	14, 26 (5) 9, 26 (5) 14, 26 (4)	11 (0.8)	10.6 (1.0)	10.5 (0.8)	10.3 (0.8)	9.8 (0.9)	9.8 (0.7)
Di Bello et al ⁵⁹	Testosterone propionate Methenolone enanthate Testosterone cypionate	300–500 300–600 200–350	10, 33 (3) — 10, 30 (7)	12.3 (0.7)	—	12.2 (0.4)	11.6 (0.5)	—	11.7 (0.4)
Dickerman et al ¹⁵	—	—	8 — 8	11.27 (0.2) [†]	—	8.74 (2.5)	12.1 (1.0) [†]	—	10.3 (2.0)
Hartgens et al ^{63,‡}	Nandrolone decanoate Stanozolol	20–250 30–140	17, 32 (7) — 15, 33 (5)	8.8 (1.1)	—	8.3 (1.0)	8.9 (0.7)	—	8.6 (0.8)
Karila et al ^{64,‡}	—	770 (310)	16, 30 (5) — 15, 26 (3)	11.2 (1.0) [‡]	—	8.9 (1.1)	11.3 (1.1) [‡]	—	9.1 (1.0)
Krieg et al ^{65,‡}	—	820 (620)	36 (7) — 36 (11)	12 (1.5) [†]	—	10.5 (1.0)	10.5 (1.5)	—	10 (0.5)
Nieminen et al ^{47,‡}	Testosterone Testosterone undecanoate	2,860 [¶] 2,660 [¶]	4, 30 (3) — —	12.75 (1.5)	—	—	13.75 (1.3)	—	—
Nottin et al ⁶⁷	—	—	6, 41 (6) — 9, 38 (6)	10.8 (1.3)	—	9.7 (1.7)	10.0 (1.4)	—	10.3 (0.9)
Palatini et al ^{38,‡}	Testosterone enanthate and propionate Stanozolol	50–1,500 50–150	10, 27 (8) — 14, 28 (5)	10.8 (2.3)	—	9.6 (0.8)	10.4 (2.3)	—	10.1 (1.3)
Sachtleben et al ⁷⁰	Stanozolol Methandrostenolone nandrolone	—	11, 27 (6) — —	11.1 (1.2)*	—	9.3 (1.2)	11.2 (1.5)*	—	9.5 (1.6)
Sader et al ¹³	Testosterone cypionate Stanozolol Nandrolone Creatine	—	13, 27 (6) 10, 37 (3) — 10, 34 (3)	10 (0.3) [‡]	—	8.7 (0.2)	9/8 (0.4) [†]	—	8.7 (0.3)
Thompson et al ^{81,‡}	Nandrolone decanoate Testosterone cypionate Stanozolol	—	12, 23 (4) — 11, 26 (7)	10 (2.0)	—	9.0 (1.0)	8.0 (1.0)	—	8 (1.0)
Urhausen et al ^{43,‡}	—	1,030	17, 31 (5) 15, 38 (7) 15, 28 (5)	12.3 (1.4) [‡]	11.5 (1.2) [†]	10.3 (1.0)	11.4 (1.3)* [‡]	10.2 (0.8)	9.4 (1.5)
Urhausen et al ⁷¹	Methandione, stanozolol Testosterone depot	630	14, 28 (6) — 7, 26 (5)	12.6 (1.7)	—	11.6 (0.9)	12.5 (1.2) [‡]	—	10.3 (1.8)
Zuliani et al ^{44,‡}	Testosterone enanthate and propionate Human growth hormone	750–1,500	6, 28 (2) — 8, 26 (2)	11.8 (0.8)	—	11.2 (0.7)	10.8 (0.7)	—	10.3 (0.5)

Achar S et al. Am J Cardiol 2010;106:893

CASES WITH CARDIAC SIDE EFFECTS FROM ANABOLICS

Author, year	Age	Echocardiographic Findings	Electrocardiographic Findings	Clinical Presentation and Other Relevant Findings	Progression
Vogt, 2002 ¹⁶	21	LVEF: 20-30% LVEDD: > 80 mm, LV wall thickness 13 mm mitral valve regurgitation	Sinus tachycardia, T-wave inversion in I, aVL, V5, V6	Dyspnea, orthopnea, bloody sputum, lung edema, pleural effusions, sinus tachycardia TSH suppressed with peripheral euthyroid state, elevated CRP, GPT, CK, urea, creatinine	After 1 y LVEF: 45% LVEDD: 80 mm
Ferrera, 1997 ¹³	24	LVEF 39% (catheterization)	T-wave inversions in II, III, aVF, V4, V5, V6	Dyspnea, chest pain/angina, pulmonary hypertension	After 1 mo LVEF: 69%
Schollert, 1993 ¹⁵	33	Dilated LV with decreased contractility	Atrial flutter with 2:1 block (ventricular rate frequency: 176 beats/min)	Fever, epigastric pain, head and extremity pain, palpitations, pulmonary congestion highly elevated liver function tests and LDH	Patient died within 1 year
Nieminen, 1996 ⁹	31	LVEF 14% LVEDD 79 mm LV wall thickness: 12 mm	Intermittent 2° AV block Mobitz I, left ventricular hypertrophy	Congestive heart failure Scintigraphy: myocardial scarring Electron microscopy: Z-line thickening, mitochondrial clustering	After 9 months of therapy: fractional shortening 27%, decrease of LV wall thickness by 1-2 mm, normal systolic and diastolic LV dimensions
Clark, 2005 ¹⁴	40	LVEF: 10-15% 4 chamber cardiomegaly Severe mitral and tricuspid regurgitation Global hypokinesis Paradoxical motion of septal wall Minimal pericardial effusion	Sinus tachycardia, occasional premature ventricular contractions, poor R-wave progression	Shortness of breath, paroxysmal nocturnal dyspnea, orthopnea, fatigue, productive cough, weight gain, dark urine, insomnia, nausea/vomiting, arthralgias, scleral icterus Pleural effusions, pulmonary vascular congestion, cardiomegaly, hepatomegaly, ascites Highly elevated liver function tests, elevated creatinine and urea, impaired coagulation	After 18 months: asymptomatic LVEF: 50-55% with mild mitral and tricuspid regurgitation

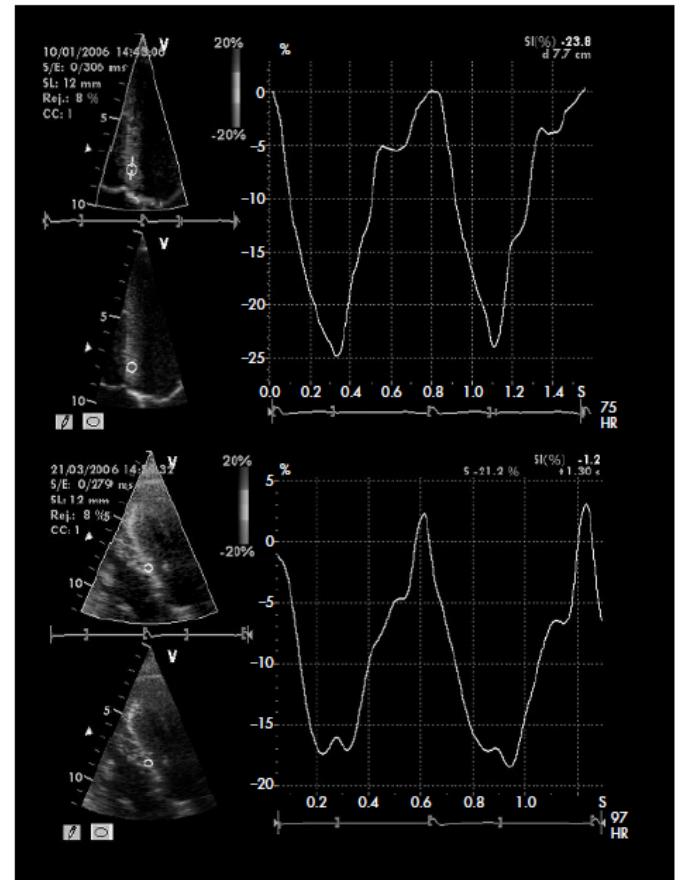
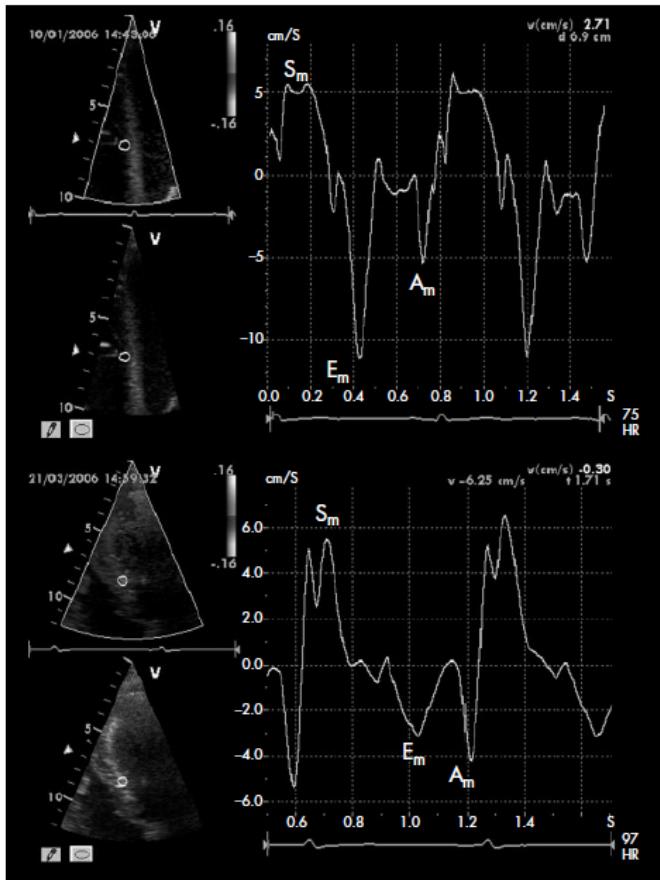
Table 1 Human echocardiographic studies investigating the effects of AAS on cardiac structure and function

Author	Journal	Year	Study design	AAS (n)	Control +Exercise (n)	Control (n)	Follow-up	Adverse effects of AAS	Main findings
Salke	Med Sci Sports Exerc	1985	CS	15	15	15	–	–	
Pearson	Am J Cardiol	1986	CS	5	11	10	–	+	DD, ↑LVmass
Urhausen	Eur J Appl Physiol Occup Physiol	1989	CS	14	7	–	–	+	LVH, ↑IVRT (DD)
Zuliani	Int J Sports Med	1989	P	6	8	–	6 weeks	–	
De Piccoli	Int J Sports Med	1991	P	14	14	14	8 weeks	+	LVH, ↑LVmass, ↑IVRT (DD)
Thompson	J Am Coll Cardiol.	1992	CS	12	11	–	–	–	
Sachtleben	Med Sci Sports Exerc	1993	P	11	13	–	8 weeks	+	LVH, ↑LVmass, ↑LVDd, ↓VO ₂ max
Palatini	J Clin Pharmacol	1996	CS/P	10	14	–	11 weeks	–	
Yeater	Br J Sports Med	1996	CS	8	27	8*	–	+	↑LVmass _I
Dickerman	Clin J Sports Med	1997	CS	8	8	–	–	+	LVH, ↓LVDd (related to BMI)
Di Bello	Med Sci Sports Exerc	1998	CS	10	10	10	–	+	LVH, ↑LVmass, ↓CVI
Dickerman	Cardiology	1998	CS	10	7	–	–	–	
Karila	Int J Sports Med	2003	CS	20	–	15	–	+	↑LVmass, LVH
Hartgens	Int J Sports Med	2003	P	(1) 17 (2) 8	15 8	– –	8–16 weeks	–	
Climstein	J Sci Med Sport	2003	CS	23	23	–	–	+	Abnormal waveforms (cardiokymography)
Urhausen	Heart	2004	CS	17+15	15	–	–	+	↑LVmass _I , LVH, relaxation abnormality
Nottin	Am J Cardiol	2006	CS	6	9	16	–	+	↑LVmass, ↑LVDd, DD
Chung	Clin Endocrinol (Oxf)	2007	P		10	10	4 weeks	–	
				10+					
Krieg	Int J Sports Med	2007	CS	14	11	15	–	+	↑LVmass _I , LVH, DD
D'Andrea	Br J Sports Med	2007	CS	20	25	25	–	+	LVH, DD, systolic dysfunction
Kasikcioglu	Int J Cardiol	2008	CS	12	14	15	–	+	↑LVmass and ↑LVmass _I , Relaxation abnormality in left and right ventricles

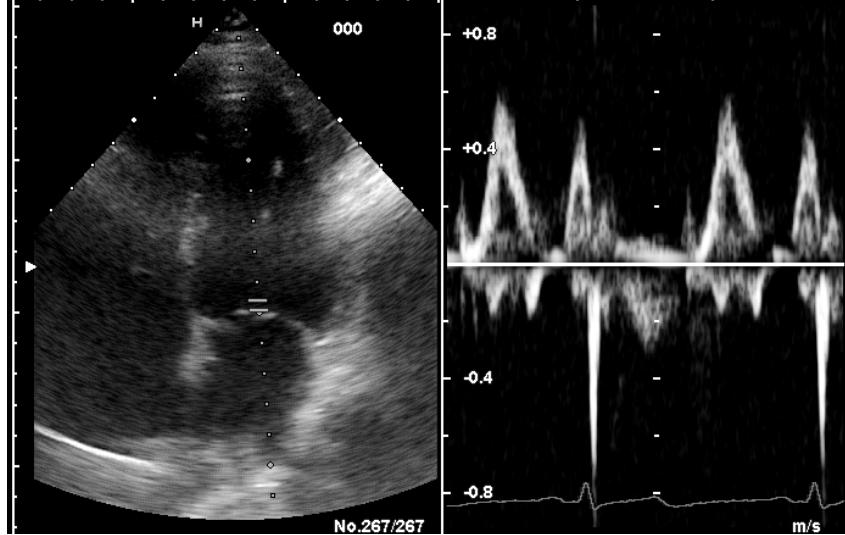
* runners

Colour reconstructed pulsed-wave Doppler myocardial imaging

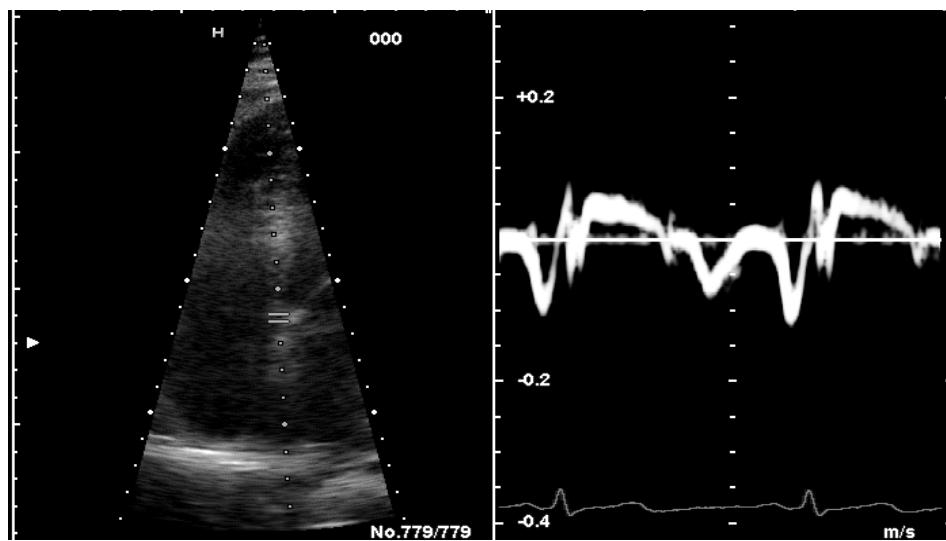
Strain Analysis



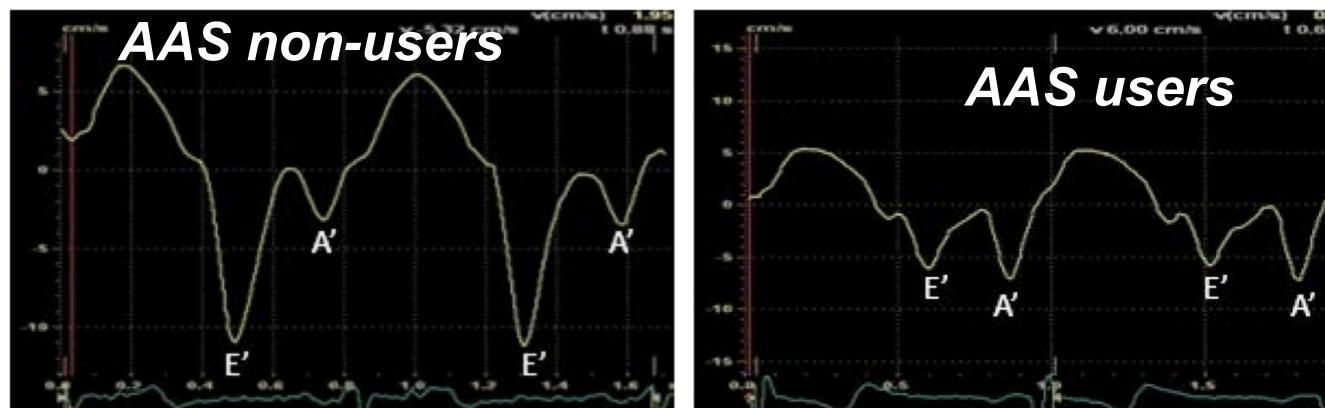
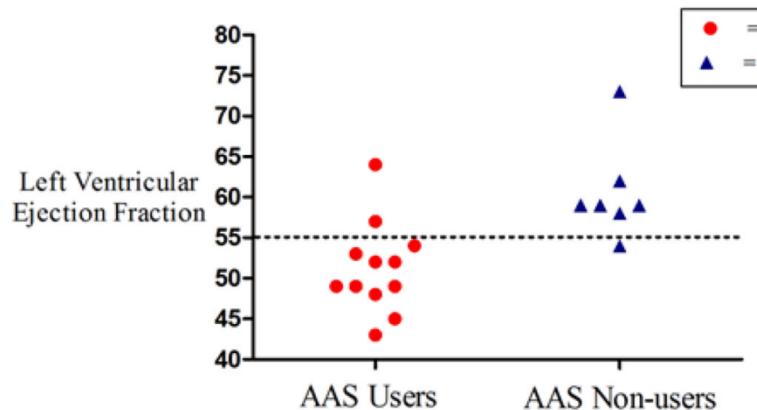
D' Andrea A, et al. Br J Sports Med 2007;41:149



a. Normal diastolic function by standard echo in an AAS user

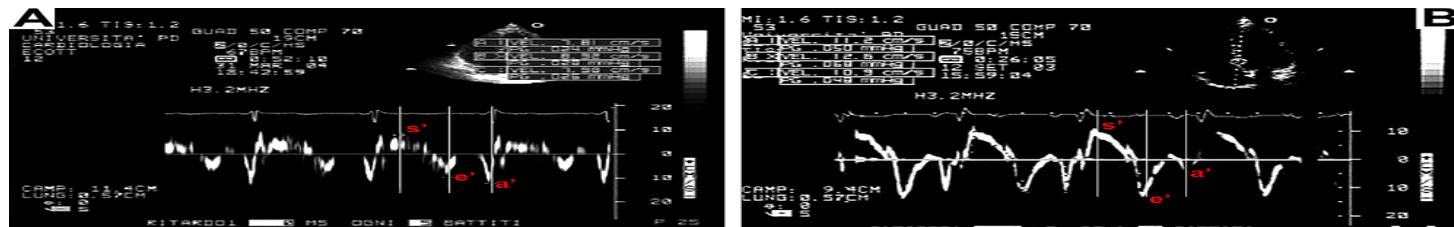


b. TDI detected diastolic dysfunction in the same athlete-AAS user



Baggish A, et al. Circ Heart Fail 2010; 34: 472

AAS non-users



Montisci R, et al. J Am Soc Echocardiogr 2010;23:516

ATHEROGENIC EFFECT OF AAS ON ARTERIAL VESSELS

**AAS INCREASE LEVELS OF LDL AND TRIGLYCERIDES
AND DECREASE HDL DUE TO A STIMULATION OF**

HEPATIC TRIGLYCERIDE LIPASE.

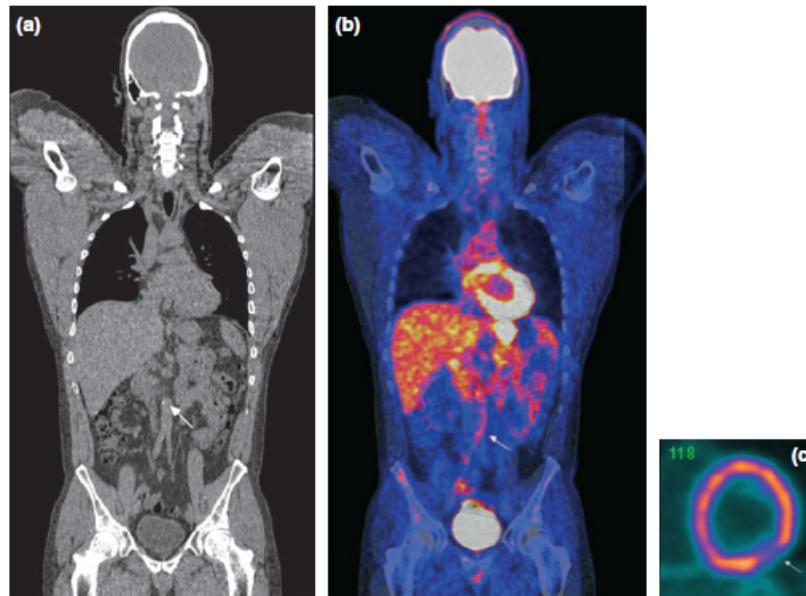
**HYPERRHOMOCYSTEINEMIA WAS FOUND IN
BODYBUILDERS USING AAS.**

Achar S et al Am J Cardiol 2010; 106 : 893

Table 1
Effects of anabolic-androgenic steroid abuse on lipoprotein concentration

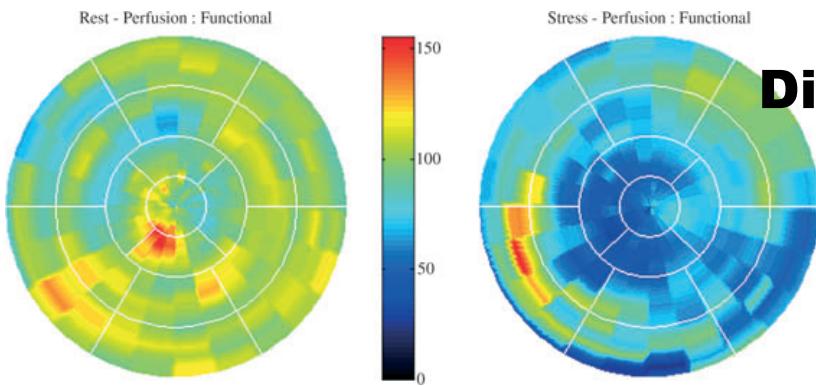
Study	Abused Agent	Dosage of AAS (mg/week)	Subjects, Age (years)			
			Users	Hx-Users	Subjects LDL (mg/dL)	Subjects HDL (mg/dL)
			Controls		HDL (mg/dL)	Ex-users LDL (mg/dL)
Rakito-Enzi et al ^{39,40}	Methenolone enanthate	100-300	14, 27 ± 5	129 ± 37	—	119 ± 17
	Testosterone cypionate	200-300	17, 25 ± 4	27 ± 11 ^b	—	48 ± 6
Fröhlich et al ⁴⁰	—	—	13, 27 ± 4	154 ± 58	—	121 ± 22
			11, 27 ± 7	23 ± 16 ^b	—	34 ± 7
Hartgens et al ^{41,42}	Stanozolol	30-140	19, 31 ± 7	—	—	—
	Nandrolone decanoate	8-250	—	17 ± 9 ^b	—	47 ± 22
			16, 33 ± 5	—	—	—
Lajarin et al ³⁹	Stanozolol	50-100	2, 27 ± 3	238 ± 8	—	—
	Methenolone enanthate	100	—	14 ± 0.4	—	—
			—	—	—	—
Lane et al ⁴²	Testosterone	—	10, 26 ± 7	113 ± 27	86 ± 23	82 ± 12
	Nandrolone		8, 32 ± 7	27 ± 16 ^b	51 ± 16	51 ± 12
	Stanozolol		10, 24 ± 4	—	—	—
Lenders et al ⁴³	Methenolone	385-690	20, 26 ± 8	206 ± 21 ^{a,b}	156 ± 9	130 ± 13
	Testosterone	310-355	42, 28 ± 7	27 ± 3 ^{a,b}	42 ± 2	46 ± 2
	Oxymetholone	580-650	13, 28 ± 5	—	—	—
McKillip and Ballantyne ³⁷	Stanozolol	280	8, 25 ± 4	243 ± 50 ^b	—	122 ± 27
	Nandrolone decanoate	200	—	16 ± 11 ^b	—	43 ± 12
			8, 25 ± 3	—	—	—
Palatini et al ^{38,43}	Testosterone enanthate and propionate	50-1,500	10, 27 ± 8	153 ± 34 ^b	—	107 ± 41
	Stanozolol	50-150	—	30 ± 10	—	57 ± 13
			14, 28 ± 5	—	—	—
Sader et al ⁴³	Stanozolol	—	10, 37 ± 3	—	—	—
	Nandrolone		—	23 ± 4 ^b	—	55 ± 4
	Creatine		10, 34 ± 3	—	—	—
Urhausen et al ⁴³	Oral (i.e., mesterolone) and intramuscular AAS (i.e., stanozolol, nandrolone)	1,030	17, 31 ± 5	139 ± 37	119 ± 30	—
			15, 38 ± 7	17 ± 11 ^b	43 ± 11	—
			—	—	—	—
Zuliani et al ⁴⁴	Testosterone enanthate and propionate	750-1,500	6, 28 ± 2	—	—	—
	Human growth hormone		—	19 ± 8 ^b	—	49 ± 6
			8, 26 ± 2	—	—	—

¹⁸F-FDG PET/CT images of AAS-associated atherosclerosis



Rest 13N-ammonia and stress 13N-ammonia PET.

Diagnosis: Microvascular disease



Golestani R, et al Eur J Clin Invest 2012; 42 : 795

THROMBOGENIC EFFECT OF AAS ON ARTERIAL VESSELS

**AAS DECREASE FIBRINOLYTIC ACTIVITY
AND INCREASE PLATELET AGGREGATION**

Zeitschrift für Kardiologie
April 2003, Volume 92, Issue 4, pp 326-331

Koronarthrombosen und -ektasien nach
langjähriger Einnahme von anabolen
Steroiden

K.-H. Tischer, R. Heyny-von Haußen, G. Mall, P. Doenecke

POSSIBLE MECHANISMS FOR ARTERIAL THROMBOSIS BY AAS

- **↑ Several procoagulant factors**
- **↓ Fibrinolytic activity**
- **↑ Platelet aggregation**
- **↓ Synthesis of prostacyclin**
- **↑ Endothelium release**
- **↑ Heparin cofactor II**
- **↑ Protein C**
- **↑ Protein S**

Nieminen et al, Eur Heart J, 1996;17:1576

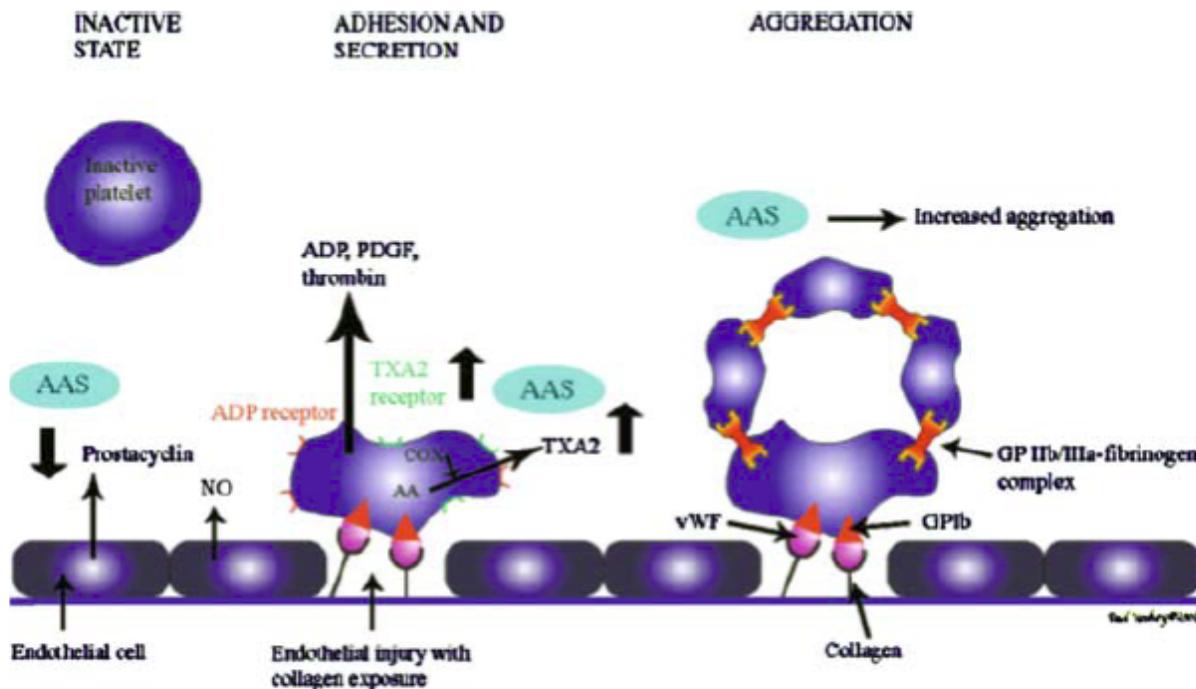
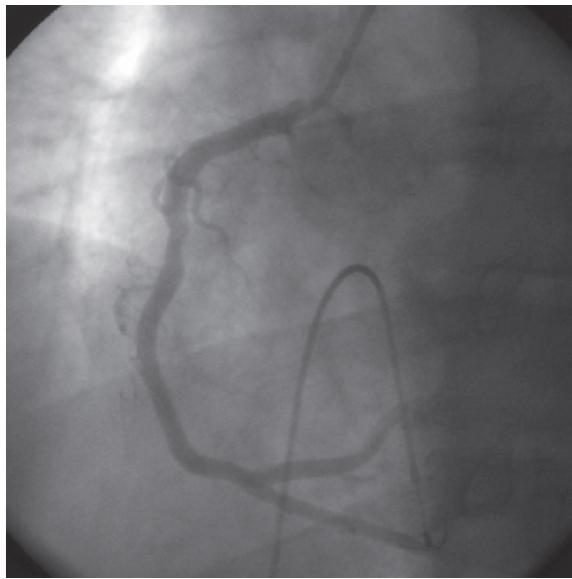
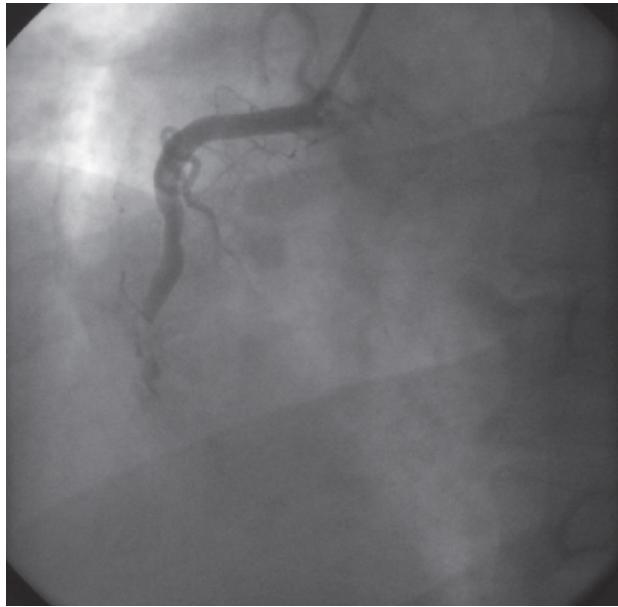
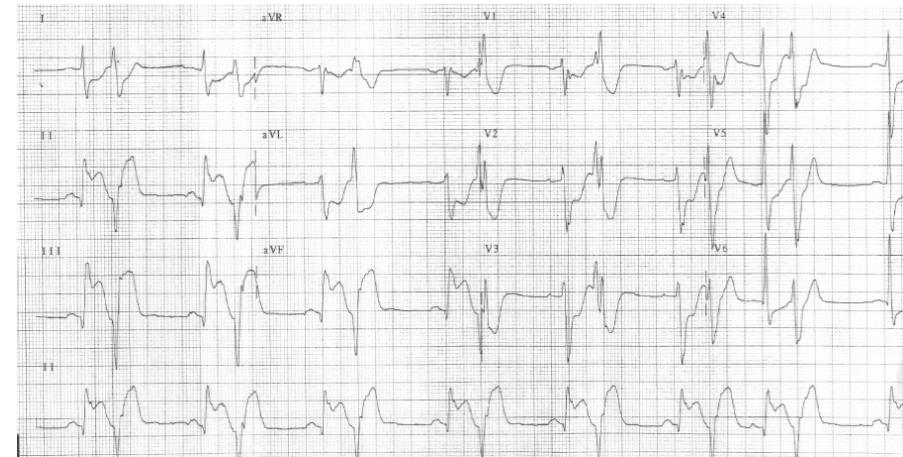


Fig. 6 The illustration shows different pathways of blood platelet activation, adhesion and aggregation. AAS appear to increase the platelet aggregation response. Experimental and human studies have indicated that AAS increase platelet production of TXA₂ and increase both platelet and vascular TXA₂ receptor density. The drugs may also decrease the production of PGI₂. ADP=Adenosine diphosphate; COX=Cyclooxygenase; NO=Nitric oxide; AA=Arachidonic acid; PDGF=Platelet derived growth factor; PGI₂=Prostacyclin; TXA₂=Thromboxane A₂; vWF=von Willebrand factor; GP=Glycoprotein

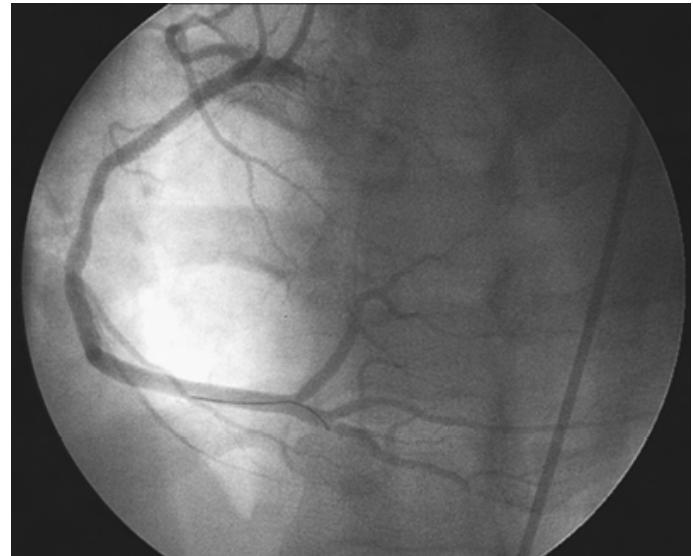
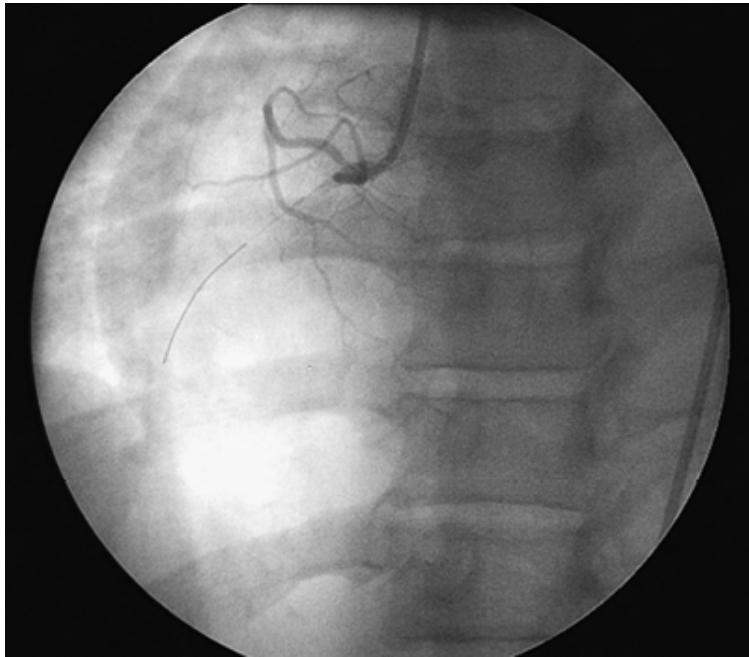


Anabolic steroids and acute myocardial infarction



Stergiopoulos K, et al. Vasc Health Risk Manag 2008;4:1475

Acute Myocardial Infarction in a Young Man Using Anabolic Steroids

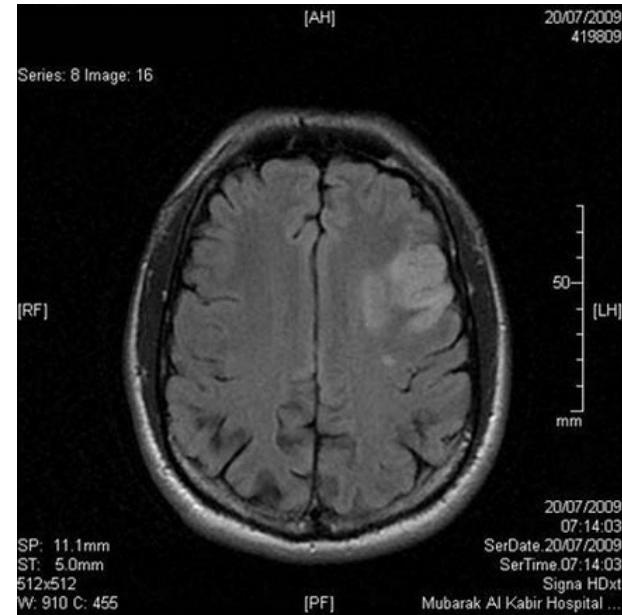


Wysoczanski M et al. Angiology, 2008 ;59: 376



Vanberg P, Atar D. Handb Exp Pharmacol. 2010;195:411

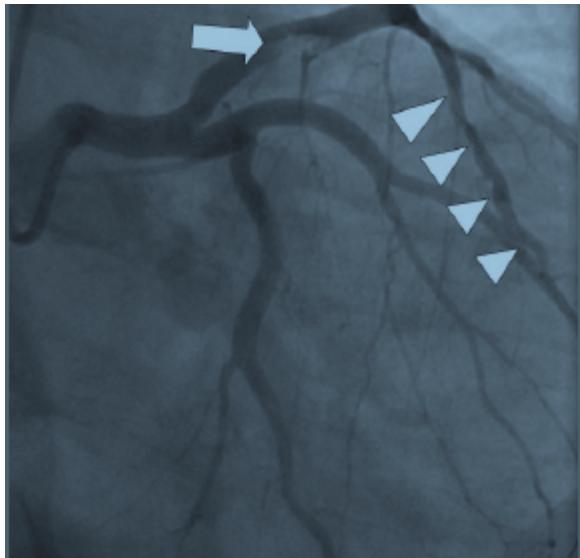
Anabolic androgenic steroid-induced cardiomyopathy,stroke and peripheral vascular disease



M Youssef et al, BMJ Case Rep, 2011; bcr 1220103650

VASOSPASM EFFECT OF AAS ON ARTERIAL VESSELS

**AAS increase vascular response to
norepinephrine and enhance coronary artery
spasm**



Smedopa J and Muler G,SAMJ 2008;98:372

CORONARY VASOCONSTRICITION THEORIES

- **THE USE OF ANABOLIC STEROIDS IS ASSOCIATED WITH IMPAIRED VASCULAR REACTIVITY.**
(Sader et al, 2001)
- **AAS CAN CAUSE ENDOTHELIAL CELL DYSFUNCTION**
(Wysoczanski et al, 2008)
- **TESTOSTERONE INCREASES THE VASCULAR RESPONSE TO NOREPINEPHRINE**
(Sullivan et al, 1998)
- **HOWEVER, TESTOSTERONE ACTS AS AN ACUTE CORONARY VASODILATOR (Webb et al, 1999)**

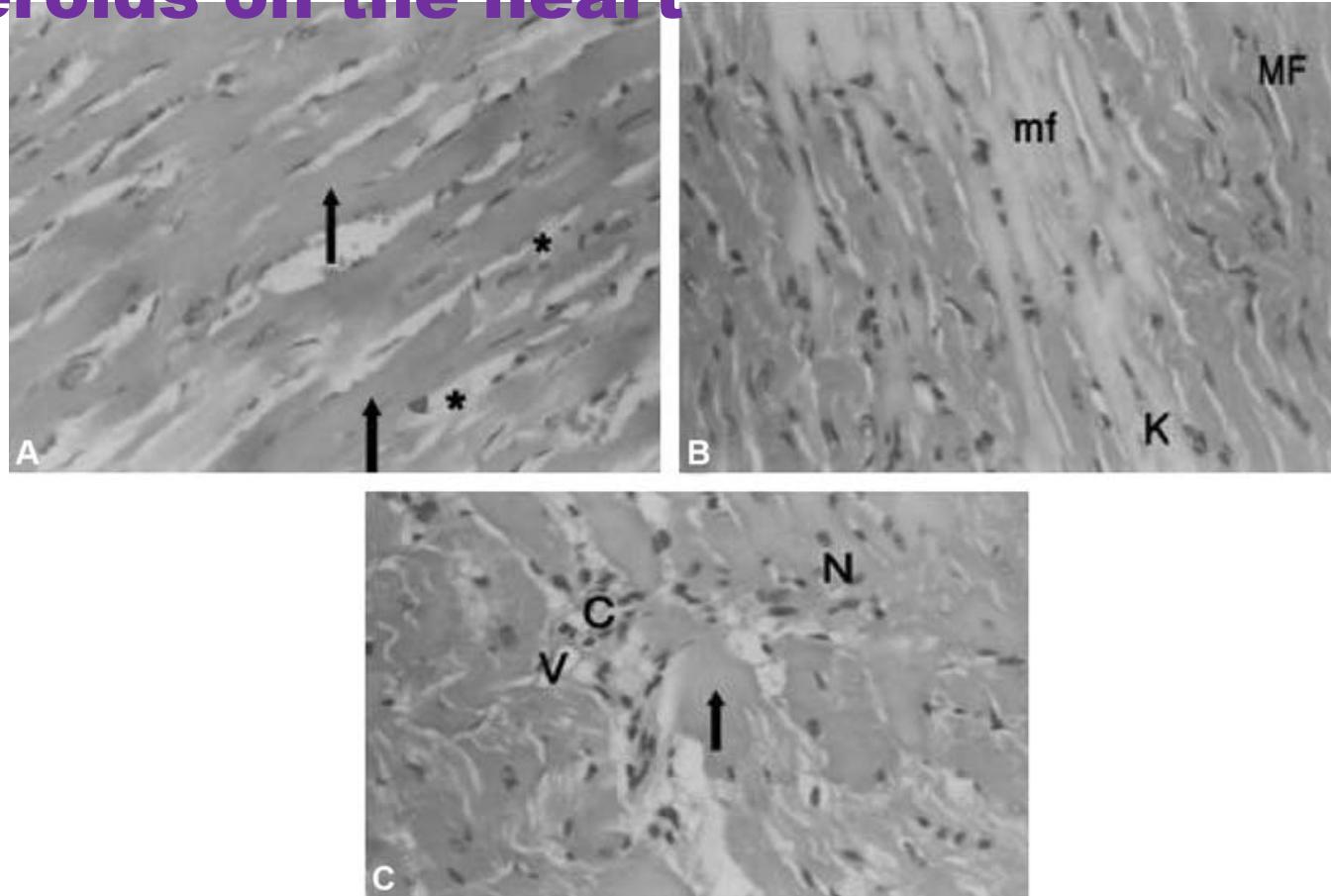
DIRECT MYOCARDIAL EFFECT OF AAS

- **MYOCARDIAL HYPERTROPHY**
- **FIBROSIS AND NECROSIS**
- **DISTURBANCES OF CONTRACTILE APPARATUS
AND MITOCHONDRIA**
- **INCREASE OF MYOCARDIAL COLLAGEN**
- **DEGENERATION OF SYMPATHETIC AXONS**
- **DECREASE OF CAPILLARY DENSITY**

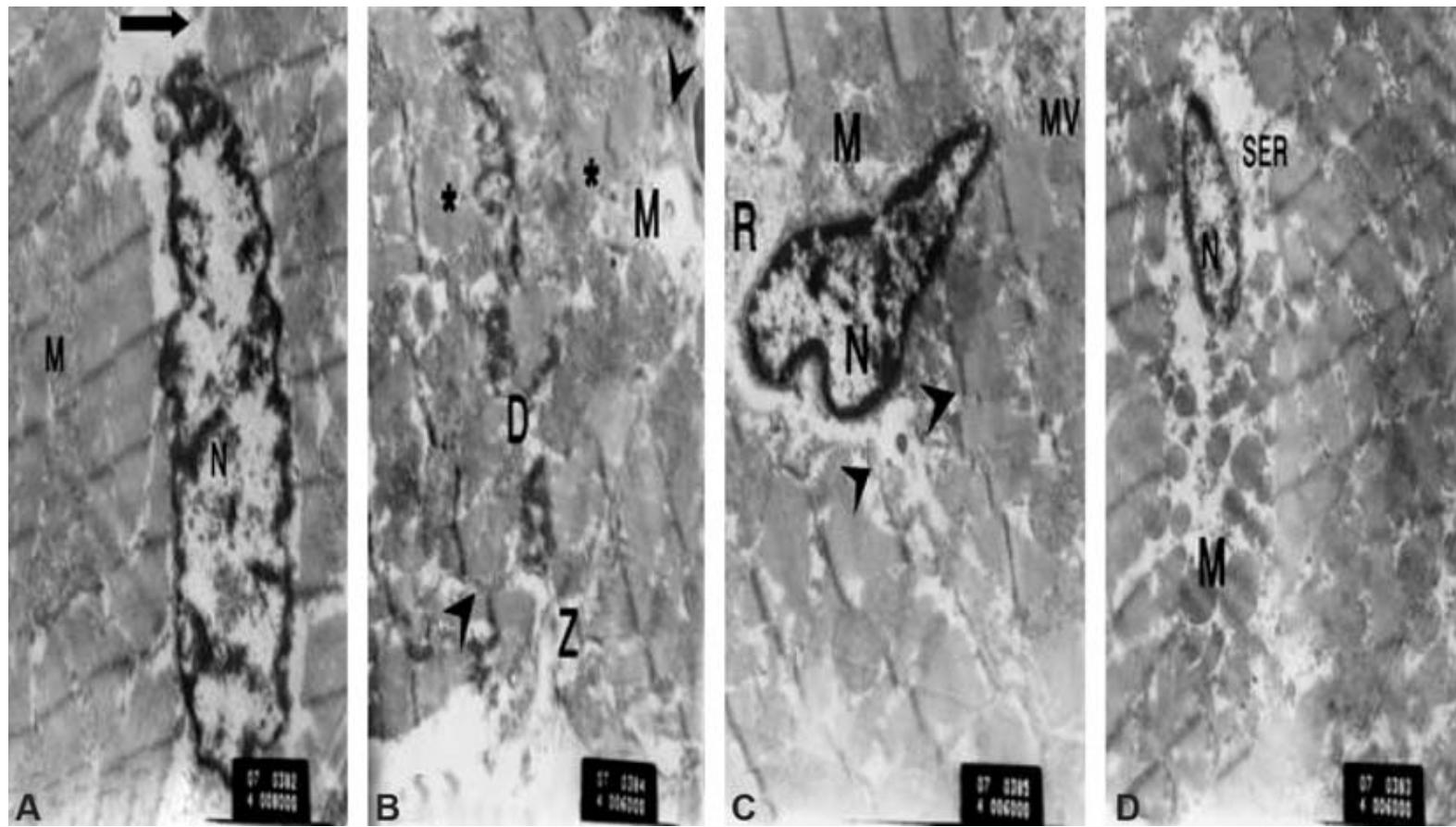
**Deligiannis A,in Biomedical Side Effects of Doping ,Sport and Buch Straub
2001;13:30**

Hassan et al ,Human and Experimental Toxicology,2009;28:273

Doping and effects of anabolic androgenic steroids on the heart



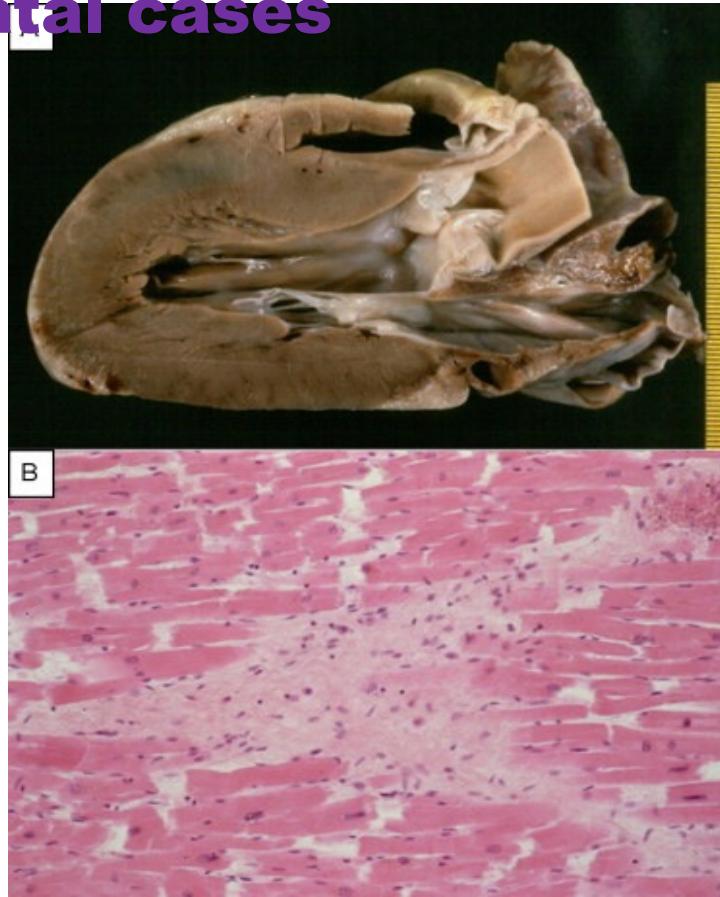
A photomicrograph of a longitudinal section in the left ventricular (LV) wall of the adult albino rat cardiac muscle 8 weeks after intramuscular injection of sustanon showing focal areas of degeneration with loss of striations (↑).



An electromicrograph of an ultra-thin section in the left ventricular (LV) wall of the adult albino rat cardiac muscle 8 weeks after intramuscular injection of sustanon showing irregular cardiac myocyte nucleus with condensed chromatin (N.), and interrupted Z-bands. Also, severely destructed mitochondria (M) can be seen

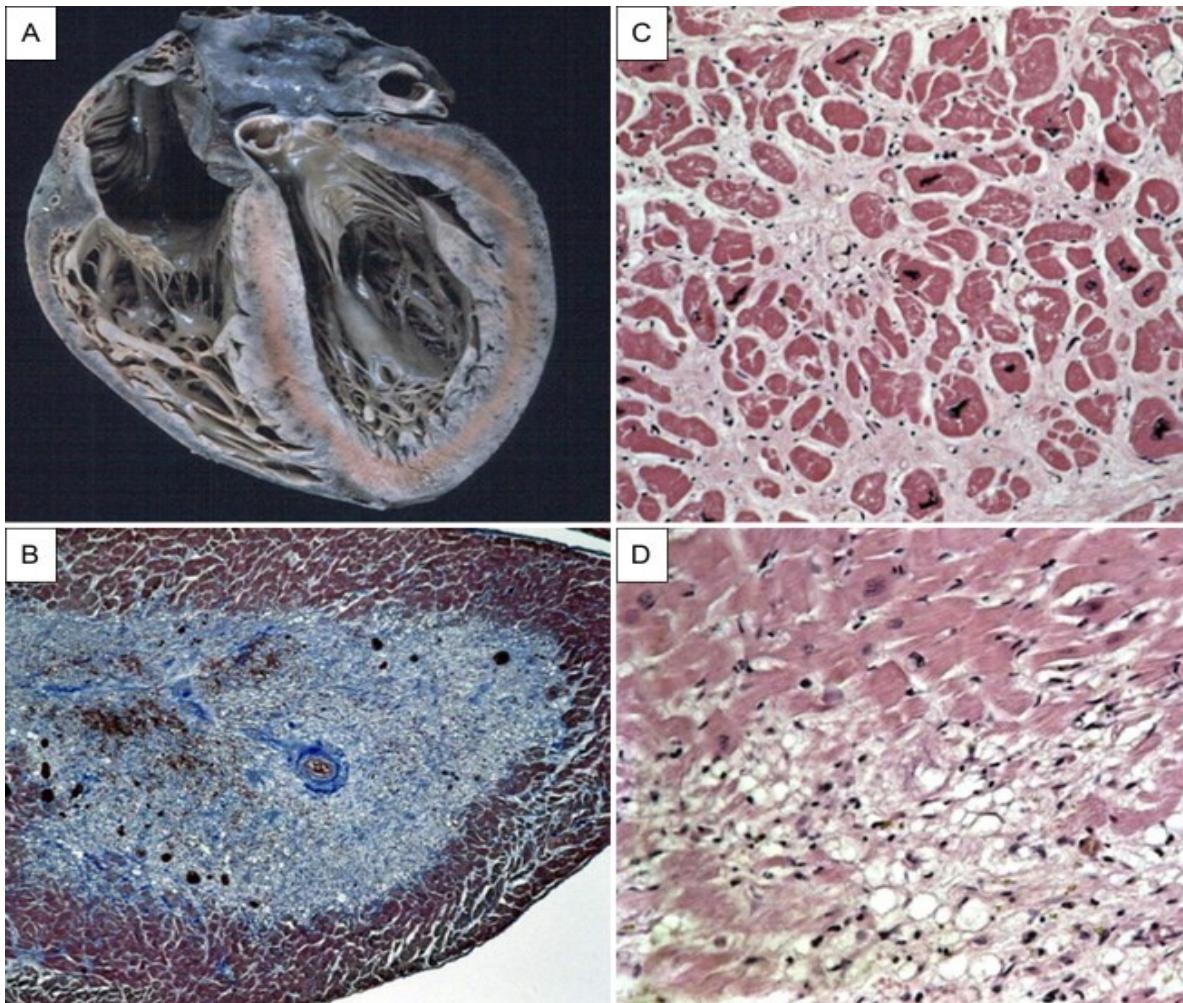
NA Hassan, et al. Hum Exp Toxicol ,2009;28:273

Anabolic androgenic steroids abuse and cardiac death in athletes: Morphological and toxicological findings in four fatal cases

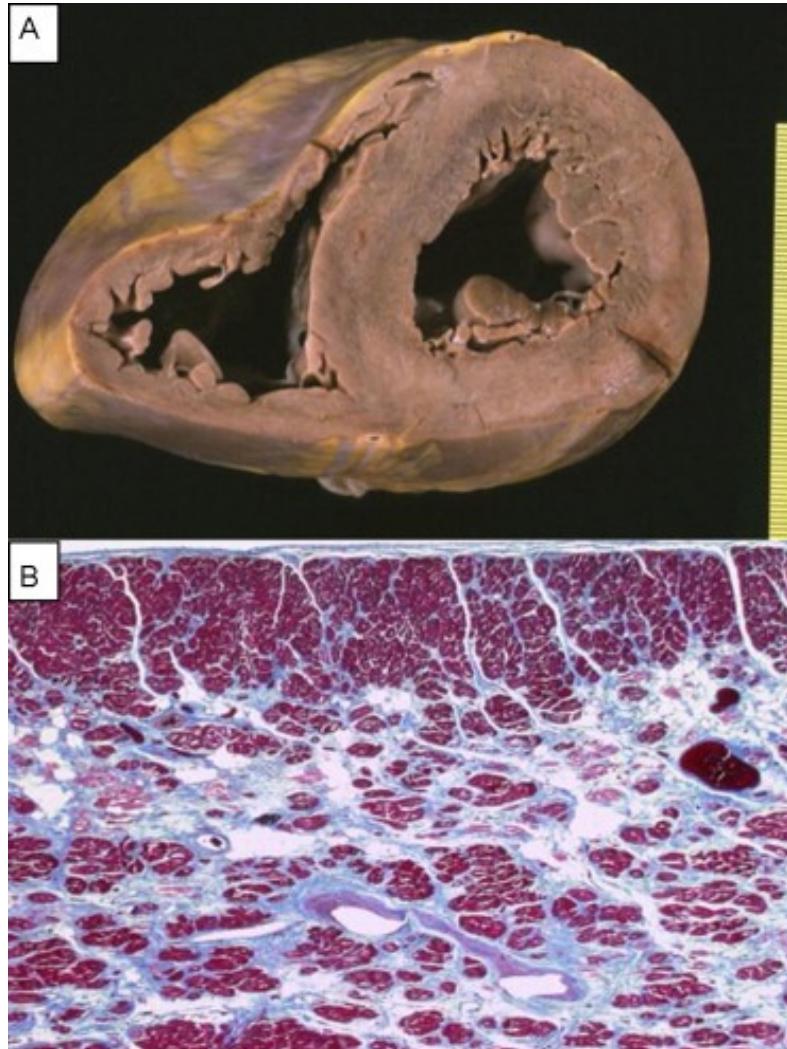


Case # 1: (A) Parasternal long axis section of the left ventricle (heart weight 450 g), with concentric left ventricular hypertrophy (interventricular septum thickness 16 mm, left ventricular free wall thickness 15 mm). (B) Spot of replacement-type fibrosis..

Montisci M , et al. Forensic Science International 2012; 217: e13



Case # 2: (A) Cardiomegaly (weight 900 g) with eccentric biventricular hypertrophy and dilatation. (B) Myocytolysis in the sub-endocardial trabeculae . (C) Hypertrophic myocytes with dysmetric and dysmorphic nuclei; interstitial and replacement fibrosis...

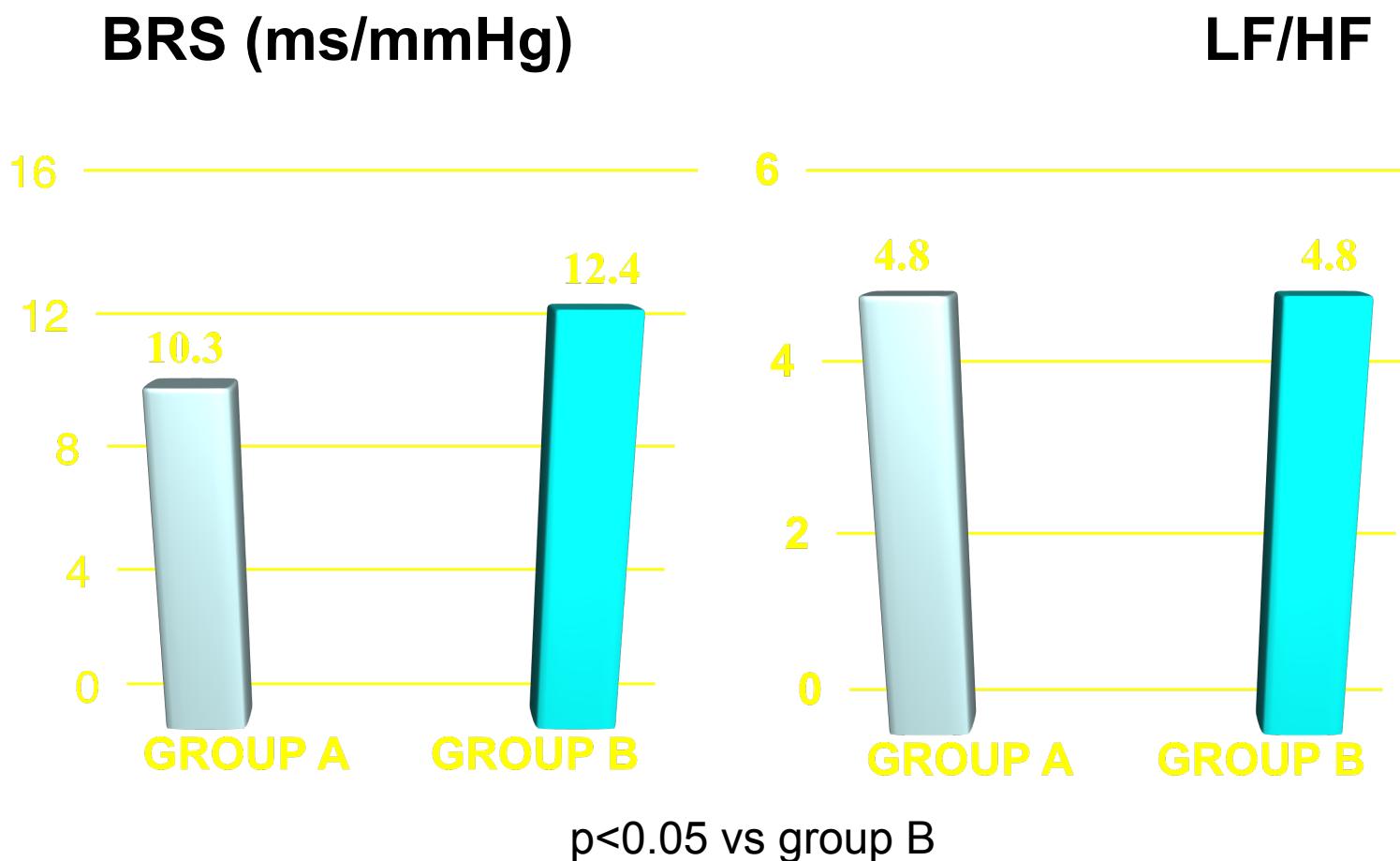


Case # 3: (A) Cardiomegaly with ventricular hypertrophy (weight 580 g, left ventricular free wall thickness 16 mm, septum 18 mm, right ventricular free wall thickness 5 mm). (B) Fibro-fatty replacement in the mid-mural region of the left ventricular free wall...

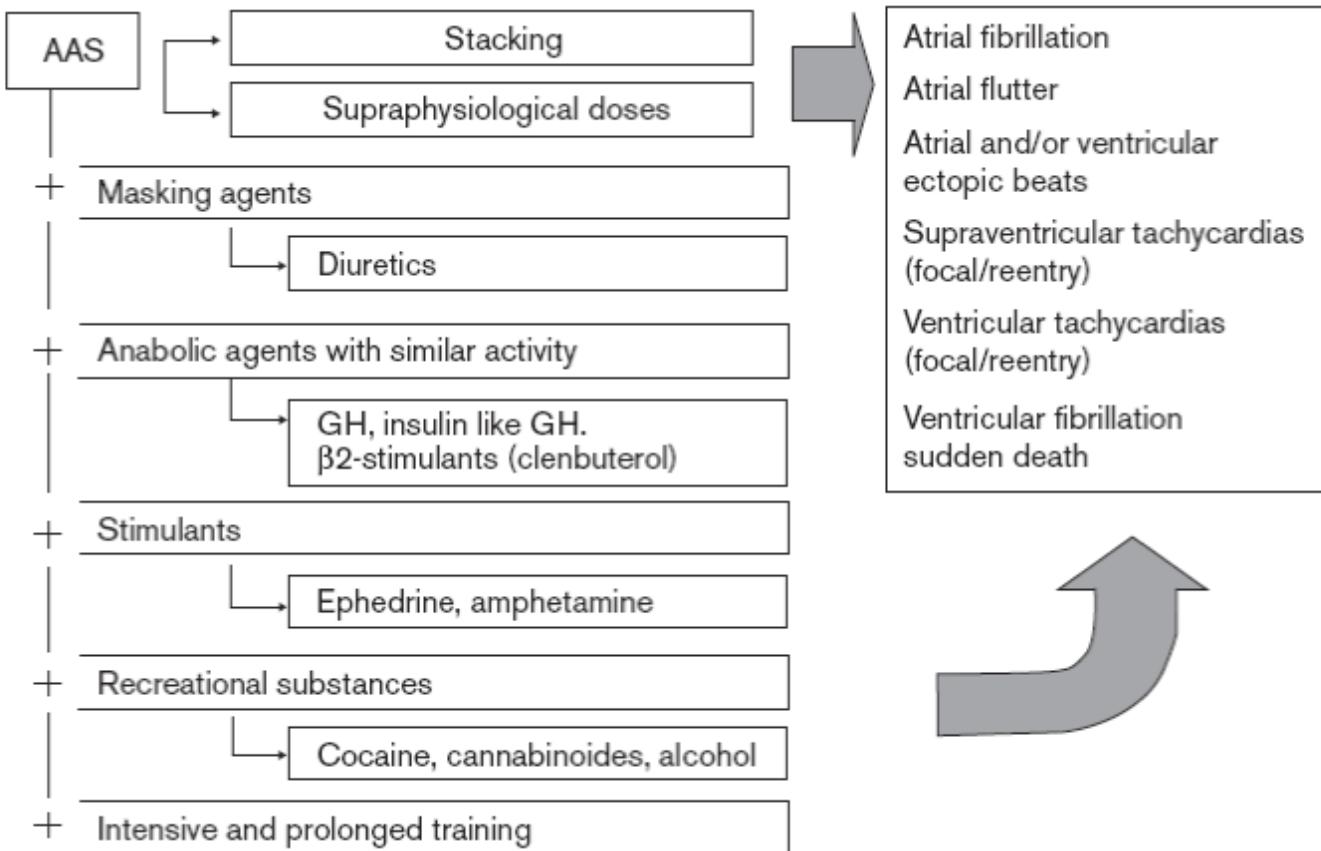
ANABOLICS AND ARRHYTHMIAS

- **AAS ELEVATE THE LEVELS OF SODIUM, POTASSIUM, CALCIUM AND PHOSPHATE.**
- **AAS CAUSE AN INCREASE IN THE HEART COLLAGEN CONCENTRATION WHICH WITH THE ACTIVATION OF THE CARDIAC RENIN-ANGIOTENSIN SYSTEM LEAD TO MALIGNANT ARRHYTHMIAS.**
- **AAS CAN ALTER CARDIAC GENE EXPRESSION, INCLUDING THOSE ENCODING ION CHANNELS THAT REGULATE REPOLARIZATION.**

CARDIAC AUTONOMIC FUNCTION IN POWER-TRAINED ATHLETES USING ANABOLIC STEROIDS



AAS AND CARDIAC ARRHYTHMIAS



Furnalello, et al. Eur J Cardiovasc Prev Rehabil 2007;14:487

ANABOLICS AND HYPERTENSION

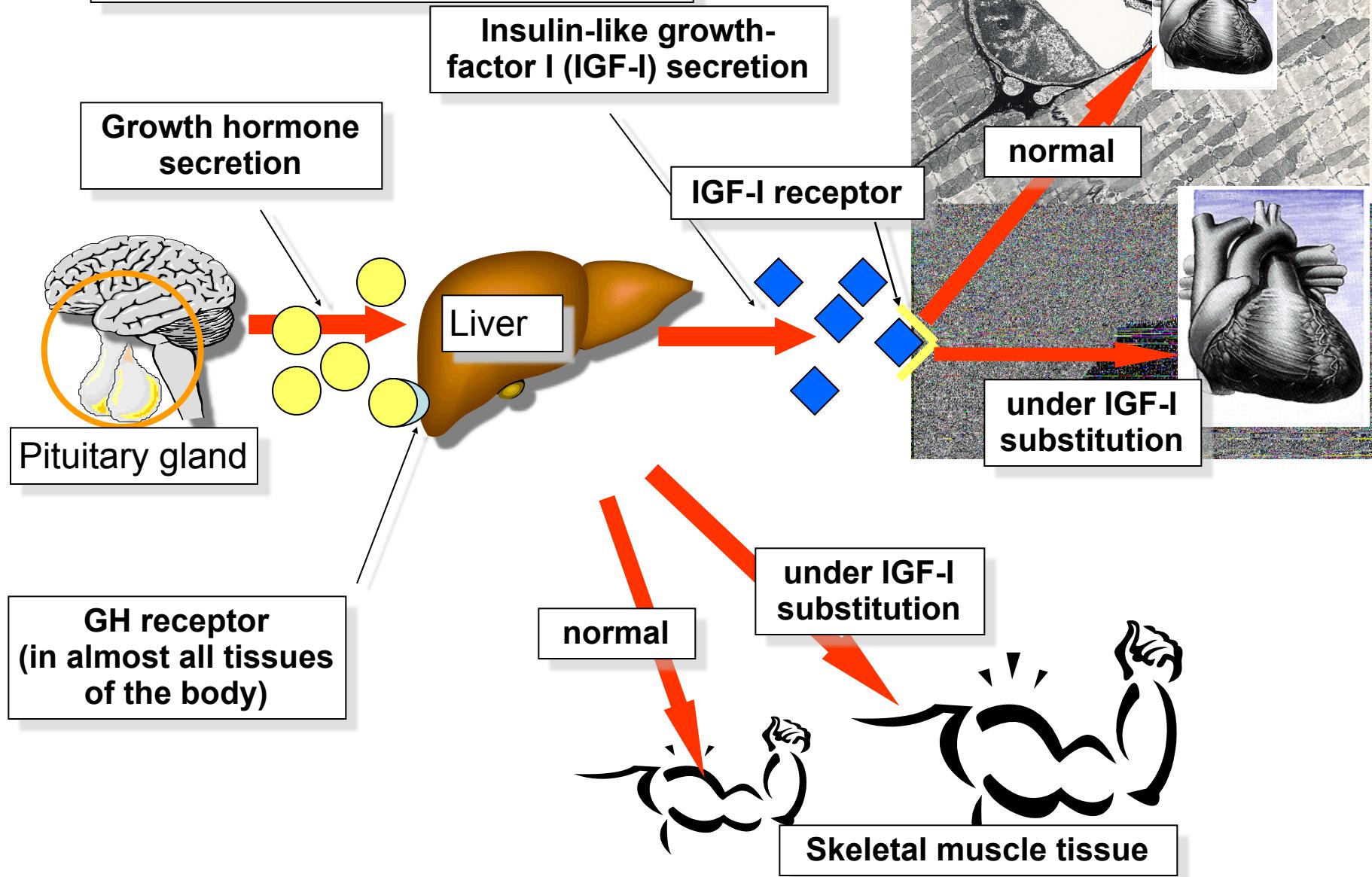
**ANDROGENS INCREASE BLOOD PRESSURE IN
SOME ATHLETES, MAINLY DUE TO SODIUM AND
WATER RETENTION.**

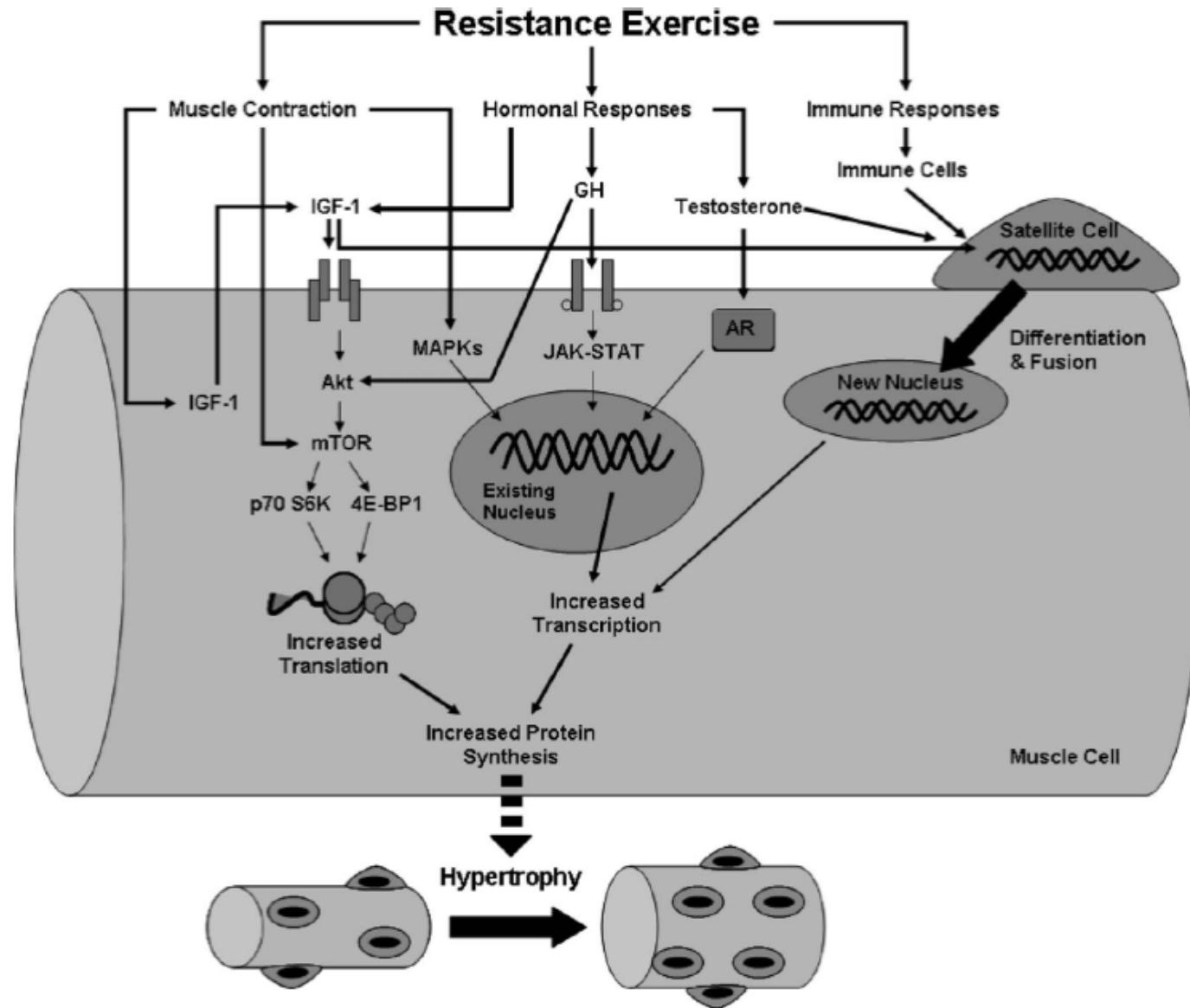
**THE RISE IN BLOOD PRESSURE APPEARS TO BE
TRANSIENT.**

**Deligiannis et al EJCPR,2006;13:687
et al J Sci Med Sport,2003;6:307**

GROWTH HORMONE (GH)

Heart muscle tissue



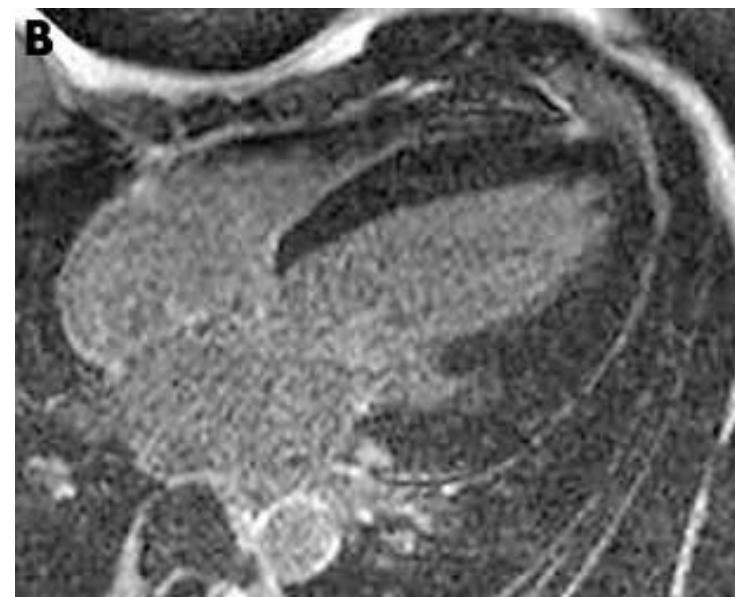
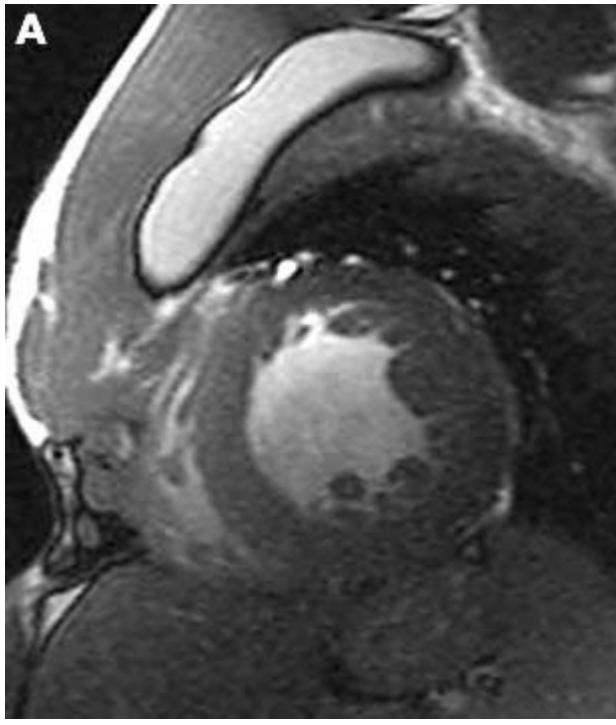


CARDIOVASCULAR EFFECTS OF GROWTH HORMONE EXCESS

**BIVENTRICULAR HYPERTROPHY
DIASTOLIC DYSFUNCTION
HYPERTENSION
ENDOTHELIAL DYSFUNCTION
VALVE ABNORMALITIES
DYSRHYTHMIAS
SUDDEN DEATH**

Palmeiro et al,Cardiology in Review,2012;20:197

Cardiomyopathy induced by performance enhancing drugs in a competitive bodybuilder



Mark PB et al. Heart 2005; 91:888

IMPROVEMENT OF ENDURANCE

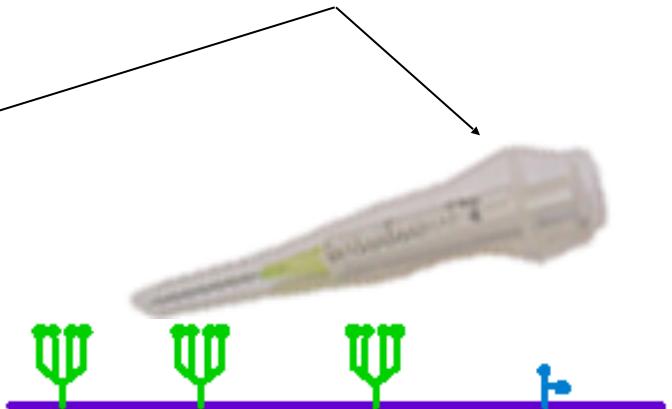
Legal



Aerobic
Training

Altitude
Training

Illegal
(DOPING)

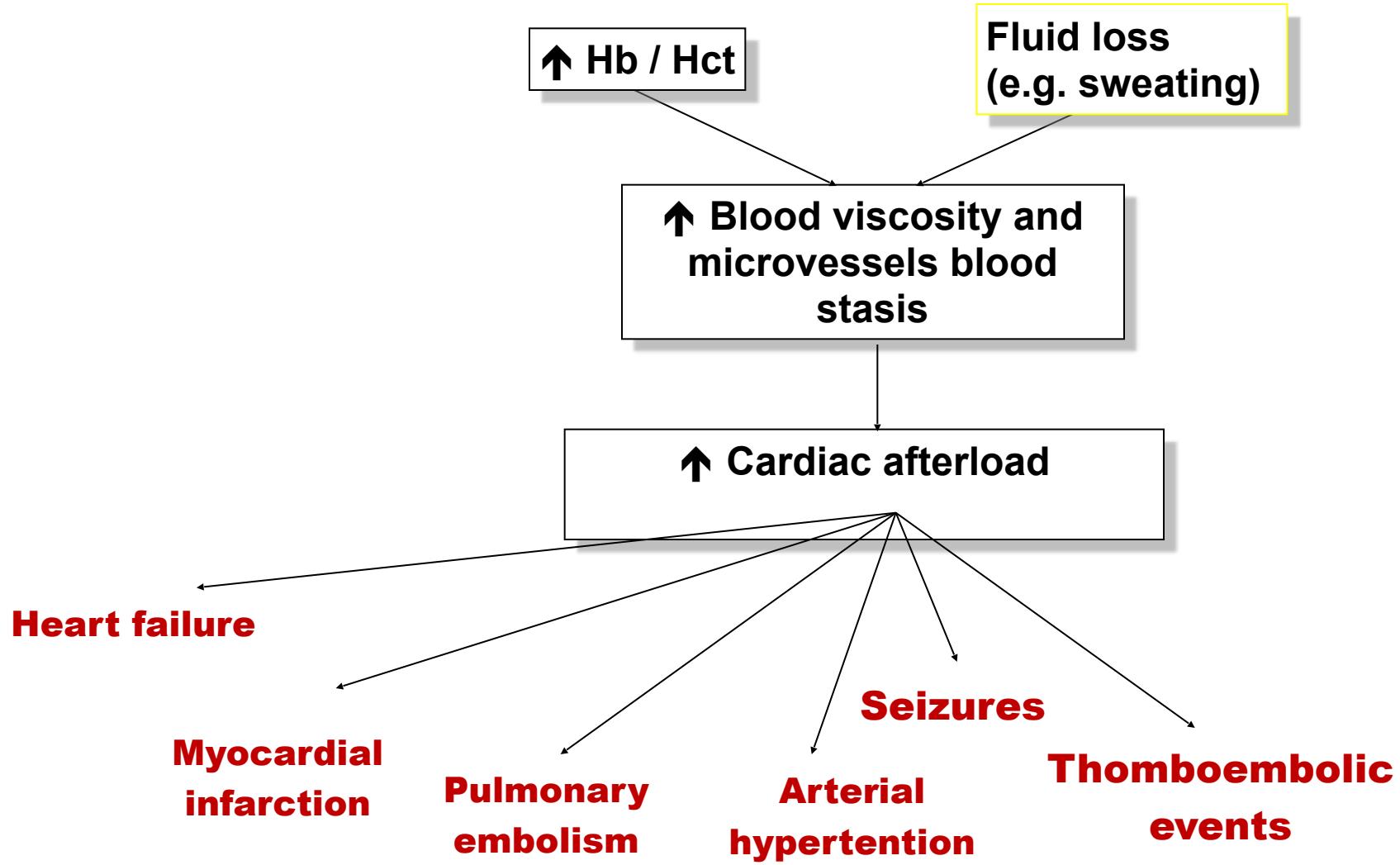


Blood
Infusion

Drugs:

**Erythropoietin
(EPO)**

rHu-EPO ABUSE SIDE EFFECTS

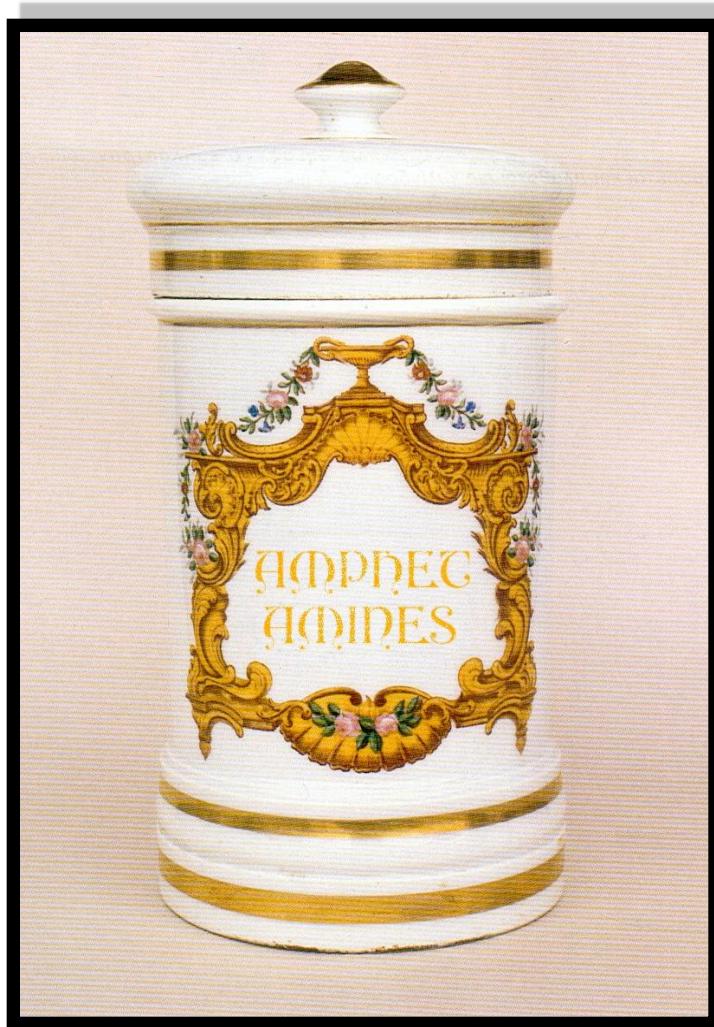


OTHER CARDIOVASCULAR SIDE EFFECTS OF ERYTHROPOIETIN ABUSE

**RhEPO promotes peripheral
sympathetic and serotonergic
overactivation and thus has
vasoconstrictor effects.**

Smith et al.,Cardiovascular Research,2003;59:538

AMPHETAMINES





1932

COMMON & BRAND NAMES

Speed; Dex; Adderall; Dexamphetamine; Vyvanse

EFFECTS CLASSIFICATION

Stimulant

CHEMICAL NAME

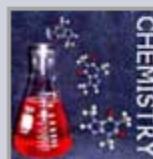
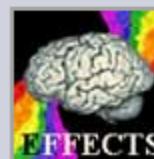
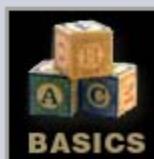
amphetamine

DESCRIPTION

Amphetamine is a strong physical and mental stimulant available widely in both prescription and street forms. It is the standard against which all other stimulants are measured.



Photo © Erowid.org



Amphetamines stimulate the central nervous system and the sympathetic part of the peripheral nervous system. Experts say that amphetamines enhance the synaptic activity of three neurotransmitters - dopamine, serotonin and norepinephrine

CARDIOVASCULAR ADVERSE EFFECTS

- **HYPERTENSION**
- **STROKE**
- **ARRHYTHMIAS**
- **CORONARY EVENTS**
- **CARDIOMYOPATHY**
- **CARDIAC FAILURE**
- **SUDDEN DEATH**

Deligiannis A and Kouidi E,HCJ,2012

COCAINE



European Heart Journal (2010) **31**, 271–273
doi:10.1093/eurheartj/ehp503

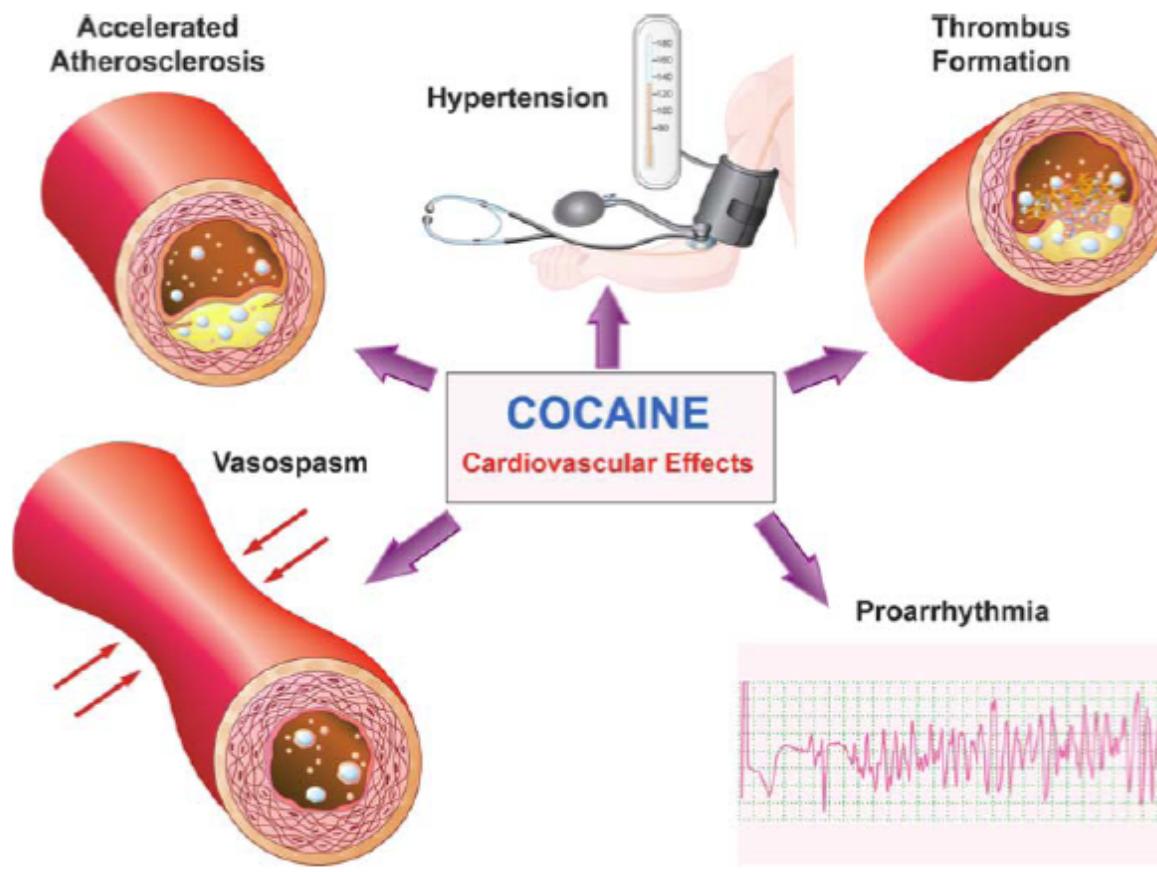
EDITORIAL

Sudden death in cocaine abusers

Richard A. Lange* and **L. David Hillis**

Department of Medicine, University of Texas Health Science Center, 7703 Floyd Curl Dr., San Antonio, TX 78229, USA

Online publish-ahead-of-print 12 January 2010



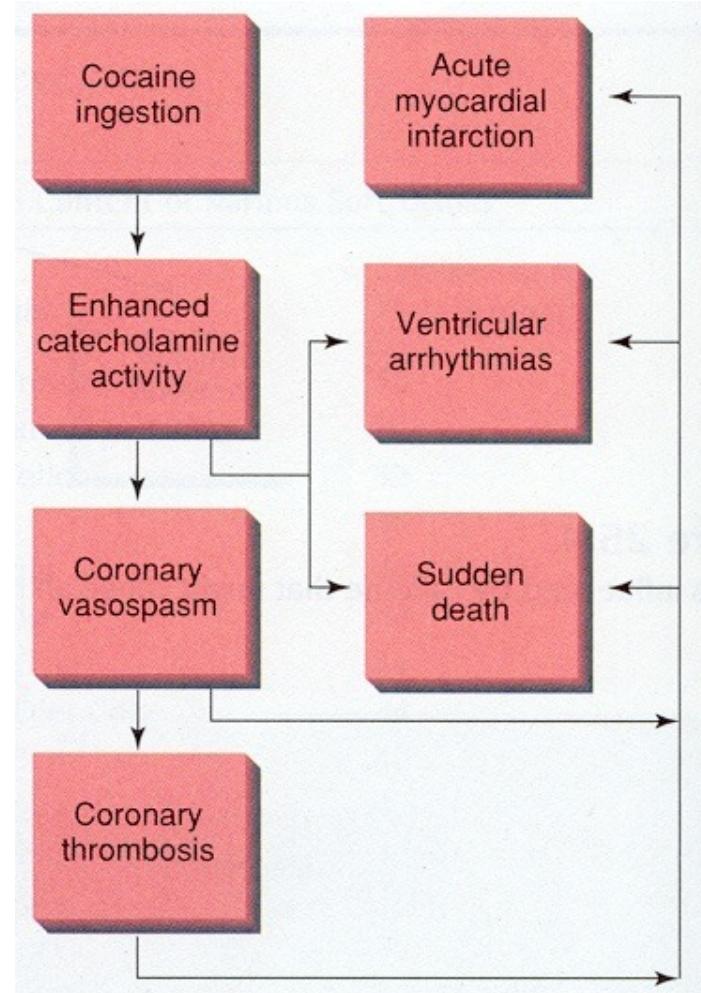
Cardiovascular complications associated with cocaine use.

COCAINE AND CORONARY EVENTS

- ↑ MYOCARDIAL OXYGEN DEMAND

CORONARY VASOSPASM

- THROMBOGENESIS



OTHER SIDE EFFECTS

- **MYOCARDITIS**
- **CARDIOMYOPATHY**
- **ENDOCARDITIS**
- **RUPTURED AORTIC ANEURYSM**
- **PULMONARY EDEMA**
- **STROKE**

Table 5 Gross and histological findings of heart specimens in 21 cocaine-related sudden death cases

Case	Heart weight (g)	LVW thickness (mm)	LVH	CAD stenosis / extent	Type of plaque	Coronary thrombosis	Myocardial infarction	Small vessel disease	Fibrosis
1	375	17	+	10%, SV	Fibrocellular	—		+++	—
2	495	18	+	30%, SV	Fibrocellular	—		—	—
3	455	17	+	60%, SV	Fibro-atheromasic		+	—	
4	460	23	+	50%, MV	Fibro-atheromasic	—	—	+	—
5	360	14	0	—	—	—	—	+++	—
6	405	15	0	60%, SV	Fibro-atheromasic	—	—	++	+
7	458	17	+	30%, MV	Fibro-atheromasic	—	—	—	++
8	370	15	0	20%, MV	Fibrocellular		—	—	—
9	300	15	0	60%, MV	Fibrocellular	Acute occlusive thrombosis (LAD)	Acute	+++	+++
10	380	20	+	40%, MV	Fibro-atheromasic	—	—	—	—
11	360	15	0	10%, SV	Fibro-atheromasic	—	—	++	—
12	370	16	+	80%, MV	Fibro-atheromasic calcified	—	—	+++	++
13	375	13	0	—	—	—	—	—	—
14	420	16	+	80%, MV	Fibrocellular	—	Acute	+++	++
15	395	15	0	—	—	—	—	—	—
16	335	15	0	80%, MV	Fibro-atheromasic	Acute occlusive thrombosis (RCA)	Acute	+	++
17	470	20	+	—	—	—	—	+	—
18	460	17	+	—	—	—	—	+	++
19	540	14	0	75%, MV	Fibro-atheromasic calcified	—	—	+	+
20	525	19	+	95%, MV	Fibro-atheromasic calcified	Re-canalized old thrombosis (RCA), acute thrombosis (LAD)	Acute and healed	++	+++
21	590	20	+	90%, MV	Fibro-atheromasic	—	Healed	+++	+++

CAD, coronary artery disease; LAD, left anterior descending coronary artery; LVH, left ventricle hypertrophy; LVW, left ventricular wall; SV, single vessel; MV, multivessel; RCA, right coronary artery; —, negative; +, mild; ++, moderate; +++, severe.

CANNABIS



ACTION OF CANNABIS (MARIJUANA, HASHISH)

ADRENERGICAL STIMULATION

- PARASYMPATHETIC BLOCKADE**

A “regular” dose of cannabis, usually contains about 20 mg tetrahydrocannabinol (THC)

CARDIOVASCULAR COMPLICATIONS OF CANNABIS

- Increased sympathetic activity (betaadrenergic stimulation)
- Interference with the peripheral vascular reflex responses.
- Arterial vasospasm
- Parasympathetic blockade?

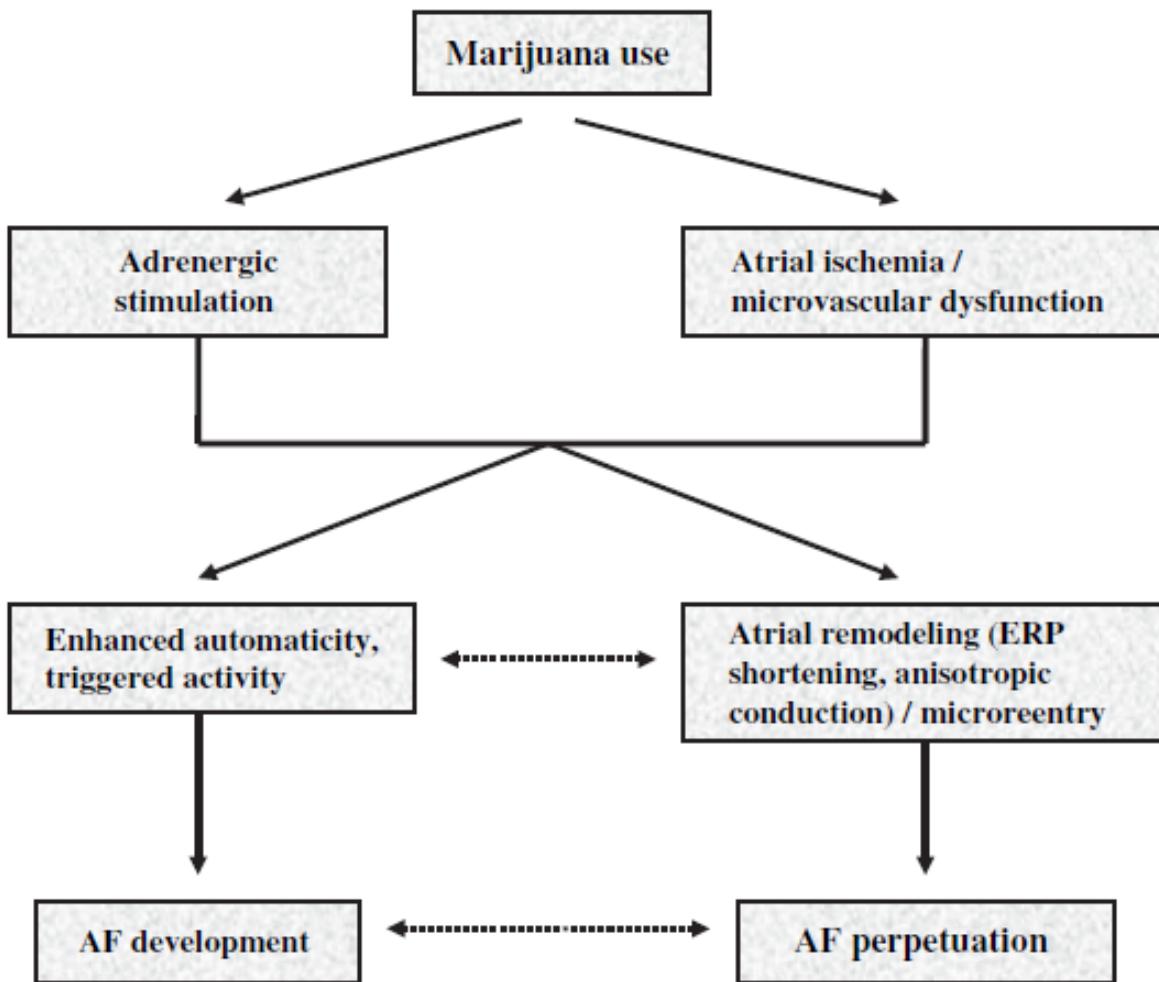


- Tachycardia
- Peripheral vasodilatation
- Peripheral vascular reflex failure
- Arrhythmia?

- Increased myocardial oxygen demand
- Decreased oxygen delivery

ISCHAEMIA

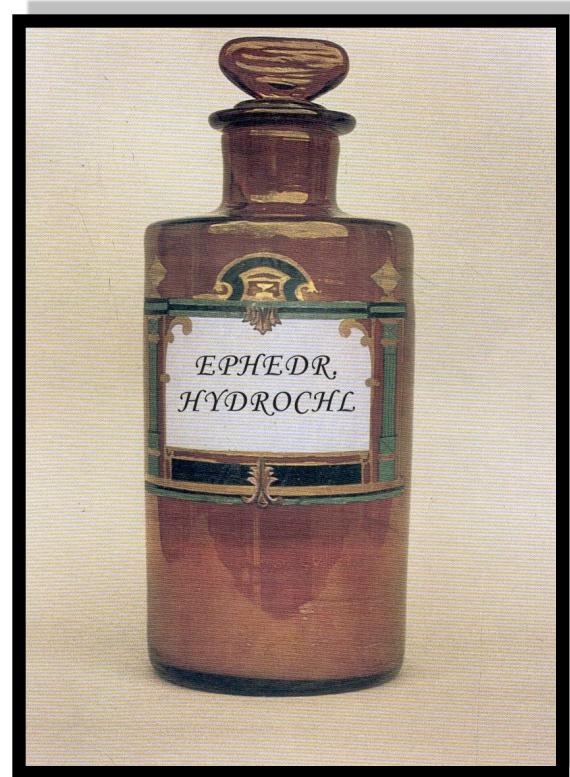
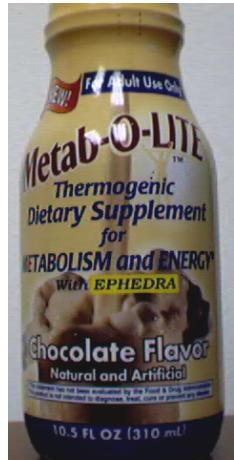
A circle containing the word ISCHAEMIA with a downward-pointing arrow.



Korantzopoulos P et al. Int J Clin Pract 2008; 62:308

EPHEDRA HERBAL SUPPLEMENTS

- MA HUANG
- IN COMBINATION WITH GUARANA OR KOLA NUT (HERBAL ECSTACY)



CARDIOVASCULAR SIDE EFFECTS

HYPERTENSION

TACHYCARDIA

ARRHYTHMIA

MYOCARDIAL INFARCTION

CARDIAC ARREST OR SUDDEN DEATH

Haller and Benowitz, N Engl J Med 2000;343:1833

ADVERSE EVENTS ASSOCIATED WITH DIETARY SUPPLEMENTS CONTAINING EPHEDRA ALKALOIDS

AGE (YR)/SEX	NAME OF SUPPLEMENT	ADVERSE EVENT	OUTCOME
35/F	Shape-Fast Plus	Subarachnoid hemorrhage	Permanent disability
22/M	Ripped Force	Arrhythmia, cardiac arrest	Permanent disability
28/F	Herbalife's Thermojetics	Cardiac arrest	Permanent disability
43/M	Ripped Fuel	Cardiac arrest	Death
37/F	Metabolife 356	Severe hypertension, cardiac arrest, hypokalemia	Death
59/F	OmniTrim Extra Vitamin-Fortified tea	Acute myocardial infarction	Coronary bypass surgery
38/M	Ripped Fuel	Arrhythmia, cardiac arrest	Death
47/F	Total Control	Hypertension, bilateral lacunar infarctions	Permanent disability
29/M	Ultimate Orange	Stroke	Permanent disability
39/M	Ultimate Orange	Hemorrhagic stroke	Permanent disability
47/M	Purple Blast	Haller and Benowitz, N Engl J Med 2000;343:1833	Permanent disability

AGE (YR)/SEX	NAME OF SUPPLEMENT	ADVERSE EVENT	OUTCOME
46/M	Diet Fuel	Stroke	Death
22/M	Ripped Fuel	Hyperthermia, abnormal electrolyte levels, cardiac arrest	Death
64/F	Fit America Natural Weight Control Aid	Atrial fibrillation, stroke	Permanent disability
47/F	Per-Form Dieter's Natural Tea	Rhabdomyolysis, hydronephrosis, hypokalemia	Prolonged hospital care
64/F	Shape-Fast	Hemorrhagic stroke	Permanent disability
34/M	Herbalife's Thermo Jetics	Atrial flutter, renal failure, hypokalemia, rhabdomyolysis	Death
32/F	Ripped Fuel	Premature delivery	Death of neonate
29/M	Ultimate Nutrition Product Ma Huang	Stroke	Permanent disability
15/F	Ripped Fuel	Arrhythmia, cardiac arrest	Death
41/F	Diet-Phen	Hypertension, multiple brainstem infarcts	Permanent disability
22/F	Magic Herb	Spontaneous abortion at 9 wk	Death of fetus
43/F	Metabolife 356	Severe hypertension, hemorrhagic stroke	Permanent disability
18/M	Ultimate Orange	Seizure, hemorrhagic stroke	Death
61/F	Metabolife 356	Hypertension, unstable angina	
26/M	Ripped Fuel	Status epilepticus, hypokalemia	Permanent disability

SIDE EFFECTS OF DIURETICS

**Loss of
water**

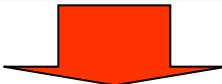
**Loss of
minerals**



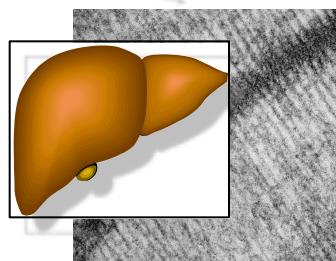
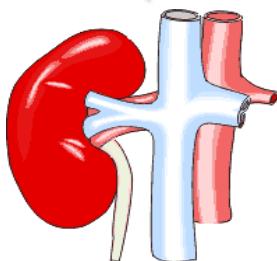
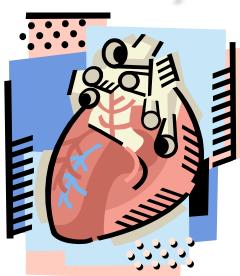
- **Weakness**
- **Drowsiness**
- **Fatigue**

**Cardiac
arrhythmias**

BETA-BLOCKERS



Antagonists of epinephrine and norepinephrine, and suppressors of sympathetic activity



β_1 -Receptors

↓ Contractility

↓ Heart frequency

↓ Myocardial excitability

β_1 -Receptors

↓ Rhenin secretion

β_2 -Receptors

↑ Muscle tension

↑ Bronchoconstriction

↓ Glycogenolysis

↓ Lipolysis

GENE DOPING

genetically modified athletes

biomedical ethics, gene doping and sport

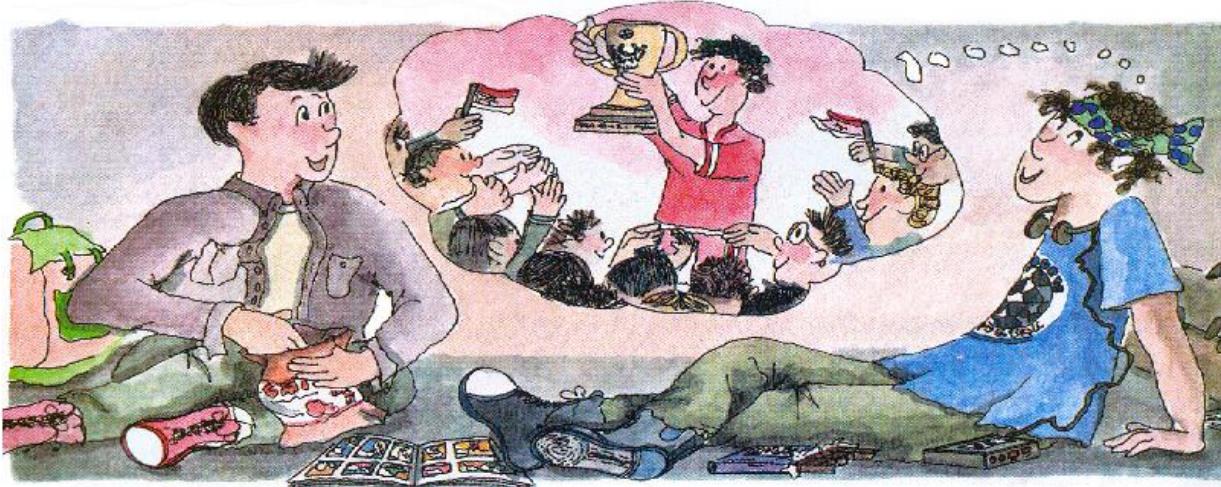
Andy Miah



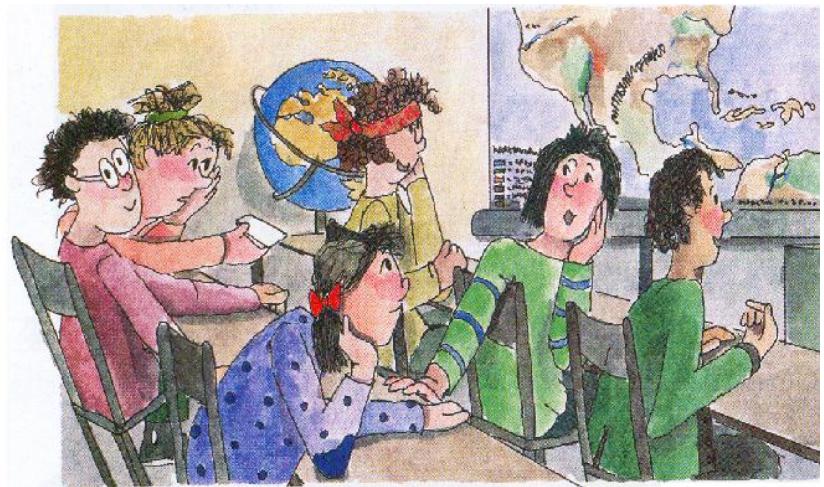
I don't know of any particular case where a person has gene doped but the technology is here. If there isn't a case I can point to today, there will be soon.

—Dr. Theodore Friedmann, World Anti-Doping Agency

FIGHT AGAINST DOPING



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International Symposium - 18 July 2002

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Institute of Biochemistry

German Sport University Cologne

Carl-Diem-Weg 6, 50933 Cologne, Germany

Tel. +49 221-4982-692, -492, Fax. +49 221-497 3236, E-Mail:
schaenzer@biochem.dshs-koeln.de



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Knowing the risks of doping!

This informational platform addresses all interested people in and out sports. Many experts have given all their recent knowledge on doping related issues. Hence, it was possible to develop this interactive internet platform and multi-level teaching materials containing versatile information.



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Explanatory movie:
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Ιατρικές παρενέργειες από τα αναβολικά-ανδρογόνα στεροειδή...

...στο καρδιαγγειακό σύστημα

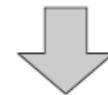
Μηχανισμοί Αθηρογένεσης

Ηπατική λιπάση τριγλυκεριδίων



HDL-χοληστερόλη ορού ↓

LDL-χοληστερόλη ορού ↑



Αθηροσκληρωτικές μεταβολές
στα αγγεία του αίματος



Tischer et al. (2003): Z Kardiol, p326-331.
Hartgens & Kuipers (2004): Sports Med, p513-554.



Busca

► Doping em geral

▼ Substâncias e métodos

Agentes anabólicos

Hormonas e substâncias relativas

Agonistas beta-2

Antagonistas e moduladores de hormonas

Modo de acção

Efeitos secundários

Diuréticos e outros agentes de camuflagem

Estimulantes

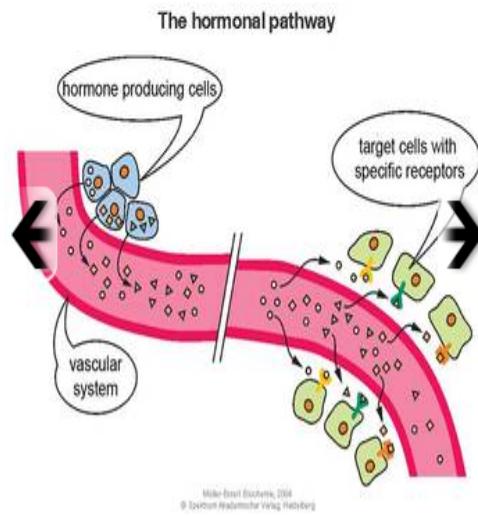
Narcóticos

Canabinóides

Você está aqui: Startpage → Substâncias e métodos → Antagonistas e moduladores de hormonas

As hormonas são moléculas mensageiras libertadas pelas glândulas endócrinas para regular funções corporais específicas, como o nível de glucose ou crescimento dos músculos. As hormonas ligam-se aos receptores na membrana celular ou ligam-se aos receptores no núcleo celular. Neste contexto, os antagonistas e moduladores de hormonas são substâncias que influenciam estes efeitos pela inibição ou que estimulam receptores específicos e, além disso aceleram ou atrasam as reacções selectivas pelas enzimas.

Os antagonistas e moduladores de hormonas fazem parte da Lista Proibida de 2008 da Agência Mundial Antidoping (AMA). São substâncias sempre proibidas (proibição dentro e fora da competição). A Lista Proibida de 2008 diferencia entre os inibidores aromatase, moduladores de selectivos de receptor de estrogénio (SERM), agentes modificadores da função da miostatina e outras substâncias anti-estrogénicas.



CONVERSA CRUZADA

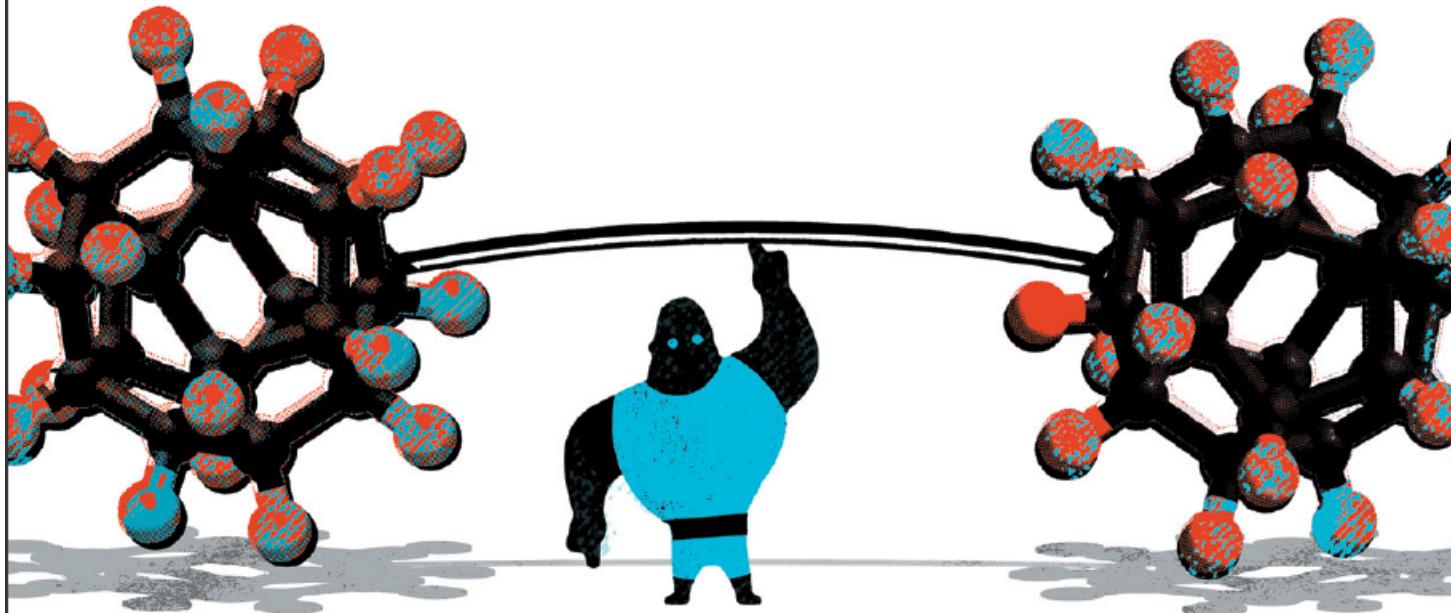
- Aparelhos de suporte e sistema músculo-esquelético
- Sistema cardiovascular
- Sistema respiratório
- Sistema gastrointestinal
- Fígado
- Sistema reprodutivo e endócrino
- Rins
- Metabolismo electrolítico
- Sistema imunológico
- Pele
- Sangue
- Sistema nervoso central
- Efeitos psicológicos e dependência

**“People do all sorts of dopey things.
The problem is, the reward isn’t worth
the danger of what could happen.”**



“WHAT WE’LL
SEE IS THE
EMERGENCE
OF ALL KINDS
OF NEW
SPORTS.”

**Eugene Goldwasser
‘the father of Epo’
Professor Emeritus of Biochemistry and
Molecular Biology
Personal interview, 18 Feb 2010**



SUPERHUMAN ATHLETES

Enhancements such as doping are illegal in sport – but if all restrictions were lifted, science could push human performance to new extremes.

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