170 Peer Brainstorming: Doping Yesterday, Today, Tomorrow: Is the Clinical Laboratory Able to Detect the Use of Doping Substances in Non-official Competitions?

Roberto Verna Prof. Dott.

2011 Annual Meeting – Las Vegas, NV

AMERICAN SOCIETY FOR CLINICAL PATHOLOGY
33 W. Monroe, Ste. 1600
Chicago, IL 60603
170 Peer Brainstorming: Doping Yesterday, Today, Tomorrow: Is the Clinical Laboratory Able to Detect the Use of Doping Substances in Non-official Competitions?

The brainstorming session will focus on the damage derived from the use of illicit substances finalized to the enhancement of performance, particularly in sports. Deep attention will be devoted to the importance of an early detection of their use and the possibility to detect it with routine laboratory methods. These methods are important either for prevention in young people or for revealing the use of hazardous substances in non official competitions, where analytical chemistry would be too expensive. A brief history and update of the doping phenomenon will open the session.

- Update their knowledge of doping.
- Update their attention to unusual emergency cases (such as children with uncertain pathology).
- Improve public health.

FACULTY:

Roberto Verna Prof. Dott.

Entire Pathology Team
Global Pathology

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Sport Medicine for the Athlete and the Sportsman. Effects and Damage Induced by Doping.

Roberto Verna MD, PhD
Professor of Clinical Pathology and Director, Clinical Research Center
“Sapienza” University of Rome

IMPORTANT: ALL THE IMAGES HAVE BEEN CANCELLED TO ALLOW PRINTING. THEY WILL BE SHOWN DURING THE LECTURE
What is doping?
Doping according to the Italian Law 14 December 2000, n° 376 (art. 1) of the Ministry of Health:

“Doping is the administration or the assumption of drugs or biologically and pharmacologically active substances and the use of medical acts without any need justified by pathological conditions and able to modify physical or biological conditions in order to achieve the best performances by the athletes”

Prof. Roberto Verna
The term **doping** comes from “doop”, a mix of ergogenic substances that Dutch seamen used already four centuries ago before facing an ocean storm.

*Prof. Roberto Verna*
From “doop” the term has become “to dope” and finally “doping” that means a substance able to modify the performance.
The term *doping* comes also from "*oop*", a mix of opium, tobacco and narcotics administered to racehorses in '800.

*Prof. Roberto Verna*
“Dope” is also an ancient South African term indicating an alcoholic drink used to stimulate during tribal ceremonial dances.

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“Doping is cheating”

(Antidoping Code - WADA)

Prof. Roberto Verna
Types of doping related to the different moments of the agonistic activity

1. Before the match, during the training, to try to increase muscular mass and physical strength or resistance (steroids- EPO )

2. After the match, to rapidly recover strength.

Prof. Roberto Verna
Types of doping related to the different moments of the agonistic activity

3. During the match, to:

- Decrease fatigue,
- Stimulate CNS,
- In some sports, to reduce anxiety (cannabinoids, beta blockers, etc)
- Try to increase oxygen transport and reduce fatigue (hemotransfusion)

Prof. Roberto Verna
Every Sport Authority is bound to:

• Protect athletes’ health
• Enforce medical and sports ethics
• Maintain the same opportunities for all the athletes during a competition

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History of DOPING

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From the Greeks....

Doping is not a recent discovery, but was already common in the antique Greek wrestlers (III century b.C.) who used a mushroom-derived drug to enhance their aggressiveness.

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...to the Romans

During their games, Roman athletes used different qualities of meat mixed with stimulating substances

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XIX\textsuperscript{th} Century

An English bicyclist, Arthur Linton, wins the Parigi-Bordeaux in 1896 dying after the race because of the use of exciting substances (ether-cocaine)
On 1904 Thomas Hicks, after winning the Olympic marathon in Athens, was seriously taken ill by the use of stricnine sulfate during the race.
Again XX century

Dorando Petri on his marathon race arrival, (London 1908) worn-out by fatigue ‘cause of the intake of stricnine with cognac
Former international efforts against doping

Prof. Roberto Verna
Prof. Roberto Verna

First cases of hematic doping
ATHENS 2004
Paralympics

Doping also affects the Paralympics in Athens: two Azerbaijani weightlifters were expelled from the Games because positive to two different substances. Sara Abbasov, 28, and Gundula Ismaylov, 31 years have fallen into the clutches of the controls after a test conducted on September 18. The two tested positive for nandrolone (the woman) and stanozolol (the man).

Prof. Roberto Verna
OPERATION QUADRIFOGLIO

84° GIRO D'ITALIA 2001

CARABINIERI FOR HEALTH (NAS)

Prof. Roberto Verna
STARTING OPERATION QUADRIFOGLIO
PERQUISITIONS AT HOTELS IN SANREMO AND NEIGHBOURING TOWNS

-184 Military employees

-507 Packs of prohibited medicines seized: (stimulants, anabolic steroids, steroids, diuretics, synthetic hemoglobin, blood products) Sequestration of large amounts of medical material (syringes, needle-cannulas, etc ..) and anonymous substances for laboratory analysis

-105 Persons reported to the Judicial Authority
**LIST OF THE DUGS FOUND DURING “HERCULES” CONFISCATION OPERATION**

<table>
<thead>
<tr>
<th>ALDACTONE</th>
<th>LASIX</th>
<th>RESTANDOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANAPOLON TABLET</td>
<td>HOMEOCUR TESTERSET</td>
<td>SAIZEN</td>
</tr>
<tr>
<td>OKSIMETOLON</td>
<td>HUMOLIN</td>
<td>SCHERING</td>
</tr>
<tr>
<td>ANDRIOL</td>
<td>JINTROPIN</td>
<td>SYNFLEX</td>
</tr>
<tr>
<td>BENADON</td>
<td>KADIUR</td>
<td>SOMATOSTATINA</td>
</tr>
<tr>
<td>CLOMIPHENE CITRATE</td>
<td>KRIPTOCUR</td>
<td>SPASMOPRONECAL</td>
</tr>
<tr>
<td>DECA-DURABOLIN</td>
<td>ISOPURAMIN</td>
<td>SPIROPENT</td>
</tr>
<tr>
<td>DIANABOL</td>
<td>LIPOSTABIL</td>
<td>SUSTENON</td>
</tr>
<tr>
<td>DEPO MEDROL</td>
<td>MASTERON</td>
<td>TAD 600</td>
</tr>
<tr>
<td>EFEDRINA LEVEL</td>
<td>METADIENON</td>
<td>TIOSIDE</td>
</tr>
<tr>
<td>EPARGRISEOVIT</td>
<td>METANABOL</td>
<td>TI-TRE LIOTIRONINA</td>
</tr>
<tr>
<td>ESICLENE</td>
<td>MONORES</td>
<td>TESTEX ELMU</td>
</tr>
<tr>
<td>ESTRUMATE</td>
<td>NAPOPSIN</td>
<td>PROLONGATUM</td>
</tr>
<tr>
<td>EUTIROX</td>
<td>NEOTON</td>
<td>TESTOSTERONE CYPIONATE</td>
</tr>
<tr>
<td>EXTRABOLINE</td>
<td>NESPO 60</td>
<td>TESTOVIRON</td>
</tr>
<tr>
<td>FELDENE</td>
<td>NOVALDEXTAMOXIFEN</td>
<td>TESTOVIS</td>
</tr>
<tr>
<td>FINAJECT</td>
<td>PARABOLAN</td>
<td>TRANSMETIL</td>
</tr>
<tr>
<td>FINASTERIDE</td>
<td>PLACENTEX</td>
<td>VENTIPULMIN CITRATE</td>
</tr>
<tr>
<td>GANABOL</td>
<td>PRIMOBOLAN</td>
<td>VIRORMONE TESTOSTERONE</td>
</tr>
<tr>
<td>GENOTROPIN</td>
<td>PROFASI HP</td>
<td>PROPINATE</td>
</tr>
<tr>
<td>GH UMATROPE</td>
<td>PROCAR FINASTERIDE</td>
<td>WINSTROL</td>
</tr>
<tr>
<td>GLOBUREN</td>
<td>PROVIRON</td>
<td></td>
</tr>
</tbody>
</table>

**APPROXIMATE AMOUNT : EURO 8,970,000,00**

Prof. Roberto Verna
**Jargon words used to order drugs, recorded during tapping**  
*COMANDO CARABINIERI PER LA SANITA' - N.A.S.*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFEDRINA</td>
<td>Mau-Wang</td>
</tr>
<tr>
<td>WINSTROL</td>
<td>double U - dresses - STROMBA</td>
</tr>
<tr>
<td>GANABOL</td>
<td>(for veterinary use)</td>
</tr>
<tr>
<td>DECA</td>
<td>&quot;the ones with the yellow cap&quot; - masterized</td>
</tr>
<tr>
<td>ANDRIOL</td>
<td>the moto</td>
</tr>
<tr>
<td>DECADURABOLIN</td>
<td>the cars</td>
</tr>
<tr>
<td>NANDROLONE DECAONATO</td>
<td>lat extension</td>
</tr>
<tr>
<td>PROVIRON</td>
<td>trousers</td>
</tr>
<tr>
<td>OXANDROLONE</td>
<td>lat machine</td>
</tr>
<tr>
<td>HASHISH</td>
<td>smoke - chocolate</td>
</tr>
<tr>
<td>GH</td>
<td>&quot;the cold one&quot; - the ice - frozen proteins - chewing gums</td>
</tr>
<tr>
<td>PRIMOBOLAN</td>
<td>P - decaffeinated</td>
</tr>
<tr>
<td>PROVIRON</td>
<td>PRO</td>
</tr>
<tr>
<td>TESTOVIS</td>
<td>&quot;those with the blue box&quot;</td>
</tr>
</tbody>
</table>

*Prof. Roberto Verna*
The medicalization of the athlete and of the sportsman

Prof. Roberto Verna
WHY ATHLETES AND SPORTSMEN USE DRUGS?

• To improve athletic performance
  • drugs prohibited and not for doping
  • creatine
  • linear and ramified aminoacids

• For a faster athletic recovery in cases of strong athletic involvement
  • Ergogenic Aids

• To recover losses due to the intense physical effort
  • Vitamins
  • Mineral Salts

• To protect from oxydative damage
  • Vitamins
  • Antioxydants

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The differences in performance among athletes are minimal

- Fractions of seconds in speed trials
- Few seconds in endurance events

**Consequences**

Exasperated search of the smallest improvement through the use of drugs believed to be capable of increasing performance

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Drugs used by athletes and by athletes banned and NOT for doping

• Medication not banned for doping
• Health products (supplements)
• Herbal products
• Homeopathic preparations

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Athletes subjected to doping controls who reported taking medication

= 65-70% (8000 athletes)

Types of drugs reported

<table>
<thead>
<tr>
<th>Type of drugs</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-steroidal anti-inflammatory drugs</td>
<td>35%</td>
</tr>
<tr>
<td>Supplements (salt, amino acids, etc.)</td>
<td>20%</td>
</tr>
<tr>
<td>Vitamin supplements</td>
<td>17%</td>
</tr>
<tr>
<td>Herbals / homeopathic products</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

Prof. Roberto Verna
For a medication, adverse effects are allowed only if the ratio risk / benefit of the treatment is favourable.

A health benefit does NOT exist in a subject who is not sick

Unreasonable risk of ADR occurrence

Prof. Roberto Verna
Recently, in Italy has been transposed the European Directive on food supplements (46/2002/EC of June 10, 2002)

**FOOD SUPPLEMENTS**

products capable of performing

“nutritional” effects  physiological effects

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FOOD SUPPLEMENTS:
(46/2002/CE del 10 giugno 2002)
capsules, tablets, tablets, bars, vials, bags
in particular, but not limited to, vitamins, minerals, amino acids, fatty acids, fibers and herbal extracts

Prof. Roberto Verna
Guidelines on foods intended to meet intense muscular effort, especially for sportsmen

Products aimed at energy integration
Products with minerals designed to restore salt and water losses (...)
Products for the integration of proteins
Products for the integration of amino acids and derivatives (creatine)
Other products with nutritional value, adapted to an intensive muscular effort
Combination of the above products

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VITAMINS AND MINERAL SUPPLEMENTS

The minerals replenish salt and water losses resulting from physical activity.

Supplementation of vitamins in the diet, in most cases, is incongruous and unnecessary.

A sportsman has seldom a vitamin deficiency.

Also, if vitamins are “good”, it does not mean they can not become "bad" if abused.

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HERBAL PRODUCTS

Even among the sportmen is becoming more widespread the culture of "natural supplement":

The erroneous belief that, just as naturally, must necessarily be harmless
The effect of word of mouth propagation, especially in clubs and gyms
Advertising campaigns not subjected to controls
The wide availability on parallel sales channels (internet)

self-medication w/out supervision

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Is the use of supplements "Safe"?

A scientific demonstration of effectiveness
Correct information of the action on the body and on the performance
Certainty of the content of products

ARE MISSING
- Health risks
- Commercial fraud
- Positivity to antidoping tests

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Potential risk of positive drug test

Different composition from that declared on the label (contamination, whether deliberate or accidental, with doping substances or their precursors)
Active ingredients contained in herbal products marked with an “unusual" name (eg, ephedrine / ma huang-...)
Unknown interactions with other drugs / metabolites and / or endogenous substances

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Potential risks to the positive doping test: an example ...

- Product based on a mixture of herbs, free for sale

- Declared ingredients: Cola nut, Passiflora, Ma-huang, Siberian Ginseng, Chinese Dandelion, Ginger, Seaweed, Pullulan, Gymnema sylvestre

- The analysis showed the presence of ephedrine (ephedrine, methylephedrine).

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Potential risks to the positive doping test: a further example ...

It was found the presence of anabolic steroids in some packages of food supplements in individual packages, NOT all the capsules were contaminated. Contaminated capsules contained steroids in amount ranging from 0.3 to 500 micrograms.

The contaminated products are often of U.S. production, almost always not available over the counter, but on safe parallel channels particularly Internet.

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Supplements and herbal products should be considered drugs?

YES, according to WHO

Editorial in JAMA, March 26, 2003: supplements should be considered in all respects and consequently medication should be adequate evidence available on their validity.

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The excessive "medicalization", represents a serious danger for the athlete,

NOT ONLY FOR THE POSSIBILITY OF A POSITIVITY TO DOPING TESTS, BUT ALSO

FOR THE POSSIBLE OCCURRENCE OF ADRs

ADR: \( \Rightarrow \) Adverse Drug Reaction

Prof. Roberto Verna
The ADRs in the U.S. (JAMA 1998; 279: 1200-05) are, incidentally, the fourth leading cause of death after cardiovascular diseases, cancer and stroke:

more than 100,000 deaths / year.

The data comes from a meta-analysis of 39 prospective studies in hospitalized patients:

- 2,216,000 patients with serious non-fatal ADRs
- 106,000 patients with fatal ADRs

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To combat doping is necessary to know the effects and damage of banned substances

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Ephedrine

- Nausea, Vomiting,
- Increased sweating,
- Thirst,
- Restlessness, Insomnia,
- Tachicardy, Hypertension, Arrhythmias.

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NARCOTICS
Prohibited only in competition

Are taken to reduce pain perception

Pain is a warning sign

Its removal may lead the athlete to "overdo"

Risk: to worsen existing injuries
to cause permanent damage.

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Narcotics

- Constipation;
- Nausea and vomiting;
- Insomnia and depression;
- Decreased ability to concentrate;
- Loss of balance and coordination;
3. CANNABINOIDS

A decrease of emotional tension before a race is postulated.

- Increased heart rate, blood pressure
- Balance and coordination disorders;
- Short-term memory loss;
- Loss of concentration, hallucinations, psychosis;
- Subnormal body temperature;
- Abnormal spermiogenesis and ovulation;

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GLUCOCORTICOIDS

Insomnia;
Hypertension;
Cataracts;
Diabetes Mellitus;
Osteoporosis;
Immunosuppression

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ANABOLIC DRUGS
Prohibited “in-out” competition

Alterations in serum chemistry

- Increased hematocrit
- Increase of platelets
- Decreased levels of FSH and LH
- Decreased levels of testosterone
- Decrease in HDL-cholesterol and total cholesterol
- Hyperglycemia, hyperinsulinemia
- Elevated liver enzymes and indices of cholestasis
ANABOLIC AGENTS
Prohibited “in-out” competition

Long lasting use

Liver Damage:
- Cholestasis
- Hepatitis
- Benign and Malignant Tumors

Mental Damage:
- Dysphoria
- Psychosis
- Dependence
- Severe Depression

Cardiovascular Damage:
- Cardiomyopathy
- Acute Myocardial Infarction
- Cerebrovascular Accident
- Pulmonary Embolism

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ANABOLIC DRUGS
Prohibited “in-out” competition

Drugs often used in combination

- **Human chorionic gonadotropin (HCG):**
  - ↑ the synthesis of testosterone contrast to the testicular atrophy

- **Diuretics:**
  - ↓ water retention dilute the urine for drug tests

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ANABOLIC DRUGS
Prohibited “in-out” competition

Drugs often used in combination

- **Antiestrogens:**
  - prevent gynecomastia in males

- **ACTH:**
  - endogenous steroids production can provoke a feeling of euphoria

Prof. Roberto Verna
4. Anabolic Agents
(testosterone, nandrolone, stanzolol…)

↑ muscle mass,
↓ body fat
↓ stamina
↑ aggressiveness
↑ catabolic action of glucocorticoids
↑ synthesis of red blood cells
↑ bone density
Anabolic Agents

Hematochemical Alterations

- Hematocrit
- Platelets
- Levels of FSH and LH
- Testosterone levels
- HDL-cholesterol and total cholesterol
- Glycemia, Insulinemia
- Liver enzymes and indices of cholestasis
Anabolic Agents

Adverse effects of using anabolic agents depend on the age and sex of the subject, the duration of treatment, the dose and type of steroid used.

Adverse effects can be divided into generic, specific to men, specific to women.
Anabolic Agents

General adverse effects

- Acne;
- Damage to the Reproductive System and Sterility;
- Hypertension;
- Increased Risk of Cardiovascular Disease;
- Abnormalities and Renal and Liver Dysfunction;
- Aggressive and Violent Behavior
- Tendon Injury and/or Bone Microfractures
Anabolic Agents

Adverse effects specific to men

Gynecomastia;
Reduced Production of Male Hormones;
Testicular Atrophy and Oligo-azoospermia;
Infertility, Impotence;
Alopecia;
Increased Risk of Prostate Cancer.
Anabolic Agents

Adverse effects specific to women

- Hirsutism and Hair Loss;
- Menstrual Irregularities and Amenorrhea;
- Atrophy of the Mammary Glands;
- Voice Change;
- Clitoris-megalia
MASKING AGENTS

Prohibited “in-out” competition

• They have the ability to alter the excretion of prohibited substances, to mask their presence in urine or other samples used in doping control, or modify the hematological parameters

Prof. Roberto Verna
MASKING AGENTS
Prohibited “in-out” competition

Useful to decrease weight in the orders divided by classes

- Dishydratation
- Amenorrhea
- Anemia
- Electrolyte Dysequilibrium
- Osteoporosis
- Hypotension

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Death for doping

“Flo Jo” Griffith (1959-1998) caught an infectious disease because of the abuse of growth hormone extracted from corpses.

She said:

“when you always get second, you can accept it or try to become the number one”.

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PEPTIDE HORMONES
Prohibited "in-out" competition

EPO increases erythrocyte production thus oxygen transport.

On the other hand, the risk of death by thrombosis increases by 400%

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BETA-2 AGONISTS
Prohibited “in-out” competition

THESE DRUGS HAVE AN EFFECTIVE ACTION ON MUSCLE MASS WITHOUT DETERMINING THE MANY SIDE EFFECTS RELATED TO THE USE OF STEROIDS. Are also used to prevent asthma triggered by exercise.

Clenbuterol produces a specific protein anabolism in both normal muscle and in the catabolic phase through the activation of beta-2 adrenergic receptors present in skeletal muscles themselves.

Growth in mass and increased muscle strength

Prof. Roberto Verna
BETA-2 AGONISTS
Prohibited “in-out” competition

Therapeutic dose range: 20-80 micrograms per day

Doses in doping: 100-140 micrograms per day

SIDE EFFECTS: Tremor (very marked), and cardiovascular effects such as tachycardia, palpitations, arrhythmias, hypertension. Were also observed anxiety, dizziness, headache, insomnia and muscle spasms.

Prof. Roberto Verna
ANTIESTROGEN AGENTS

Prohibited in and out competition

Prohibited in and out competition, exclusively for men

Clomiphen
Cyclophenil
Raloxifen
Tamoxifen
Toremifen
Aromatase inhibitors (Aminoglutethimide, Anastrozole, Exemestane, Letrozole, Fludrocortisone and Desossicortone)

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ALCOHOL
Prohibited in particular sports

- Alcohol activates the ventral area of the brain and releases dopamine by changing all the positive feelings.

Prof. Roberto Verna
ALCOHOL
Prohibited in particular sports

• Damage from alcohol include severe liver disease and risk for infants of drinker mothers: the fetal alcohol syndrome

Prof. Roberto Verna
The world of sport, professional or not, looks for a "magic" and harmless ingredient that can improve physical performance and increase the level of competitiveness.

The companies promote the spread of specialized products designed specifically for sports.

These substances are not always safe.

Prof. Roberto Verna
Incongruous / Hazardous use of supplements and health products.

Raw materials and production processes are not always controlled.

Extreme vagueness in the indication of the dosages.
Belief that the dosages are not critical as for medicines.
Lack of references to age, sex, body weight, in place to pathological situations (hypertension)

Lacks a real assessment of the effectiveness and toxicity

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Incongruous / Hazardous use of supplements and health products.

Presence of pharmacologically active molecules quite often with misleading names:

*ma-huang, guarana, pullulan, etc.* ...

Different composition versus the one shown on the label (contamination, whether deliberate or accidental).

*Prof. Roberto Verna*
Incongruous/hazardous use of supplements and health products.

“ETERNAL LIFE "(slimming)
Dictamnus dasycarpus plant contains numerous toxins
3 cases of liver failure, 1 death

“JIN BU HUAN "(sedative, analgesic)
Lycopodium serratum plant containing a alkaloid morfinosimile
7 cases of hepatotoxicity and acute liver failure
Can the sports physician, motivated by the need for prevention (no disease) administer drugs without violating the law and professional ethics?

**TUE:** Therapeutical Use Exemption

The physician of professional societies should make a note of the use of supplements/health products

*Prof. Roberto Verna*
SPORTS YES, DOPING NO

DOPING IN SPORT IS A CRIME AND MAY SERIOUSLY HARM YOUR HEALTH

Prof. Roberto Verna
<table>
<thead>
<tr>
<th>Prohibited substances</th>
<th>Prohibited methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stimulants</td>
<td>• Administration of blood, RBCs and/or similar products</td>
</tr>
<tr>
<td>• Narcotics</td>
<td>• Administration of artificial oxygen transporters or plasma substitutes</td>
</tr>
<tr>
<td>• Anabolizing Agents</td>
<td></td>
</tr>
<tr>
<td>• Diuretics</td>
<td></td>
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<tr>
<td>• Peptide Hormones, mimicking substances</td>
<td></td>
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<tr>
<td>• Local Anesthetics</td>
<td></td>
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<tr>
<td>• Alcohol</td>
<td></td>
</tr>
<tr>
<td>• Cannabis sativa and indica</td>
<td></td>
</tr>
<tr>
<td>• Glucocorticosteroids</td>
<td></td>
</tr>
<tr>
<td>• Beta - blockers</td>
<td></td>
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</tbody>
</table>
HEMATOCHEMICAL MARKERS OF THE PHYSICAL CONDITION OF THE ATHLETE

- Testosterone
- Diidrotestosterone
- ACTH
- Cortisol
- DHEAs
- delta-4-androstenedione
- GH

- Evaluation of the agonistic stress and involvement

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HEMATOCHEMICAL MARKERS OF THE PHYSICAL CONDITION OF THE ATHLETE

- LDH
- CPK

- Study of the muscular characteristics of an athlete

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MOUNTAIN SPORTS

- Complete Blood Count
- Sideremia
- Transferrin
- Ferritin
- Hb dissociation curve
- Diphosphoglycerate
INDICATORS OF THE USE OF PROHIBITED SUBSTANCES AND METHODS

Prof. Roberto Verna
Analytes for analyzing substances

- FSH ↓
- LH ↓
- PT ↓
- PTT ↓
- LH ↓
- Total Chol. ↓
- HDL Chol ↓
- GH
- CPK ↑
- AST - ALT ↑
- LDH ↑
- Total Proteins
- Testosteron ↓
- Estradiol ↓
- Estrone ↓
- LDL Chol ↑
- C- Prot.
- S-Prot
- D-Dimer
- PAI-1
- ATIII
- APO A ↓
Tests to reveal the use of Corticosteroids

- Blood Glucose
- Blood Potassium
- Blood pH

Tests to reveal the use of Narcotics and Analgesics

- LH
- ADH
- GH
- Prolactin
- Testosterone

Prof. Roberto Verna
Tests to reveal the use of EPO and analogues

- Peripheral blood examination including RBC indices
- Reticulocytes
- Transferrin
- Ferritin
- Folic Acid
- Vitamin B12
- Iron
- CD 71
- Glycophorin A
- Bilirubin
- CFU-E
- BFU-E
Tests able to detect the use of GH

- GH
- LH
- FSH
- Cholesterol
- TG
- Creatinine Clearance
- BUN
- Glucose

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Tests to detect the use of beta-blockers

- TSH
- fT3
- fT4
- HDL-Chol
- TG
- NEFA
- Glucose

- Renin
- Emogas analysis

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Tests able to detect the use of diuretics

- Na
- K
- Cholesterol
- Ht
- Plasma and Urine electrolytes
- 17-OH corticosteroids
- Urine pH (or blood)
- Uric acid
- Glucose
- Urinary aldosterone
- Na, K Pump
- Na, K Cotransport

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Genetic Doping

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Genetic Doping

- Based on the manipulation of genes.
- Using the results obtained in gene therapy.
- Is it a future threat for athletes?

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Gene Therapy

- Artificial insertion of genes into the body of the patient.

Purpose:
- Kill or weaken cancer cells.
- Making the body able to reproduce on its own substances now available only on administration.
- Replace defective genes with healthy copies.

Problems: lack of control on the expression of artificial gene.

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The prospect of gene doping

• An alternative to the administration of drugs that the body can produce itself
• Changing the natural regulation of genes
• Enhancement of protein in the body

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Examples of the potential of gene doping

- Increase in hematocrit by EPO
- Increased muscle strength by IGF-1
- Increased muscle mass by the removal of myostatin
- Increased blood flow through VEGF

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Direct injection of DNA into a muscle

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Removing the gene that controls the growth of muscle mass (myostatin)

Foreleg of a normal mouse

Foreleg of a mouse lacking the myostatin gene


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VEGF gene therapy on humans

Blood vessels of a patient who received the inoculation of a virus carrying the gene for VEGF

Before

After

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Can we discover genetic doping?

• The protein produced is equal to the endogenous protein
• The artificial DNA is present only locally after an injection with pure DNA or genetically modified cells
• You should know the sequence of artificial DNA to be able to detect it

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POSSIBLE COUNTERMEASURES

• Making the gene doping illicit
• Establish close contacts with companies that produce gene therapies
• Develop DNA tests that can detect artificial genes used in gene therapy
• Developing indirect methods to detect gene doping, if possible

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WHEN?

• Gene doping is already present and constitutes a serious risk to the athlete

• It will be easier when gene therapy becomes a standard procedure (in 10/20 years)

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