How to Improve the Fight Against Doping
A perspective from the German Sport University and the Institute of Biochemistry

Wilhelm Schänzer

Cologne - 5th October 2011
Manfred Donike
23.8 1933 – 21.8.1995

1966 First publication -
dope analysis based on GC
separation techniques

1969 Synthesis of MSTFA

1972 Dope testing
Olympic Games Munich
GC and MS

1977 Professor (appointment)
Institute of Biochemistry
German Sport University

1980 Member of the IOC MC-
subcommission „Doping and
Biochemistry“
Tour de France 1967

Tom Simpson
tragic death
Mont Ventoux
amphetamine
alcohol
Manfred Donike
23.8 1933 – 21.8.1995

1966 First publication - dope analysis based on GC separation techniques

1969 Synthesis of MSTFA

1972 Dope testing Olympic Games Munich GC and MS

1977 Professor (appointment) Institute of Biochemistry German Sport University

1980 Member of the IOC MC-subcommission „Doping and Biochemistry“
List of prohibited substances for the Olympic Games in Munich 1972

a) Stimulants
b) Narcotics
## Stimulants

<table>
<thead>
<tr>
<th>a) Psychomotoric Stimulants e.g.</th>
<th>c) Different Substances of the Central Nervous System e.g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylamphetamine</td>
<td>Amiphenazol</td>
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<tr>
<td>Amphetamine</td>
<td>Bemegrid</td>
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<tr>
<td>Benzphetamine</td>
<td>Leptazol</td>
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<tr>
<td>Cocain</td>
<td>Nikethamide</td>
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<tr>
<td>Diäthylaminopropiophenon</td>
<td>Strychnin</td>
</tr>
<tr>
<td>Dimethylamphetamine</td>
<td>and related substances</td>
</tr>
<tr>
<td>Fencamphetamine</td>
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<tr>
<td>Methylamphetamine</td>
<td></td>
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<tr>
<td>Methylphenidate</td>
<td></td>
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<tr>
<td>Norpseudoephedrine</td>
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<tr>
<td>Phendimetrazin</td>
<td></td>
</tr>
<tr>
<td>Phenmetrazin</td>
<td></td>
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<tr>
<td>Prolintane</td>
<td></td>
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<tr>
<td>Dimethylamphetamine</td>
<td>Narcotics</td>
</tr>
<tr>
<td>Methylamphetamine</td>
<td></td>
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<tr>
<td>and related substances</td>
<td></td>
</tr>
<tr>
<td>d) Narcotics and Analgetics e.g.</td>
<td></td>
</tr>
<tr>
<td>Dextromoramide</td>
<td></td>
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<tr>
<td>Dipipanone</td>
<td></td>
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<tr>
<td>Heroin</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
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<tr>
<td>Morphine</td>
<td></td>
</tr>
<tr>
<td>Methoxyphenamine</td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td></td>
</tr>
<tr>
<td>and related substances</td>
<td></td>
</tr>
</tbody>
</table>

### b) Sympathomimetic Amines e.g.

- Ephedrine
- Methylephedrine
- Methoxyphenamine

### and related substances

and related substances
The 2011 Prohibited List - World Anti-Doping Code

Substances and Methods prohibited in competition

S0  Non-approved substances and methods
S1  Anabolic agents
   - Anabol androgenic steroids (AAS)
   - Other anabolic agents
S2  Peptide hormones, growth factors and related substances
S3  Beta-2 Agonists
S4  Hormone antagonists and modulators
S5  Diuretics and other masking agents
S6  Stimulants
S7  Narcotics
S8  Cannabinoids
S9  Glucocorticosteroids

M1  Enhancement of oxygen transfer
   - Blood doping
   - Artificial oxygen uptake, transport or delivery
M2  Chemical and physical manipulation
M3  Gene doping

Substances prohibited in particular sport

Alcohol, Beta-Blockers
Detection of Testosterone misuse

1983

Testosterone / Epitestosterone
T/E - ratio > 6

Nachweis von exogenem Testosteron

The detection of exogenous testosterone

M. Donike, K.-R. Bärwald, K. Klostermann, W. Schänzer, J. Zimmermann

Institut für Biochemie der Deutschen Sporthochschule Köln

Anschrift für die Verfasser: Prof. Dr. rer. nat. M. Donike,
Institut für Biochemie der Deutschen Sporthochschule Köln, Carl-Diem-Weg 2, 5000 Köln 41
1981 Opening of a new laboratory - Institute of Biochemistry at the 7th floor of the new building - German Sport University

1981 Symposium organized under participation of the Medical Commission of the IOC and the Medical Commission of the IAAF

1983 1st Cologne Workshop on Dope Analysis

Next year
2012 30th Cologne Workshop on Dope Analysis “Manfred Donike Workshop for Dope Analysis”
World Association of Anti-Doping Scientists

- Experts in dope analysis
- Working in an accredited laboratory
- Sharing of knowledge (new substances, new methods)
- Exchange of reference material
New Doping Methods  Doping Control
### WADA List of Prohibited Substances and Methods 2011

<table>
<thead>
<tr>
<th>Category</th>
<th>Substances (N)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S0 Non-approved Substances</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>S1 Anabolic Substances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Anabol Androgenic Steroids (AAS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Exogenous AAS:</td>
<td>46 Substances</td>
<td>&gt; 46</td>
</tr>
<tr>
<td>b. Endogenous AAS:</td>
<td>21 Substances</td>
<td>21</td>
</tr>
<tr>
<td>2. Other Anabolic Substances</td>
<td>4 Substances</td>
<td>4</td>
</tr>
<tr>
<td>SARMs</td>
<td></td>
<td></td>
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<tr>
<td>S2 Peptide Hormones</td>
<td></td>
<td></td>
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<tr>
<td>EPO + Analogs</td>
<td>&gt; 20</td>
<td></td>
</tr>
<tr>
<td>Choriogonadotropin</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Growth Hormone</td>
<td>1</td>
<td>GHRH, GHRP</td>
</tr>
<tr>
<td>Insulin Analogs</td>
<td>5</td>
<td>Human Insulin</td>
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<tr>
<td>SARMs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S3 Beta-2 Agonists</td>
<td></td>
<td>6 Substances &gt; 6</td>
</tr>
<tr>
<td>S4 Hormone Antagonists and Modulators</td>
<td>12 Substances</td>
<td>12</td>
</tr>
<tr>
<td>S5 Diuretics and other Masking Agents</td>
<td>18 Substances</td>
<td>&gt; 18</td>
</tr>
<tr>
<td>S6 Stimulants</td>
<td></td>
<td>63 Substances &gt; 63</td>
</tr>
<tr>
<td>S7 Narcotics</td>
<td></td>
<td>11 Substances &gt; 11</td>
</tr>
<tr>
<td>S8 Cannabinoids</td>
<td></td>
<td>1 Substance 1</td>
</tr>
<tr>
<td>S9 Glucocorticosteroids</td>
<td></td>
<td>16 Substances &gt; 16</td>
</tr>
<tr>
<td>M1 Enhancement of Oxygen transfer</td>
<td>3 Methods</td>
<td>3 blood transfusion</td>
</tr>
<tr>
<td>M2 Chemical and Physical Manipulation</td>
<td>diff. Techniques</td>
<td>diff. Techniques</td>
</tr>
<tr>
<td>M3 Gene Doping</td>
<td></td>
<td>2 Substances 1</td>
</tr>
<tr>
<td>P.1 Alcohol</td>
<td></td>
<td>1 Substance 1</td>
</tr>
<tr>
<td>P.2 Beta Blockers</td>
<td></td>
<td>19 Substances &gt; 19</td>
</tr>
</tbody>
</table>
Improved Analytical Techniques

(especially for detection of anabolic androgenic steroids, but also for several peptides)

1995 - High Resolution Mass Spectrometry

1997 - Tandem Mass Spectrometry

... Continuous improvement in Mass Spectrometry
High Resolution Mass Spectrometry

Applied at the
- Olympic Games Atlanta 1996
- IOC accredited
Dope control laboratories had to install this technique or a similar sensitive MS technique

Monseigneur,

Regarding our discussion in Düren about the advantages of High Resolution MS in dope control I would like to present you our results in the screening of anabolic steroids from January to August 1995. From the 82 positive cases 50 cases were only found by the use of High Resolution MS. This project was initiated by Prof. Donike and it was also his intention to introduce High Resolution MS to the IOC accredited laboratories.

With kind regards

Willi Schänzer
Identification of a Longterm Excreted Metabolite of Metandienone (anabolic steroid)

- 2006 Cologne Laboratory

- Additional reporting of about 53 cases for the abuse of metandienone
  (would have not been reported with the standard MS procedure)
Dope Analyis 1972 – Olympic Games Munich

Mass Analyser with Gaschromatograph

Atlas MAT CH-5 - with On-line-Data System (left) – Gaschromatograph (right)
Mass Analyserer with Gaschromatograph

**GC-MS-MS Quantum** (Thermo Fisher Scientific)
Gaschromatograph (GC) – Mass Analyser (MS)
Financial Support for Modern Analytical Equipment

Who will pay?

How to keep 35 laboratories worldwide on a comparable level (harmonisation of analytical methods)?

- Sport federations, Governments, WADA, IOC?
2002

Foundation of a Centre for Preventive Doping Research at the German Sport University Cologne

- using the full scientific competence of other institutions of the German Sport University
- Improvements in protein analysis
- Research on new substances possibly of interest for doping purposes
Research projects (peptide hormones)

- Hemoglobin-based oxygen carriers (HBOCs)
- Synthetic insulins
- IGF-1 and synthetic analogs
- LH-RH
- Synacthen
- Growth hormone releasing hormones & metabolites
- Recombinant growth hormone hGH
- HEMATIDE (EPO-mimetic)
- Proteases (manipulation)
- Desmopressin
Research projects (gene doping & other)

- **Small interfering RNA (siRNA)**
- **Generic screening assays** (Development of for targeted and non-targeted doping control analysis)
- **Multi-analyte detection methods** (Development particularly for peptide hormones)
Research projects (small molecules)

- Selective androgen receptor modulators (SARMs)
- GW1516 (gene doping substance)
- AICAR (gene doping substance)
- Hypoxia-inducible-factor (HIF) stabilizers ("EPO mimetics")
- JWH-018 (synthetic cannabinoid)
- S-107
Centre for Preventive Doping Research at the German Sport University Cologne

- Doping control and anti-doping research are working in a manner of “hand to hand“
- Highly effective anti-doping strategy
- Case related research
- Best model for other anti-doping research groups
Centre for Preventive Doping Research at the German Sport University Cologne

2011
Foundation of an European Monitoring Centre for the early identification of new substances and methods having a potential for an abuse for doping purposes.

supported by the Federal Ministry of the Interior (Germany)
Identification of Doping Traps

- Protection of athletes
- Inadvertent Doping Cases
- Case related research
- Contamination of Nutritional Supplements with prohormones (since 1999)
- Fakes of Nutritional Supplements with anabolic steroids and stimulants
- Food contamination - clenbuterol
Summary

- Following the Cologne experience in dope control and anti-doping research we consider the situation (in Germany and several other countries) as follows: