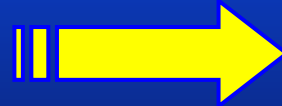


# **HEALTH ISSUES IN DOPING**

**Professor Nikos Sakellaridis MD, PhD**

# What is Doping?

Doping



Use of prohibited substances  
and/or methods



Enhancement of performance  
in sports

# Doping Definitions

- **European Union:** ([www.europa.eu.int](http://www.europa.eu.int))

Doping in sport means use of substances and/or any other available methods of artificially enhancing performance in a sporting event, or when preparing for it, in a way which violates sporting ethics and damages the athlete's or player's physical and psychological health

- **WADA:** ([www.wada-ama.org](http://www.wada-ama.org))

Doping is defined as the use of an artifice, whether substance or method, potentially dangerous to athletes' health and/or capable of enhancing their performances, or the presence in the athlete's body of a substance, or the ascertainment of the use of a method on the list annexed to the Olympic Movement Anti-Doping Code

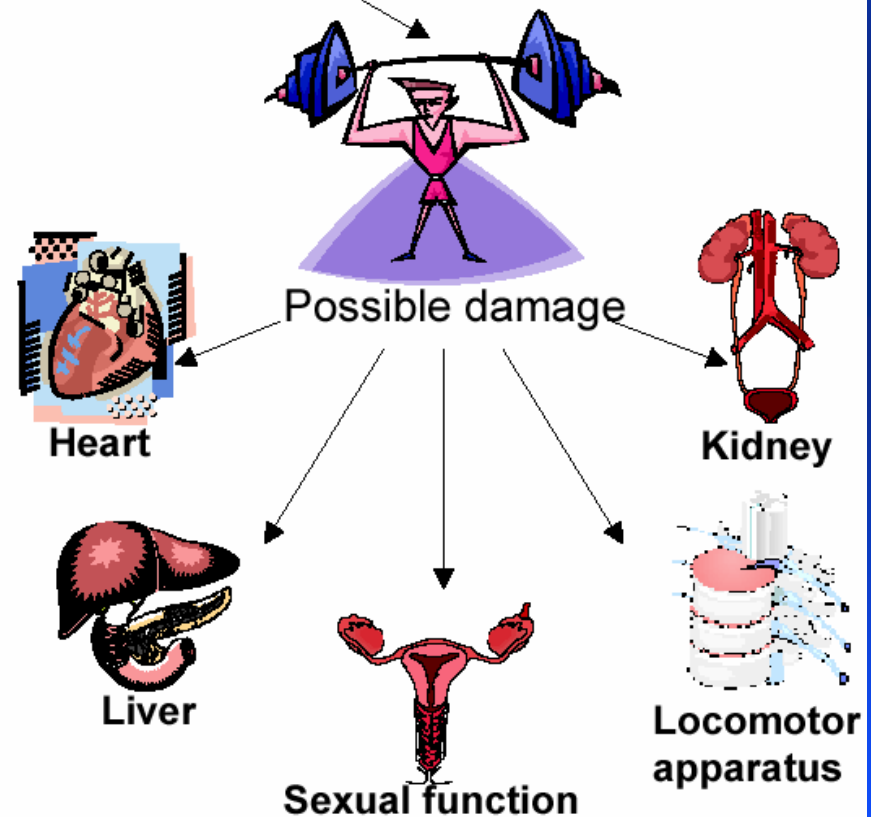
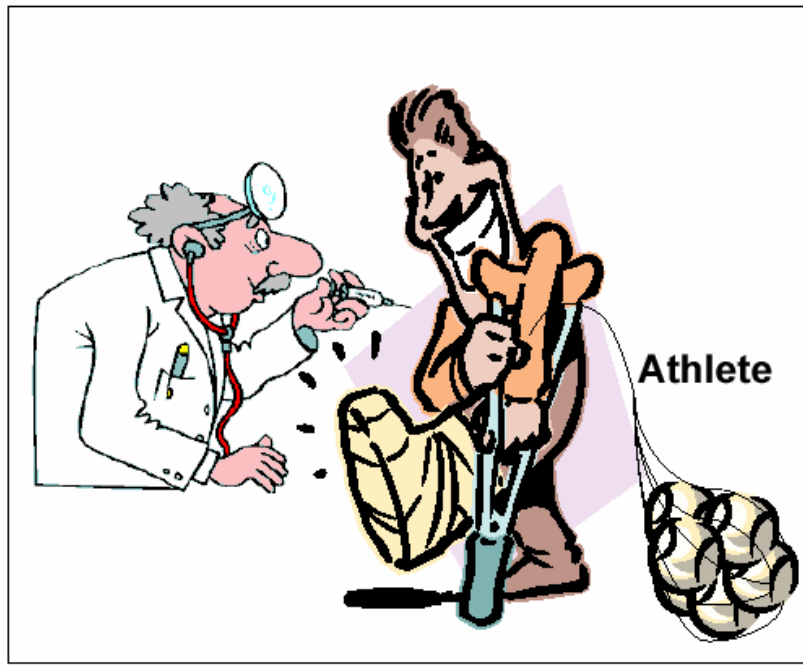
- **Practical definition:**

Doping is using anything in the Doping list

# EFFECTS AND SIDE EFFECTS OF DRUGS

Drugs can be life-saving when used for therapeutical purpose

Drug abuse for doping purpose in sport is unethical and potentially dangerous for the athlete's health





**Every drug is a poison**



**Ωφελείεν η μη βλάπτειν**

# Doping: a growing public health issue

- Doping methods are complex, and the available drugs are so numerous, that doping has become more and more dangerous for top athletes
- Doping is becoming more and more widespread and begins increasingly early in young, and unsupervised, athletes
- Doping is linked to a lack of objective information concerning the risks involved in the use of the most recent substances
- Since their positive effects are felt well before their negative side effects, it is difficult to convince athletes and coaches not to use them
- More than a cheating problem
- Doping issue concerns society as a whole
- Increased risk of health problems with athletes



**WORLD  
ANTI-DOPING  
AGENCY**  
play true

# **WORLD ANTI-DOPING CODE**

**(WADA valid since 01.01. 2006)**

## **Substances**

**Prohibited classes of  
substances**

**Classes of substances which  
are prohibited under  
certain circumstances**

### **Exceptions:**

**A few substances have limits of concentration**

**A few substances are allowed under medical prescription**

## **Methods**

**Prohibited methods**



## PROHIBITED CLASSES OF SUBSTANCES

(WADA valid since 01.01. 2006)

### **C. Anabolic Agents (e.g.):**

- Anabolic androgenic steroids (e.g. nandrolone, stanozolol)
- $\beta$ 2-agonists (e.g. clenbuterol)

and related substances

### **B-blockers**

(in some sports)

### **A. Stimulants (e.g.):**

- Amphetamine
- Ephedrine
- Caffeine
- Cocaine

and related substances

### **D. Diuretics (e.g.):**

Acetazolamide, furosemide

### **E. Peptide hormones, mimetics and analogues (e.g.):**

hCG, LH, hGH, EPO, insulin

and related substances

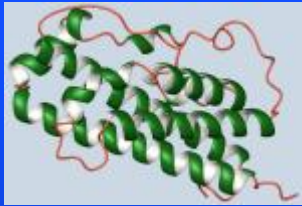
### **B. Narcotics & Analgesics (e.g.):**

Heroin, Morphine, Methadone

and related substances

### **F. Agents with anti-oestrogenic activity (e.g.):**

Aromatase inhibitors

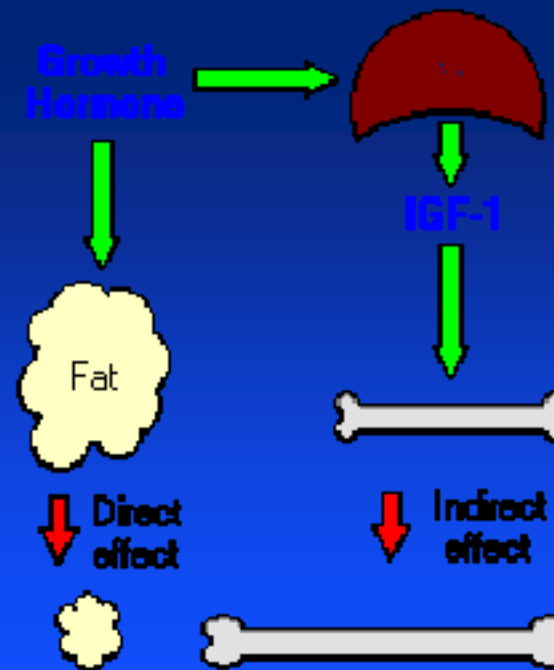
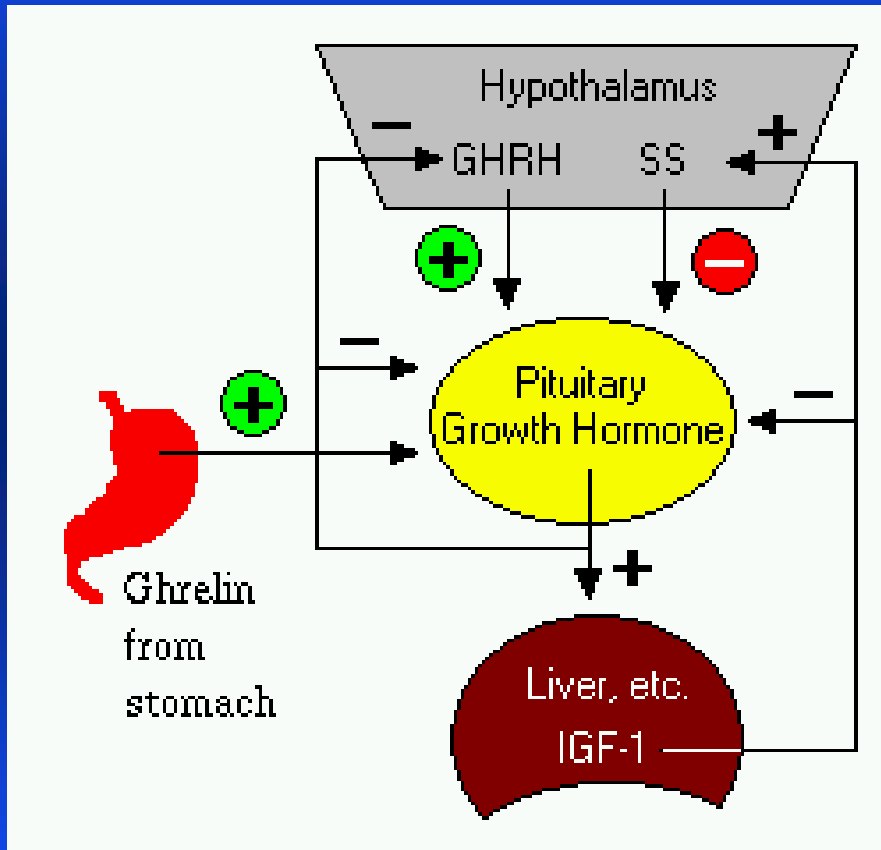


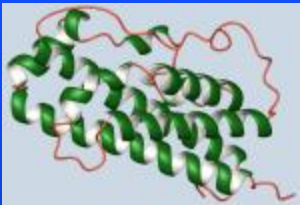
# Growth Hormone (hGH)

**Protein metabolism:** stimulates protein anabolism, increased protein synthesis and decreased oxidation of proteins

**Fat metabolism:** enhances the utilization of fat

**Carbohydrate metabolism:** maintain blood glucose within a normal range, enhance glucose synthesis in the liver



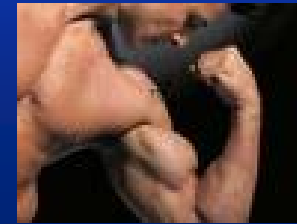


## Growth Hormone (hGH)

Increase of training motivation



Increase of muscle mass



**Purpose of abuse**

Decrease of body fat



Increase of body size



Improvement of performance



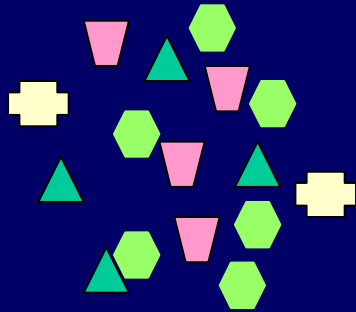
# Growth Hormone

## How can we *possibly* detect it ?

### Markers of hGH action

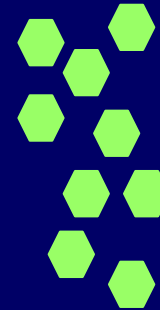
- IGF-1
- Pro-III-NP (amino-terminal peptide of pro-II collagen)
- ICTP (carboxy-terminal crosslinked telopeptide of Type-1 collagen)

### Native pituitary hGH



Several distinct isoforms

### Recombinant hGH



22 kDa isoform only

So we can detect it but is that a solution?

Problems with native GH

# Side effects of hGH abuse

## CHILDHOOD Gigantism

### ACUTE

- Infections
- Water retention
- Headache
- Fatigue/ weakness of muscles
- Joint and muscle pain (arthritis)
- Blood glucose increase



### CHRONIC

- Acromegalia
- Diabetes mellitus
- Dysrhythmias
- Myocarditis and  
myocardiopathy



- Tumors



# PROHIBITED METHODS

(WADA valid since 01.01. 2006)

**Enhancement of Oxygen transport**  
"Blood Doping"

**Gene Doping**

**In the future...**



**Blood Transfusion**  
(homologous/eterologous)

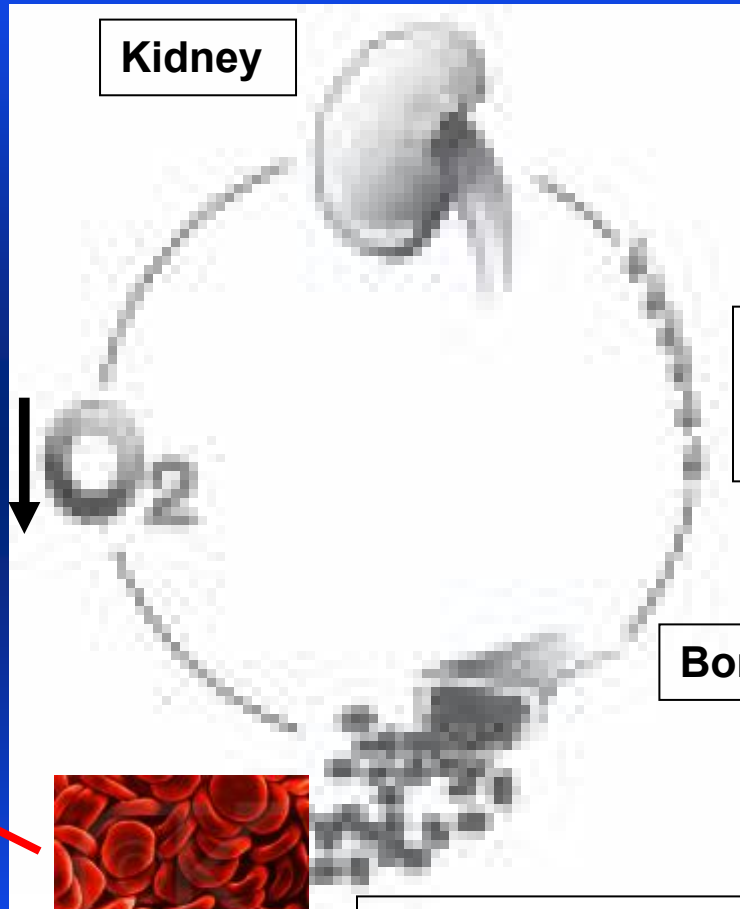
**Erythropoietin (EPO)**



# EPO



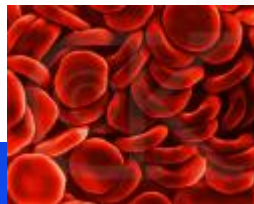
Increase the oxygen carrying capacity of the blood



Kidney

**EPO**  
(glycoprotein hormone,  
5 pmol/l)

Bone marrow

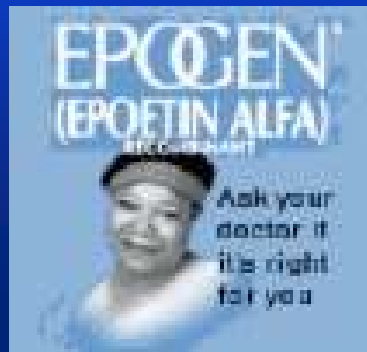


Increase in Red Blood Cells production

**Recombinant EPO  
(rh EPO- USA)  
(USA patent till 2015)  
produced in cultured animal cells**

**Recombinant EPO  
(rh EPO- EU)  
produced in cultured human cells**

1989

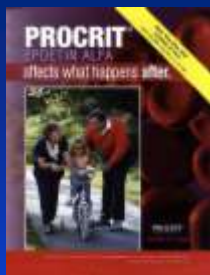


2006

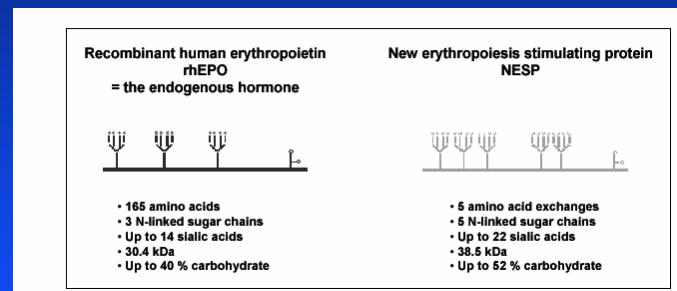


**DynEpo: produced in human cells- authentic pattern of human glycosylation**

1991



2001



**Longer lasting EPO analogue**

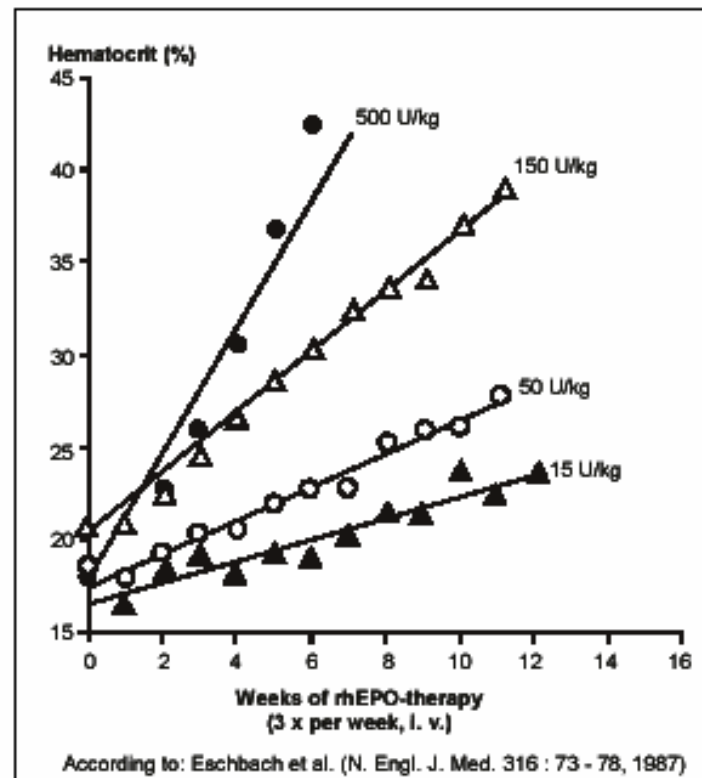
# MEDICINE

## What is the use of EPO?

### Dose response to rhEPO

#### Treat anemia

- Chronic Renal Failure
- Cancer
- Chemotherapy
- Pre-operative



**SPORTS**

## What is the use of EPO?

### Blood Doping Agent in endurance sports

- Competitive Cycling
- Triathlon
- Marathon

*“The cycling drug of choice”*



Stimulates RBCs production

More O<sub>2</sub> is delivered to the muscles

Delays the onset of fatigue

Increase endurance

Induces muscle recovery

An athlete can fight harder and for longer

1998: "Tour de France" = Tour of Shame



Willy Voet



2000, Tour de France



French National Laboratory  
for Doping Detection (LNDD)

Urine Test: distinguish pharmaceutical  
From endogenous EPO

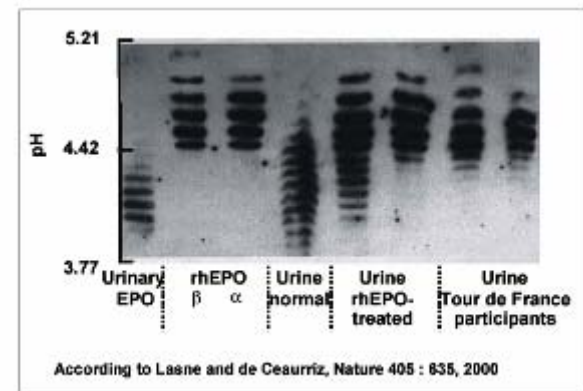
## Proposed techniques for detection of EPO doping

### Indirect

- **Blood: Hb / Hct, MCV, MCH** (Casoni et al.: Int J Sports Med 1993)
- **Blood: Reticulocyte parameters** (Parisotto et al.: Int J Sports Med 2000)
- **Serum: [Soluble transferrin receptors] / [ferritin]** (Gareau et al.: Nature 1996)

### Direct

- **Serum: EPO level** (Souillard et al.: Br J Clin Pharmacol 1996)
- **Serum / Blood: Profile of serum EPO and red blood cell parameters** (Parisotto et al.: Haematologica 2001)
- **Urine / Serum: Electrophoretic demonstration of (rHu-) EPO** (Wide et al.: Br J Haematol 1990, Med Sci Sports Exercise 1995, Lasne and de Ceaurriz: Nature 2000)



*Radioimmoblots of commercial rhEPOs and human urine following isoelectric focusing*

SPORTS MEDICINE\_DRUG TESTING

## News & Analysis All Doped Up— and Going for the Gold

Misdeeds by the International Olympic Committee frustrate scientists developing tests for the performance-enhancing drugs erythropoietin and human growth hormone

This coming September, alongside the stirring spectacle of Olympic competition in Sydney, there will be another struggle so complex that the average viewer will probably have a hard time grasping the rules, let alone getting excited about it. Unfortunately, the loser will be fair competition.

The use of performance-enhancing drugs has long been one of the darkest aspects of sport, but the shadow has grown longer in recent years as evidence accuses athletes of increasingly turning to two drugs relatively new on the doping scene: erythropoietin and human growth hormone. Hundreds of other substances have been banned by the International Olympic Committee (IOC), but these two are harder to catch.

With sporadic funding from the IOC and other sources, researchers in half a dozen countries have been working feverishly over the past couple of years to come up with reliable tests for the two drugs. Unfortunately, although they have come tantalizingly close, the tests will probably not be ready in time for the Sydney games, several researchers say. More troubling, scientists in those of the labo-



Better dead than second

BLACK-MARKET BIOTECHNOLOGY: ATHLETES ABUSE EPO AND HGH

CYCLING IN THE FRANCE, police in Reims, questioning. Seven teams

about 95 to 2,700 milligrams, a military official of the U.S. Olympic Committee (USOC) who asked not to be identified. government bicycle race, was thrown into a van as investigators found caches of the drug in team vans, in car trunks and

1987-1990

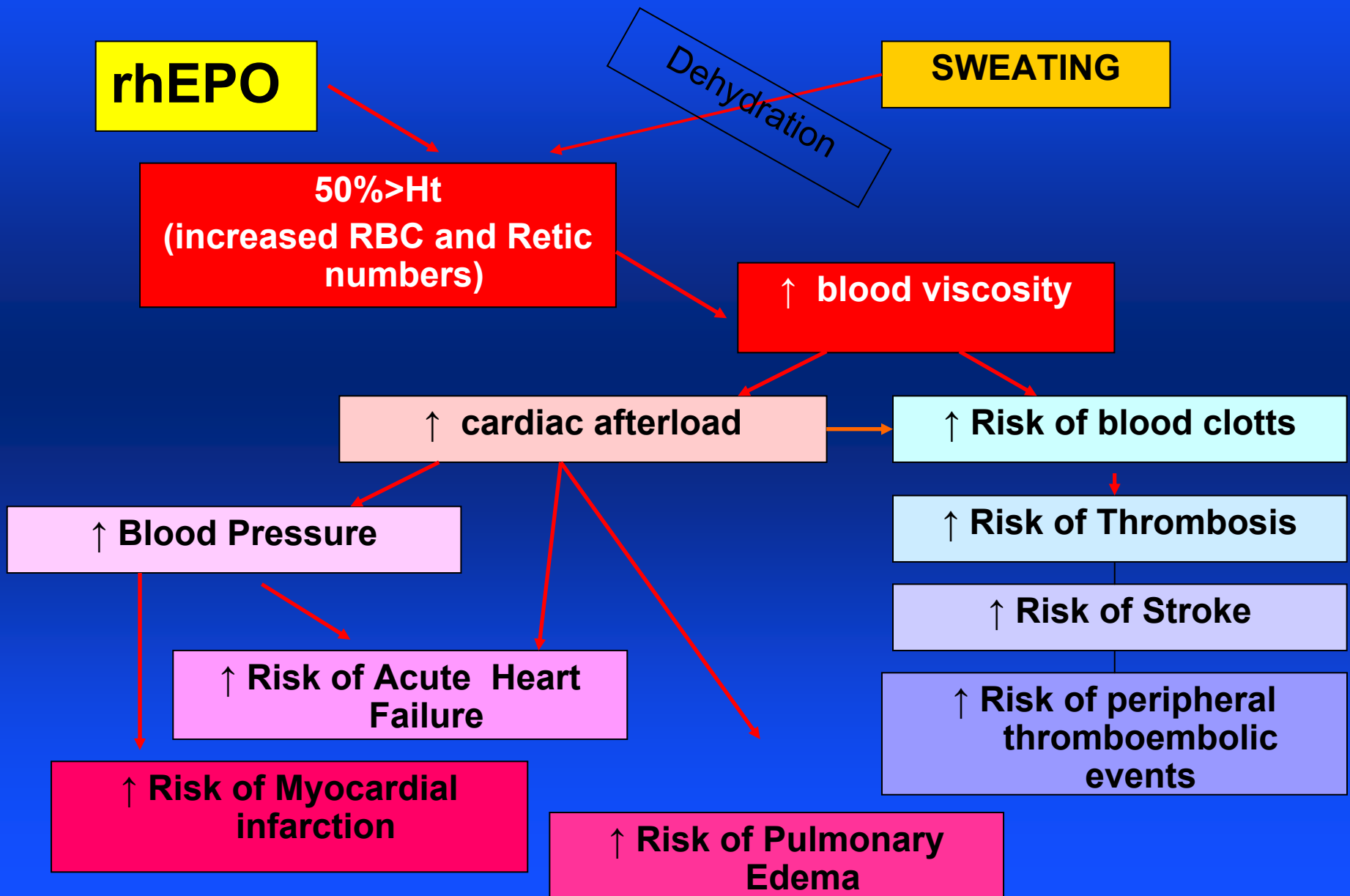
14 Dutch and 4 Belgian cyclists  
(young, healthy and elite athletes)  
died suddenly

Overwhelming probability:  
these unexpected deaths were associated  
With the use of EPO

*Independent, July 14, 1991*

**EPO may well be the most dangerous, in health terms,  
of all the performance-enhancing drugs currently available !!!**

## Side Effects of rhEPO abuse



Thank You to:  
Dr. Stella Zissopoulou, MD

- **Between 1963 and 1985, about 7,700 people received human growth hormone (hGH) made by the National Hormone and Pituitary Program (NHPP). Twenty-six of them got CJD.** In June 1999 when we last sent you an update, we knew of 22 people who received hGH who got CJD. Unfortunately, we learned of 4 others recently. One has been confirmed. We are still studying the other three, but it is likely that all of these illnesses are CJD. None of those with CJD began hGH treatment after 1977, when a new purification step was added to hormone production.

*May 19, 2006*