Doping in unorganised sports

Gezondheidsraad **President**
Health Council of the Netherlands

To the Minister of Health, Welfare and Sport

Subject : presentation of advisory report *Doping in unorganised sports*
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Dear Minister,

In response to your request for advice dated 23 April 2008, I hereby present to you the advisory report Doping use in unorganised sports. The advisory report was drafted by a committee appointed for this purpose, and was reviewed by two Health Council Standing Committees on Medicine and on Health Ethics and health Law. Additionally, a number of external experts were consulted.

The Committee would like to emphasise the importance of unorganised sports, including fitness training, in terms of the positive contribution that exercise (sports) makes to public health. It would be unjust if the recommendations outlined in this report are used to negate this positive contribution.

In the advisory report before you, the Committee describes the risks of doping use in unorganised sports. It is of the opinion that given the nature of the substances used, the way they are used and risk perception among users, use of doping in unorganised sports is associated with significant risks.

In order to present the true extent of the health problems – in terms of disease burden and care consumption – the Committee used existing health services data collections. However, these health problems have only partially been mapped. This has largely to do with the nature and objectives of these data collections.

The doping issue is not so large as to make default registration a logical or practical desirable. The Committee therefore recommends further research be conducted in order to gain insight into the consequences (short and long term) of doping use in unorganised sports.

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Furthermore, the Committee sees a number of possibilities for expanding current doping policy with specific measures focused on doping use in unorganised sports. It makes a number of concrete suggestions for limiting or preventing severe individual health damage to users. To this end, the Committee has attempted to coordinate with Dutch drug policy, in part due to combined use among doping users.

The Committee feels it is important to determine whether and which harm reduction measures can be used to expand to current doping policy. Additionally, the Committee feels it is desirable to further investigate whether effective interventions currently used in other fields (drugs, alcohol, smoking) can be used as part of doping policy; an additional reason for this approach is that combined use of doping and other psychotropic substances is relatively common.

I endorse the committee's conclusions and recommendations.

Your sincerely,
(signed)
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to:

the Minister of Health, Welfare and Sport

No. 2010/03E, The Hague, April 13, 2010

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Housing, Spatial Planning & the Environment, Social Affairs & Employment, Agriculture, Nature & Food Quality, and Education, Culture & Science. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

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INAHTA

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Contents

Executive summary

Request for Advice

In recent years, reports from the former Netherlands Centre for Doping Issues (NeCeDo) and the subsequently founded Doping Authority showed that doping in sports is likely a growing problem in our country. Use of doping in sports is largely associated with professional sports. However, in addition to organised sports (at both professional and amateur levels), doping is supposed to be widespread in unorganised sports.

The Minister of Health, Welfare and Sport has asked the Health Council of the Netherlands to investigate the nature and severity of doping use in unorganised sports, particularly with regard to the harmful effects on health, both short- and long-term, the implications of high-risk drugs in terms of health risk, disease burden and care consumption, and to make recommendations regarding these topics. Additionally, the Council is asked to provide a vision statement on improving prevention of health damage based on current scientific insights.

The request for advice defines doping in unorganised sports as improper use of authorised or unauthorised medicinal products with the objective of obtaining a muscular or slim physique. It indicates that the use of anabolic steroids and stimulants by gyms and fitness centre attendees in particular is worrying.

Doping in sports

Defining what counts as doping, the reason doping is used, and the way doping policies should be drafted is context dependent. Within organised sports, doping is used to improve performance. The use of doping is combated vigorously there due to the unfair competitive advantage and the harmful health effects for users. In the Netherlands, the primary responsibility for these activities lies with national sporting organisations, that can perform doping tests and issue sanctions if required.

Within unorganised sports, doping is not only used to improve performance, but also to obtain a slim, muscular physique. Within the framework of this advisory request, the Committee defines unorganised sports as: “any form of recreational sporting activity not organised by regular sports organisations”. Fitness is the most common sport performed in this context. The majority of this sporting activity takes place in gyms and fitness centres.

The primary task to counter the risks of doping use in unorganised sports lies with the government. To counter the risks of improper use of medicinal products (with or without marketing authorisation), the Doping Authority has been tasked with raising awareness and advising amateur athletes (particularly gym visitors) and people in their direct environment. Trade and manufacturing are countered via legislation.

Doping substances

Many substances are used as doping. A rough classification – according to the use they are put to is:

- Performance-enhancing substances
- Substances to counter the effects of other doping substances
- Substances to obtain a slim and/or muscular physique
- Other substances.

The substances listed in the advisory report are discussed one at a time; the risks of use and – insofar as available – the extent of use are outlined per substance.

Prevalence and characteristics of doping use in unorganised sports

About 2 million people visit gyms and fitness centres in the Netherlands. Recent research performed by TNO examining the prevalence of doping among gym

visitors aged 15 and older showed 8.2% of them – 160,000 individuals - used doping substances in the past year.

In addition to research focused specifically on the use of performance-enhancing substances by fitness centre visitors, research is conducted every four years in the Netherlands into substance use (alcohol, drugs, tobacco, sleeping medication and sedatives, and performance-enhancing substances) in the general population: the National Prevalence Study into Substance Use (NPO). A secondary analysis of NPO data from 2005 regarding the use of performance-enhancing substances in the general population shows that more men use performance-enhancing substances than women. Of note is also combined use; doping users were found to use more (other) substances compared with the general population (cannabis, cocaine, amphetamines, XTC, LSD, heroin and alcohol). This suggests that doping users exhibit higher risk behaviour than the general population. Doping use is more common in urban than in rural areas; stimulants are more common in urban areas, anabolic steroids in rural areas.

Data from different population groups shows that the percentage of doping users among non-western immigrants is 4.9%, among western immigrants it is 3.1% and among native Dutch people 1.9%.

Contrary to previous findings, internet was found to play an important role as a place for purchasing doping substances. Gyms and fitness centres are still the main place to make contact with dealers.

Short- and long-term consequences of doping use for disease burden and care consumption

The Committee searched multiple databases. This revealed that while data was available on various disease entities, the degree to which these are caused by doping use is unclear. Many registries record substance and/or medicinal product use, but not the indication for the use of the substance in question. There are ways to gain greater insight into the consequences of doping use in terms of disease burden and care consumption. These are outlined in this advisory report.

Regarding the short-term effects of doping use in unorganised sports, the Council noted it causes health damage. With regard to long-term effects, negative effects on the cardiovascular system are certainly present, and potential carcinogenicity of substances must also be considered. A survey of available literature showed that renal, hepatic, skin, tendon and muscle conditions have also been described. Additionally, a broad array of psychiatric issues related to doping use has been described. This includes addiction, effects on mood (depres-

sion) and (aggressive) behaviour. The harmful effects of doping are not controversial, but the extent of the damage remains unclear.

Current and future doping policies

While exact data on the consequences of doping substance use on disease burden and care consumption are lacking, the Committee is of the opinion that, given the knowledge regarding harmfulness of doping substance use and the potential severity thereof, it would be useful to determine in which regard the current doping policies could be modified and/or improved in order to prevent/minimise unnecessary and unwanted severe harm to individual user health.

The Committee is of the opinion that doping policies cannot be addressed separately from the broader substance use policies regarding harmful substances implemented by the Dutch government. These policies focus on prevention. Taking the available data into account, the Committee sees no reason to deviate from these policies.

Taking into consideration the development of future preventive policies, the Committee recommends new research be conducted into the determinants of doping use, in other words to identify the factors that influence this behaviour. In anticipation of this research, the Committee makes a number of recommendations influenced by parallels in other areas. The incidence of combined use among doping users led the Committee to establish a connection with the Dutch drug policies. The Committee believes future doping policies should be differentiated both in terms of target groups and intervention types.

Conclusions and recommendations

The Committee wishes to emphasize the importance of unorganised sports and exercise in making a positive contribution to promoting public health. The Committee would greatly regret it should the findings included in this advisory report be used selectively and in an oversimplified manner so as to negate this positive contribution.

The Committee is of the opinion that current doping use in unorganised sports, given the nature of the substances used, the method of use and users' risk perception, entails significant risks.

Although this affects (particularly compared to issues such as obesity and smoking) a relatively small group (recent use among about 8% of gym visitors

and 1% of the Dutch population), but in absolute terms the group is significant (about 160,000 people have used doping substances in the past year).

The precise nature and severity of the health problems associated with doping are only partially known. Databases are available that may help map the effects of doping use in unorganised sports and gain further insight into various aspects of doping use. A separate study could be initiated via ZonMw.

The Committee sees a number of possibilities for supplementing/improving current doping policies. The Committee has four general recommendations: 1) approaching doubters and users differently; 2) addressing the foundations of permissive ideas (attitudes) towards doping use, namely: that the risks are acceptable in relation to the goals pursued; 3) differentiating more specifically between various target groups; 4) combining interventions focused on demand reduction, harm reduction and supply reduction.

These general recommendations may be translated into a number of concrete points for improvement in the areas of awareness raising and facilities. For example, more extensive awareness raising – based on hard, objective evidence should be provided; various parties (gym and fitness centre directors and staff, GPs and sports doctors) should be involved more actively. Furthermore, the Committee feels it is important to investigate whether and with which harm reduction interventions current doping policies should be supplemented. Further research should clarify how and to what degree this approach, desired by doping users, should be implemented. For example, research could be conducted into how the healthcare system could address doping users more specifically. Another possibility would be to investigate to what degree a programme similar to the Drugs Information and Monitoring System (DIMS) – focused on doping – could be developed/set up to counteract the risks associated with doping substance use.

Chapter 1

Introduction

1.1 Request for advice

On 23 April 2008, the Minister of Health, Welfare and Sport asked the Health Council of the Netherlands to 'investigate the harmful effects of doping use on health' and publish an advisory report on the subject (Annex A).

The reason given by the Minister for the request are reports from the former Netherlands Centre for Doping Issues (NeCeDo) and the subsequently founded Doping Authority in the past years that showed doping in sports is likely to be a growing problem in our country. According to the request for advice, research figures indicate that about 50,000 people use doping each year. In addition to organised sports (both professional and amateur), doping use is apparently most prevalent in unorganised sports. The use of anabolic steroids and stimulants by gym and fitness centre attendees is particularly worrying. According to the request for advice, various descriptions of disease cases in medical literature show that athletes run serious health risks in both short and long term when using doping substances. This harm may be caused by: 1) (side) effects of the substance itself, 2) method of use (for example, combined with other medicines), 3) poor quality of the substances.

The goal of the advisory report is to obtain greater insight into the nature and extent of the doping problem, particularly with regard to the chances of severe long-term effects of using doping. Greater insight is considered to be essential

for the assessment of current doping policies and may provide handholds for adjusting preventive measures in this field, such as directed awareness-raising.

1.2 Committee and review

As requested, the President of the Health Council decided to appoint a committee (for Committee membership, see Annex B). This Committee met five times. The advisory report drafted by the Committee was subsequently reviewed by the Standing Committees on Medicine and on Health Ethics and Health Law.

1.3 Terminology and delimitation

This advisory report focuses solely on doping use in unorganised sports. This means doping in organised sports is not addressed. The Committee defines unorganised sports as: “any form of recreational sporting activity not organised by regular sports organisations”. The vast majority of this type of sports activity is practiced in gyms and fitness centres.

This focus on unorganised sports means doping policies that have been implemented for organised sports do not apply. Combating doping use among competitive athletes in the Netherlands is primarily the purview of the sports organisation in question; for unorganised sports, this is primarily a task for the government. Chapter 2 will examine this policy difference in greater detail.

1.4 Structure of the advisory report

Chapter 1 outlines the request for advice, the terminology used and the delimitation of the advisory report. Chapter 2 addresses the historical background of doping in sports, and examines the organisation of doping policy and legislation and regulations in this field. Chapter 3 describes the substances and their intended effects, the risks associated with use and the extent of use. Prevalence and characteristics of doping use in unorganised sports are examined in Chapter 4. Chapter 5 looks at the short-term and long-term effects of doping use on disease burden and care consumption. Current and future doping policy is outlined in Chapter 6, and the advisory report ends with conclusions and recommendations.

Chapter 2

Doping in sports

Sports have an important function in our society. One of the phenomena that is often linked to sports and given a great deal of attention is doping. While doping is usually associated with professional sports, it is generally assumed that amateur athletes and even recreational athletes use doping. There is little reliable data on this subject.

The extensive media attention doping receives is disproportionate to any demonstrated performance-enhancing effects. The assumed large-scale use of such substances is largely based on irrational ideas regarding effectiveness. It has long been assumed that doping use by health individuals may entail significant health risks.[1]

While the focus of this advisory report lies on doping use in unorganised sports, the Committee feels it is important to provide a brief general overview of doping use in sports in this chapter. Indicating the different contexts for organised and unorganised sports provides a framework for doping issues associated with unorganised sports. Paragraph 2.1 provides a historical overview of the use of performance-enhancing substances. Paragraph 2.2 gives definitions of doping in organised and unorganised sports. Finally, the organisational differences between doping policy in organised and unorganised sports are examined (Paragraph 2.3).

2.1 Historical background

The history of performance-enhancing substance use is long. The first recorded mention dates back to 2700 B.C. in ancient China.[2] The ancient Greeks also used a panoply of products to improve athletic performance. In the mid-19th century, scientists started performing experiments in which substances were administered to athletes in order to improve performance. Criticism of such practices was limited. The increasing interest in 'the authenticity of the human being' during the interwar period caused a culture shift. An international consensus slowly developed regarding the reprehensibility of doping activities by medical scientists, doctors and pharmacologists.[3] After the Second World War, use and trade in doping substances became a dubious affair. Trade moved underground, doping use entailed increasing health risks, and the number of users increased.[4]

The first time doping received major social attention was during the 1960 Summer Olympics. Danish cyclist Jensen died of the effects of what would later be called doping substances during the event. In 1962, the Health Council published a report on the use of doping in Dutch sports.[5] The conclusion was that it was not a general public health risk. It did conclude that 'the top cyclists and possibly a number of other top athletes in other sports' used doping. Therefore, the Health Council recommended the introduction and implementation of a ban on doping use by sports organisations. The recommendation also called for illicit trade in doping substances to be combated.

The first doping checks during competitions were performed by the Royal Dutch Cycling Union (KNWU) in 1965. This was in response to a number of incidents that had given the sport of cycling a bad name. The International Olympic Committee (IOC) drafted rules for combating doping in Olympic sports in the same year. During the 1968 Olympic Games, the IOC started performing doping checks. Since then, the IOC has regularly updated its list of doping substances, and routine doping tests are performed during all Olympic Games. As athletes only use some of the doping substances during training periods, in 1988 the IOC decided not only to perform tests during competitions, but also at other times. These tests look for evidence of anabolic substances, diuretics, peptides and glycoprotein hormones and analogues thereof.

The Dutch government initially did not implement any active policies, as doping was not considered to be a significant public health risk. In 1987, the 'Sports medicine supervision and sport healthcare' memorandum was published, which examined the doping issue in great detail. It made several recommendations

regarding doping issues. Among other things, it called for the creation of a national doping institute. The Netherlands Centre for Doping Issues (NeCeDo), established in Rotterdam in 1989, was given a coordinating, awareness-raising and implementing role in the field of doping issues and medicine use in sports.[2] The Netherlands Doping Check Foundation (DoCoNed) was founded in 1999 as a central organisation for doping testing. On 1 July 2006, the NeCeDo and DoCoNed merged into the Netherlands Anti-Doping Authority Foundation, also called the Doping Authority. This merger brought prevention and testing together under one roof.

In 2001, another memorandum was published by the Ministry of Health, Welfare and Sport: 'Sports, exercise and health', which once again addressed prevention and reduction of doping use.

Internationally, the Netherlands committed to combating doping when it ratified the Council of Europe's Anti-Doping Convention in 1995. Additionally, the Netherlands supports the World Anti-Doping Agency (WADA), an organisation created by the IOC and numerous governments to combat doping. The Netherlands is also a member of the International Anti-Doping Arrangement (IADA), in which various countries strive to attain the highest possible quality standards for their own anti-doping programmes. Furthermore, the Netherlands accepted the UNESCO International Convention Against Doping in Sport on 17 November 2006.

2.2 Definitions of doping

The word 'doping' comes from a term referring to a 'thick sauce'. Although doping has become a common term, an exact definition has proved difficult. The Health Council used the following definition in 1962: 'Doping is the use of certain medicines with the intention of achieving better performance than the user considers possible without use of these substances, and use by a person who does not normally use these medicines or use them in the same concentrations.'

The Committee of Ministers of the Council of Europe drafted the following definition in 1967: "Doping is the administration to a health individual or use by said individual – in any way – of substances foreign to the body, or physiological substances administered in abnormal amounts or via abnormal routes, with the sole purpose of artificially and unfairly influencing this individual's performance when participating in a competition".

An old IOC definition of doping is: “Doping is understood to mean the use of active substances and/or application of methods designed to improve the suitability for performance and competition results. Doping is harmful to health, falsifies athletic performance and competition, undermines the standing and purpose of sports and is an offence against the principles of fair play”.

In 1994, the IOC published an updated definition based on its experiences. In the opinion of the IOC, doping is in contravention of both sports and medical ethics. The definition of doping by the IOC's Medical Committee currently consists of two points: 1. The administration of substances belonging to banned groups of medicines and/or 2. the use of various prohibited methods. This new definition is very pragmatic. All previous definitions were unclear or provided athletes with loopholes. The new definition basically amounts to maintaining a list of prohibited substances and methods. Use of these substances or methods is an offence.

The request for advice indicates that in the context of unorganised sports, doping is described as 'unintended use of authorised or unauthorised medicines to obtain a muscular or slim physique’, and encompasses the use of anabolic steroids, growth hormone, epo, insulin, thyroid hormone, amphetamines and various other substances. The request for advice also indicates that athletes seek out veterinary medicines such as clenbuterol.

The use of anabolic steroids and stimulants by gym and fitness centre visitors is particularly worrying; according to the request for advice, the description of disease cases in medical literature shows that athletes run serious health risks when using doping substances, in both the short and longer term. This harm may be caused by: (side) effects of the substance itself, the method of use (for example, combined with other medicines), or poor quality of the substances.

2.3 Organisation of doping policy

When describing the organisation of doping policy in sports, it is important to differentiate between organised and unorganised sports. In the Netherlands, combating doping use in organised sports (within the context of competition) is primarily a task for the sports organisation in question. Combating the risks of doping use in unorganised sports is primarily a task for the government.

2.3.1 Organised sports

Doping use is combated aggressively in Dutch (professional) sports. Unfair competition and health risks are the underlying reasons for this approach. Sports organisations in the Netherlands have a large degree of autonomy, as defined by the right of association: they are free to draft and uphold their own rules. As the responsibility for combating doping use lies primarily with the sports organisations in question, they must perform doping tests when necessary and punish offenders based on their own regulations. The government supports sports organisations in this task, in part due to its responsibilities to promote public health and other social values, as well as based on various obligations relating to international treaties (see Paragraph 2.3.3) the Netherlands is signatory to. If a sports organisation fails to implement adequate anti-doping policies, the government may cut its subsidies. Sports organisations that do not organise competitions are exempt.[2,6]

National sports organisations are members of the corresponding international sports federation or umbrella organisation, and are expected to keep their anti-doping regulations in line with those of the international sports federation. For the majority of these federations, doping regulations issued by governments and the World Anti-Doping Agency (WADA) define policy.[2] The WADA, jointly founded by the IOC, strives for global harmonisation of anti-doping regulations and procedures. A key instrument is the – WADA drafted – World Anti-Doping Code, which was formally introduced for governments, sports organisations and national anti-doping organisations in March 2003. The Code is the fundamental, universal document all global anti-doping activities are based on. Among other things, the Code addresses the definition of doping, sanctions, the doping list, checks, awareness-raising, research and laboratory testing. All athletes and sports organisations are obliged to adhere to the Code; however, the Code is not mandatory for many governments (unlike the previously discussed Anti-Doping Conventions of the Council of Europe and UNESCO).

In November 2007, WADA drafted a new World Anti-Doping Code. As part of the required harmonisation with this code, the Doping Authority developed the National Doping Regulations (NDR): a Sports Organisation regulation that must be defined for all organisations with one or more accredited professional sports disciplines before 1 January 2009 [www.dopingautoriteit.nl].

Since 1 January 2004, the doping list is defined annually by the World Anti-Doping Agency instead of the IOC. A substance may be added to the doping list if two of the following three criteria are met:

1 The substance improves performance
2 The substance is harmful to health
3 The substance goes against the 'Spirit of Sport'.

The 'Spirit of Sport' refers to the values and standards of sports, such as fair play and respect for the rules of the sport and for each other.

A new doping list is published by WADA every year in January, which applies to all (inter)national sports organisations that acknowledge the World Anti-Doping Code [www.dopingautoriteit.nl].

2.3.2 *Unorganised sports*

Where doping in organised (professional) sports is primarily focused on improving athletic performance, use of doping in unorganised sports has the goal of, in addition to improving performance, obtaining a muscular and slim physique. Fitness is the most common sport performed in this context.[7] The vast majority of this type of sports activity is practised in gyms and fitness centres. As the desire for a muscular/slim physique or improved performance is not a sufficient medical indication for obtaining these substances via official channels (GP, pharmacy), they are obtained through other means (contacts/dealers at gyms, friends, internet and sometimes doctors who do issue the substances for doping purposes). In such cases, use generally occurs without medical supervision or adequate provision of information, with all of the associated health risks for users this entails. Additionally, a lot of fakes are available on the market.[4,8,9]

In contrast with organised sports, the primary task of reducing doping use in unorganised sports lies with the government. It has the constitutional task of taking measures to promote public health. Instruments the government may use to this end include awareness-raising and legislation and regulations.

With a subsidy from the Dutch government, the Netherlands Anti-Doping Authority Foundation (hereafter referred to as the Doping Authority) focuses, among other things, on providing information and advice to athletes (particularly fitness enthusiasts) and their direct environment. The prevention programme 'Eigen Kracht' (True Strength) developed by the Doping Authority in 2004 focuses specifically on athletes in fitness centres and gyms. Fitness entrepreneurs, gym owners and instructors are a key intermediate target group. The over-

all goal of the programme is: to prevent or reduce the use of doping by athletes in fitness centres and gyms. Key programme elements are:

- Information published on the website – www.eigenkracht.nl
- The book 'Op eigen kracht', which indicates how to obtain (and maintain) a slim, taut, muscular body in a responsible fashion
- The Doping Info number that people can call every weekday with questions about substance use
- A monthly publication in Sport & Fitness magazine, in order to provide bodybuilders with objective, reliable information
- Giving guest lectures on doping for training courses in the fitness field (CIOS, ROC, Fit!vak and private courses such as Fysio Physics)
- Providing content-rich contributions to trade shows (including Fitnessvakdagen, EFAA convention) and further and additional education (including training for GPs, sports physiotherapists, sport masseurs, sport dieticians, drugs detectives from the Royal Netherlands Military Police).

The sector itself is also involved in combating doping: the sector organisation of the recognised gyms Fit!vak requires all Fit!vak member centres to be certified by the National Fitness Centre Certification Regulation (LERF). Among other things, this regulation sets requirements in the area of doping. Fit!vak members sign an anti-doping covenant.[6] In doing so, the centre declares it will implement policy within the centre that combats the use of doping substances, on penalty of loss of LERF accreditation [www.keurmerkfitness.nl].

In their 1998 publication on doping trade, Koert and Van Kleij indicate that – over time – a split has developed between so-called hardcore schools where bodybuilders are a significant proportion of attendees, and fitness and movement centres, where every effort is made to avoid any association with bodybuilding (and extreme doping use that it is often associated with). According to the authors, sector organisation Fit!vak may be seen as a representative of the latter group.[3]

2.3.3 *Legislation and regulations*

Council of Europe Anti-Doping Convention

The Council of Europe Anti-Doping Convention, ratified by the Dutch government, engenders certain treaty obligations.[2,6] The explanatory report for the convention emphasises that the primary responsibility regarding doping lies with the corresponding sports organisations. Signatory states are obligated to take legisla-

tive, regulatory or administrative measures where necessary in order to reduce the availability (including trade, possession, import, distribution and sales) as well as use of prohibited doping substances – particularly anabolic steroids - or methods in sports. The signatory states are obliged, among other things, to support the sports organisations in combating doping. If the organisations are insufficiently active in this role, the signatory states are obligated to impose sanctions (Article 4). Additionally, the convention entails a number of obligations in the fields of awareness-raising and education. Such programmes and campaigns must focus both on youths in schools, sports clubs and parents as well as on adult athletes, officials, coaches and trainers. Educational programmes aimed at doctors will have to emphasise respect for medical ethics (Article 6 Paragraph 1).

The Netherlands meets these obligations through the Doping Authority. Using a subsidy from the Dutch government, the Authority focuses on: planning and implementing doping checks; raising awareness among professional athletes and their direct environment; raising awareness among other athletes (particularly fitness enthusiasts) and their direct environment; providing information and giving advice; developing and monitoring anti-doping regulations; collection and performance or initiation of scientific research; realising international coordination.

The Anti-Doping Convention also requires the Netherlands, where necessary, to take specific measures to combat the illegal production of and trade in doping substances.

UNESCO Anti-Doping Convention

On 1 February 2007, the UNESCO International Convention Against Doping in Sport came into effect in the Netherlands.[10] The convention is a formalisation of government obligations flowing from agreements made within the context of the WADA. The global scope of this treaty (there are currently 128 treaty states) and explicit recognition of the WADA mission are new items compared with the Council of Europe Anti-Doping Convention (currently ratified by 50 countries). By meeting the requirements flowing from the Council of Europe Anti-Doping Convention, Dutch anti-doping policy already meets practically all treaty requirements.[11]

The UNESCO treaty does not encompass mandatory implementation or harmonisation of legislation, but gives treaty partners the freedom to choose the instruments used to meet treaty requirements. This allows the Dutch government to meet its requirements through self-regulating policies. In addition to repres-

sion through doping checks and sanctions, the treaty also emphasises prevention through information and education.[12]

National legislation and regulations

In contrast with a number of countries where legislation exists that criminalises doping, the Netherlands has no specific national legislation regarding doping.[13] In order to meet the treaty requirements to implement specific measures to combat the illegal production and trade in doping substances, the Netherlands has the Medicines Act and the Opium Act. Substance use itself is not illegal in the Netherlands, even if the substances are illegal or may cause harm to an individual's health. Only if third parties are endangered, for example in traffic, is the use of certain substances prohibited.[2]

Medicines Act

The Medicines Act (MA) applies if a product meets the definition for a medicine as defined in Article 1, paragraph 1, under b of the MA. A medicine is defined as: “A substance or composite of substances designed to be administered or used for, or presented as being suitable in any way for: 1) healing or preventing a disease, deficiency, wound or pain in humans, 2) making a medical diagnosis in humans, 3) restoring, improving or otherwise modifying physiological functions in humans by achieving a pharmacological, immunological or metabolic effect.”

Medicines may be categorised as follows (Article 1, paragraph 1, under s, s1, t, u MA):

- Medicines solely available on prescription (PM medicines)
- Medicines available without prescription, but only via a pharmacy (PO medicines)
- Medicines available without prescription, but only via a pharmacy or drugstore (PDO medicines)
- Medicines that are freely available over the counter (OTC medicines).

One reason to make certain medicines only available on prescription is if normal use may entail direct or indirect danger if used without medical supervision (Article 57, paragraph 1, under a, MA) or if the medicines in question are designed for parenteral use, in other words must be administered by injection (Article 57, paragraph 1, under d, MA).

The doping substances described within the framework of this advisory report (see Chapter 3) are largely PO medicines and can only be obtain on pre-

scription. The doping substance amphetamine described under 3.2.6 is also one of the medicines covered on list I of the Opium Act. This medicine is therefore not only covered by the MA act, but also – and in specific cases primarily – by the Opium Act.[14]

The actions listed in the MA that may be performed with medicines (including preparation, supply and issuing – giving a medicine to a patient) may only be undertaken by specific parties with appropriate licences or authorisations. It is prohibited to market a medicinal product without marketing authorisation (Article 40 MA), to perform actions with medicinal products without manufacturing or wholesale licences (Article 18 MA) and to issue PM/PO medicines without authorisation (Article 61 MA).[14]

With the objective of combating trade in doping substances, since May 2001 the unauthorised manufacture and delivery of medicines, as well as the preparation, sale, delivery, import, trading or keeping in stock for the purposes of delivery of unregistered medicines has been classified as an economic crime, punishable under the Economic Crimes Act (WED); combating the illegal manufacture and trade of doping substances has been made easier thanks to this.[6,8,13]

Opium Act

The Opium Act prohibits possession, trade, sale and production (the Act mentions bringing into or taking out of the Netherlands borders, growing, preparing, processing, selling, delivering, issuing, transporting, having present) substances present on the lists belonging to the Opium Act (Articles 2 and 3, Opium Act). List I encompasses hard drugs – substances for which use entails unacceptable risks – and list II covers soft drugs. The maximum penalty for prohibited actions with substances on List I is generally higher than the maximum penalty for prohibited actions with substances on List II.

It is prohibited to prescribe a substance listed on list I or II, unless the substance is – in the interests of public health – explicitly permitted by a general administrative measure (Article 4, paragraph 1, Opium Act). The prohibition regarding preparation, processing, sales, delivery, issues, transporting or having present a substance on List I or II does not apply to (among others) pharmacists and GPs with pharmacies, if said actions are performed within the framework of normal performance of tasks (Article 5, paragraph 1, under a, Opium Act); the prohibition regarding issuing, transporting or having present a substance on List I or II does not apply to individuals performing actions within the framework of the performance of (among other things) medicine (Article 5, paragraph 2, Opium Act).

The Attorney General has drafted guidelines for investigation and prosecution of Opium Act crimes: large-scale trade and production of hard drugs is the highest priority. The sale of smaller quantities of soft drugs in coffee shops is technically illegal, but in practice is only prosecuted if coffee shops do not adhere to the AHAY-L criteria: no Advertising, no Hard drugs sales, causes no Annoyance, no access to coffee shops for Youths (under the age of 18) and no sale of Large amounts (more than 5 grams) per transaction.[15]

Criminal Code

The Criminal Code may play a role in the potential harmful effects of doping substance use. Crimes that may apply include: abuse, (severe) physical harm or involuntary manslaughter; concealing danger when transacting harmful substances, and misrepresentation.[2]

Chapter 3

Doping substances

3.1 Introduction

There are many substances that are used as doping. In this chapter, they are classified by the goal they are used for.

A global categorisation is:
- Performance-enhancing substances
- Substances that counteract side effects of other doping substances
- Substances for obtaining a slim and/or muscular physique
- Other substances.

The discussion of each group begins with an overview table listing the substance in question, the desired effect, the risks and, if known, the extent of use. A substance may be used for multiple purposes.

Annex D contains a more extensive description of each substance (pharmacological properties and epidemiological data).

3.2 Performance-enhancing substances

Table 1 lists the key substances used with the objective of improving performance.

Table 1 Performance-enhancing substances:

Substance	Desired effect	Risks	Extent of use
Anabolic androgenic steroids (AAS)	Increasing strength and muscle mass[16]	Various, including: breast growth in men[16] acne[17,18] cardiovascular diseases[19,20] liver damage[21-24] psychiatric conditions[25-27] muscle damage[16]	0.5 % [28]- 1%[29-32] of the general population
'Prohormones'	The same as AAS, but circumvent the toxic effects of AAS	Changes in fat and female sex hormone levels in the blood[33]	unknown
Growth hormone	Increasing muscle mass	Joint pain[34] Diabetes[35] Thickened heart muscle[36] Creutzfeldt-Jakob disease[37,38]	6.6% of the group 'have used at some point'[28] 4.5% of the group who has used doping in the past year[39]
Insulin-like Growth Factor 1 (IGF-1)	Same as growth hormone	Severe lowering of blood sugar level, potentially leading to brain damage and coma[40]	unknown
Insulin	Combined with growth hormone, increases protein storage with the goal of building muscle mass	Severe lowering of blood sugar level, potentially leading to brain damage and coma[41,42]	unknown
Amphetamines, ephedra and amphetamine derivatives	Combating fatigue Increasing strength explosion	Tremors, sleeping disorders, palpitations, hypotension, psychosis or psychotic symptoms[43,44] Addiction[45]	41.8% of the group 'have used at some point'[28] 2.4% of the recent use group[46,47]
Erythropoietin (EPO)	Increases red blood cell creation, leading to increased stamina	Flu-like symptoms [48] Cardiac arrest[1] Thrombosis[49]	3.8% of the group 'have used at some point'[28]
Yohimbe	Muscle strengthening	Interactions with medicines and foods In case of overdose: among other things: arrhythmias, restlessness, arousal[50]	unknown
Gamma Hydroxybutyric Acid (GHB) and similar substances	Promoting muscle growth	Decreased breathing in case of overdose somnolence [51]	0.5% of the group 'have used at some point' and 0,1% of the used in the past year group[52-54]

3.2.1 *Anabolic androgenic steroids*

Properties

Anabolic androgenic steroids (AAS) can be divided into artificial anabolic steroids such as danazol, nandrolon and stanozolol, and natural steroids that occur in the body, such as testosterone and dihydrotestosterone. In the Netherlands, danazol, nandrolon (deca-durabolin) and testosterone are registered as medicines.[48] Androgens lead to the development and maintenance of secondary gender characteristics and sexual functions in men. They also have anabolic (protein-sparing) functions.

The use of anabolic androgenic steroids as doping

This form of doping was widely implemented by the former East-German government, which led to the dominance of East-German women in sports.[55,56] Of the many publications on anabolic steroids, only a limited number are of sufficient scientific quality, meaning a double-blind, placebo-controlled method was used. An additional methodological problem is that many users of anabolic steroids use a variety of drugs in often varying (far too high) doses.[57] There are major differences between dosages used in practice and dosages studied in scientific research. In practice, the dosages are far higher.[58] Furthermore, some of the substances are sourced on the black market, so no statements can be made regarding their quality. Research has shown that 50-60% of the products do not deliver what is promised on the package.[8]

Hartgens and Kuipers found that use of anabolic steroids increased strength by 5-20% compared to baseline. Weight increases by 2-5 kg thanks to an increase in lean body mass.[16] There appears to be no decrease in fat mass.

Side effects

Short-term use of anabolic steroids can already have negative effects. In general, it may be stated that negative effects are more pronounced in cases of extended use and at higher doses.

There are clear gender differences: when used by women, the consequences are lasting and generally severe.

In men, the following side effects of anabolic steroid use have been reported: breast growth, libido increase, long lasting erections, inhibition of sperm formation, acne, liver damage, unfavourable fat distribution in the blood, water and salt retention, and increase in prostate size.

While both men and women are likely to use the same substances, the effects of administration are different in part. The natural levels of androgens in women are only a fraction of those found in men. Women therefore experience the anabolic effects of androgen administration at lower doses compared with men. Side effects that are only seen in women are lowered voice, excessive hair growth, male pattern hair loss, clitoral enlargement, menstrual cycle disruption and involution of breast tissue. The side effects mentioned are largely reversible and, compared with men, occur at relatively low doses.

Extent of use

Extensive literature is available on the use of anabolic steroids in sports.

It is estimated that 1 to 3 million inhabitants of the United States have used steroids. An estimated 50,000-100,000 of the 9 million inhabitants of Sweden are thought to have used steroids, amounting to about 1% of the population.[31] Other studies in a variety of European countries[32] show steroid use by 1-5% of the population. These figures do not, however, reveal the true risks of long-term use.

A study among 6,000 16- and 17-year-old Swedes using anonymous multiple-choice questionnaires showed that 3.2% of young men had used steroids, but none of the questioned young women had.[16,29,30]

German figures report alarming use among fitness centre attendees, particularly among young people aged 18-26 years.[18]

Another study in Brazil, conducted in 13 gyms among 288 weight lifters, showed a prevalence of 11.1% for current and past use of steroids, and 5.2% for use of other hormones. The most commonly used steroids were nandrolon and stanozolol. The other hormones were gonadotrophin and triiodothyronine. Additionally, other medication use was charted. This revealed a prevalence of 4.2%, and concerned substances including lipostabil, diuretics and veterinary medicines.[59]

Research into doping use among the Dutch population between the ages of 15 and 64 (n=20282) revealed that 1.0% had used doping in the past year. 2.1% indicate they have used doping at some point. In 22.2% of the cases in this ‘used at some point’ group, the substance in question was anabolic steroids.[28]

3.2.2 *Precursors of anabolic steroids, so-called 'prohormones'*

Properties

In order to avoid the side effects of anabolic steroids while profiting from the advantages, substances that play a role in the formation of anabolic steroids have been marketed; in past years, there have been aggressive advertising campaigns promoting these products.

Prohormones (also called precursor or andro prohormones) are substances that are turned into testosterone by the body's metabolism. Examples are androstenedione and dehydroepiandrosterone (DHEA).

The use of anabolic androgenic steroids as doping

Manufacturers claim these substances increase the serum concentration, leading to an increase in muscle strength and volume, a decrease in body fat and improvement in mood and libido. However, most studies dispute these claims.[60,61]

Side effects

Various studies with oral Andro show that oestrogen-related hormone levels are abnormally high. Most studies also show a significant drop in high-density lipoproteins, which may be linked to an elevated risk of cardiovascular diseases. In summary, this means the industry's claims remain unsubstantiated, and that the potential long-term effects, particularly due to the influence on blood fat metabolism and oestrogen levels are cause for concern.[33]

In the United States, an appeal from the FDA in 2004 led to the Anabolic Steroid Control Act being passed. This act covers androstenedione and 17 other steroids which – as is the case in the Netherlands – may not be sold without a doctor's prescription. It is worth noting that this development led to the marketing of so-called designer nutritional supplements, containing new 'fantasy steroids', where the question is to what degree the substances are still anabolic steroids.[62]

Extent of use

No precise figures are available on the use of prohormones. What is clear is that many so-called nutritional supplements are used to address assumed vitamin and mineral deficiencies. It is known that these supplements may be polluted by, among other things, prohormones.[63]

3.2.3 *Growth hormone*

Properties

There are a number of registered medicines available containing growth hormone (somatropin) made using recombinant DNA techniques. Somatropin is a protein created using recombinant DNA technology, which is analogous to human pituitary growth hormone. It stimulates longitudinal growth in children with growth hormone deficiency. Somatropin also stimulates tissue growth by increasing the number and size of skeletal muscle cells. The Committee has noted that human growth hormone has also been marketed.

The use of growth hormone as doping

The goal growth hormone (GH) is primarily used for in sports is its effect on muscle mass. GH lets the muscles grow indirectly, not directly, by increasing the capacity for protein formation: this mechanism increases the amounts of insulin and anabolic steroids a person can use effectively. Many dosage schedules are used. Muscles may increase in mass under the influence of GH, but this does not automatically equate to an increase in muscle strength.[34,64] Available research data do indicate an increase in lean body mass, although this is also associated with a decrease in stamina and an increase in side effects. In order to show any effect at all, large amounts of anabolic steroids – and often insulin – need to be used alongside the growth hormone.

Side effects

Use of human growth hormone is associated with a risk of developing Creutzfeldt-Jacob disease (prion disease).[38,65] A comparative study found higher rates of joint pain and carpal tunnel syndrome (nerve impingement) among growth hormone users.[34] Additionally, soft tissue swelling, breast growth, insulin resistance with an increased risk of diabetes mellitus[35] and extreme growth of hands,

feet, nose and jaw (acromegaly) have been described. In a double-blind, placebo-controlled study with supra-physiological amounts of growth hormone, Cittadini found an increase in the relative thickness of the left ventricle of the heart[36] in the growth hormone group.

Extent of use

Growth hormone is used as an anti-aging substance by body builders. The majority of trade with this objective takes place on the black market. This has led to a large number of illegally important combined preparations on the market. Industry sources suggest that in the United States alone, trade with this purpose yields a turnover of 2 billion dollars per year.[35] In the Netherlands, 6.6% of the 'have used at some point' group indicated they had used growth hormone.[28] Danish research among 702 general practices showed that 182 patients had used doping in the past year, nine of whom had used growth hormone.[39] The high costs limit the use of growth hormone, and anabolic steroids are also more attractive to users.[66]

3.2.4 Insulin-like Growth Factor I

Properties

Insulin-like Growth Factor I (IGF-I) is often used alongside growth hormone and insulin. IGF-I plays a role in growth hormone effects.

The use of Insulin-like Growth Factor I (IGF-I) as doping

The increase in IGF-I stimulates conversion of glycogen into glucose and of fats into fatty acids. IGF is more effective than GH in directly stimulating muscle growth and increase in muscle density. IGF can also be used on its own. Unlike GH, it is not necessary also to use large amounts of anabolic steroids as well as insulin to achieve results.

Side effects

The use of IGF-I can lead to severe hypoglycaemia (low blood sugar).[40]

Extent of use

No precise figures are available on the use of IGF-I.

3.2.5 *Insulin*

Properties

Insulin has an effect on carbohydrate, fat and protein metabolism. The effect on carbohydrate metabolism is based on promoting uptake of glucose in liver, muscle and fat tissues. Additionally, insulin inhibits the production of glucose in the liver and promotes glycogen creation from glucose. The effect on fat metabolism consists of stimulating fat formation. It also inhibits fat breakdown and release of free fatty acids from fat tissue. Finally, insulin promotes protein formation.

The use of insulin as doping

By combining growth hormone and insulin, users hope to stimulate the production and uptake of proteins.

Side effects

Insulin lowers blood sugar levels. A major drop can lead to hypoglycaemic coma.[41,42] Common injection sites may develop atrophy or hypertrophy of subcutaneous fat, often due to incorrect injection techniques.

Extent of use

No precise figures are available on the use of insulin as doping.

3.2.6 *Amphetamines, ephedra and amphetamine derivatives (ecstasy)*

Properties

Amphetamines are medicines registered for the treatment of ADHD and depression. They are also used as appetite inhibitors in the treatment of weight problems. The main desired effects of amphetamines are arousal

and inhibition of fatigue. The latter effect in particular led to wide use in sports. The street names of the illegal variants are Crystal Meth or Speed.

Use of amphetamines as doping

Amphetamines have a performance-enhancing effect during short, explosive bursts of activity. For high-intensity endurance effects such as cycling, they have a performance decreasing effect.[67] For explosive activities such as shot-put and brief exertion like a 100-400 meter sprint, use appears to increase performance by 1-2%.

Side effects

Use is associated with a variety of psychological and physical effects. Euphoria, hyperalertness, emotional hypersensitivity with stress and anger may occur. There are also influences on heart rate, and pupil dilation and blood pressure changes occur.[45] In rare cases, liver disorders and epileptic seizures may occur. Amphetamine dependence may occur quickly, and is apparent in the inability to sustain normal social and professional activities. In order to experience the same feeling, increasing amounts of the substance must be used. Physically, this may lead to severe weight loss, psychologically to paranoid delusions.

Extent of use

A great deal of data is available on amphetamine use in general, but little specific information is present on the extent of use in unorganised sports. In the Dutch ‘have used at some point’ group, 41.8% indicated they had used stimulants.[28] In another study, the figure was 2.4% for the ‘recent use’ group.[46,47]

3.2.7 Erythropoietin

Properties

Erythropoietin (EPO) is a glycoprotein hormone produced in the kidney that, among other things, stimulates the production of red blood cells in the bone marrow. Currently, EPO or (long-acting) pegylated erythropoietin variants produced using recombinant DNA techniques are available.

Haematopoietic growth factors (blood growth factors) can specifically stimulate the production and functional activity of certain types of blood cells. In this way, they play a key role in the regulatory process of blood cell formation. The physiology of these factors has been known for some time; however, therapeutic application only became a possibility when recombinant DNA techniques allowed production on an industrial scale. Currently, the following erythropoiesis-stimulating substances may be identified: Arbepoietin, epoietin-α, epoietin-β, epoietin-∂ (Dynepo) and Cera. Erythropoiesis-stimulating substances stimulate erythrocyte production. These substances are produced using recombinant DNA techniques, and immunologically and biologically identical or closely related to human erythropoietin (EPO), a glycoprotein primarily created in the kidney that regulates erythrocyte production in the bone marrow.

Erythropoiesis-stimulating substances are used to treat a variety of forms of anaemia.

The use of Erythropoietin (EPO) as doping

It has been shown that the use of EPO causes changes in performance comparable to blood doping. Maximum power and the ability to sustain a specific exertion improve significantly within 6 weeks of EPO administration. There may also be a direct effect on muscles.[68]

Side effects

The primary side effect of erythropoietic is flu-like symptoms. Blood pressure elevation is sometimes noted. There is also a significant risk of thrombosis.[49] During sports, particularly in warm weather, this may also lead to an increase in blood cell content (hematocrit), which leads to increased blood viscosity, which ultimately may lead to circulatory problems or even circulatory arrest.[1]

Extent of use

EPO use gained widespread attention due to its use by professional cyclists and top athletes.[69] The death of almost 20 European cyclists in the late 1980's and early 1990's is suspected to be related to EPO use. In 1998, a Tour de France team was removed from the competition due to EPO use, and six other teams left the competition.[70]

A Danish study among 702 general practices revealed 182 patients had used doping in the past year.[39] In this group, anabolic steroid use was common, but none of the interviewees had used EPO. In a group of Dutch people who had admitted to using doping at some point, 3.8% indicated they had used EPO.[28] That EPO is also used in unorganised sports may be deduced from the content of a variety of websites.[71,72]

3.2.8 *Yohimbe*

Properties

Yohimbe is the name for the dried bark of *Pausinystalia Yohimbe* or *Corynanthe Yohimbe*, a tree native to the tropical forests of West Africa. Double-blind studies have shown that yohimbe works as an aphrodisiac and a potency-increasing substance.[73]

The use of Yohimbe as doping

The promotional text on a pot of Yohimbe makes the following claim: 'Yohimbe is known in the athletic world for its positive effect on strengthening muscles. This dietary supplement provides its positive contribution to muscles, joints and the stomach. This formula is particularly recommended for bodybuilding, high level athletics, weight lifting and fitness.' Research does not support this claim.[74]

Side effects

Interactions are possible with certain medicines (SSRIs like Prozac, seroxat, etc. and MAO inhibitors) as well as with certain foodstuffs.[75] Particular care regarding eating food with high tyramine content is required when used together with MAO inhibitors.[50] These include fermented proteins, meat and yeast extracts, soy products and sour dairy products, certain types of cheeses (including Camembert, Cheddar and Stilton), certain alcoholic beverages (including red wine and heavy beers), chocolates, meat and fish products that are not fresh, avocados, overripe bananas and fava beans.

Extent of use

No specific data is available on the use of Yohimbe in unorganised sports.

3.2.9 Gamma Hydroxybutyric Acid (GHB) and similar substances

Properties

Gamma Hydroxybutyric Acid (GHB) occurs naturally in the body. It is a building block of the neurotransmitter Gamma Amino Buteric Acid (GABA). GHB is converted to water and carbon dioxide by the body's metabolism.

The use of Gamma Hydroxybutyric Acid as doping

In the late 80s, GHB gained notoriety as a substance that could stimulate growth hormone production, promote muscle growth and lead to fat tissue breakdown. This led to use among bodybuilders in particular. In the United States, GHB was sold in health stores until the FDA banned it in 1990.[76]

Side effects

GHB became popular as a recreational drug, as the substance may cause euphoria and supposedly worked as an aphrodisiac. At higher doses, GHB is used as a sleeping medicine. After an incident in which six people became comatose after using GHB together with alcohol, the substance has been banned in the Netherlands since 1996 unless prescribed as a medication.

In the media, GHB has been associated with sexual abuse, and is known as the date rape drug.

Extent of use

The use of 'smartdrug' GHB appears to be increasing steadily among gym visitors. It is used as an alternative to anabolic steroids and to supplement a course of steroids. In both cases, the assumption is that GHB helps build muscle by stimulating growth hormone release. Australian research shows an incidence of 0.5% for use at some point and 0.1% for use in the past year.[52-54]

3.3 Substances that counteract side effects of other doping substances

Table 2 lists the key substances that counteract the side effects of other doping substances.

Table 2 Substances that counteract side effects of other doping substances

Substance	Desired effect	Risks	Extent of use
Selective Estrogen Receptor Modulators (SERMs)	Countering AAS side effects, stimulating male gender hormone formation	Hot flushes, nausea, vomiting. Severe side effects in exceptional cases[48]	One third of AAS users[77] 14-18% of a group of bodybuilders[57]
Aromatase inhibitors	Countering AAS side effects	Hot flushes, nausea, diarrhoea[48]	unknown
Gonadotropic hormones	Stimulate the formation of male gender hormone	Fluid and salt retention breast growth in men[78,79]	unknown
Isotretinoin (Roaccutane)	Countering acne formation	Various, including liver and kidney problems, disrupted fat metabolism in the blood, harm to unborn children, loss of vision[80]	unknown

3.3.1 *Selective Estrogen Receptor Modulators (SERMs)*

Properties

Clomifene is a non-hormonal ovulation induction substance. Tamoxifen primarily has anti-oestrogen effects due to blocking of oestrogen receptors in hormone-sensitive conditions such as breast cancer.

The use of SERMs as doping

Various substances are used to combat the effects of female hormones caused by AAS (Anabolic Androgenic Steroid) use, including SERMs. The degree to which bodybuilders suffer from oestrogen overdose is insufficiently clear; the type of AAS used – aromatizable versus non-aromatizable – plays a part.

Side effects

Of Clomifene: gastrointestinal complaints such as tenderness, bloated feeling and ‘hot flushes’. The most common for Tamoxifen: hot flushes, nausea and vomiting.

Extent of use

Two British studies performed 10 years ago showed that Tamoxifen is the most commonly used SERM. User percentage was 5% in one study and 23% in the other. The Dutch study by de Boer among Dutch professional bodybuilders

showed that Tamoxifen and Clomifene were particularly popular.[57] 18% of men used Tamoxifen regularly, and 14% used Clomifene. A more recent study by TNO (2003) showed that one-third of anabolic steroid users use substances to counter the side effects. Which substances are used is unknown, however, as this information was not collected.

3.3.2 *Aromatase inhibitors*

Properties

Aromatase inhibitors prevent the conversion of androstenedione and testosterone into estron and estradiol in peripheral tissues; this conversion normally takes place under the influence of enzyme aromatase.

The use of aromotase inhibitors as doping

Aromatase inhibitors slow the production of oestrogens, as compared to a substance like Tamoxifen which blocks the effect of oestrogen. The effects are largely analogous to those of SERMs: preventing breast growth and build-up of subcutaneous fat, stimulation of natural testosterone production.

Side effects

The key side effect of selective aromatase inhibitors are symptoms of oestrogen deprivation such as hot flushes, headaches, nausea and diarrhoea.

Extent of use

No precise figures are available on the use of aromatase inhibitors as doping. The doses recommended to bodybuilders in underground books are equivalent to those used clinically in women.

3.3.3 *Gonadotropic hormones*

Properties

Two gonadotropic hormones are formed in the anterior pituitary gland: follicle stimulating hormone (FSH) and lutenising hormone (LH). The effects are different for men and women. In men, FSH stimulates the development of seminal

tubules (channels in the testicles that produce sperm) and the formation of spermatozoa, while LH stimulates leydig cells to form testosterone. In women, the gonadotrophins have no effect on testosterone production and therefore do not work as doping.

The use of Gonadotropic hormones as doping

As testosterone production drops dramatically after a course of anabolic steroids, human choriogonadotrophin (HCG) is used as doping to stimulate testosterone production. As this does not restore the natural cycle, it merely delays natural production.

Side effects

In men, high doses may lead to water and salt retention due to excessive androgen production. Cases of breast growth have been described.

Extent of use

No precise figures are available on the use of Gonadotropic hormones as doping.

3.3.4 Isotretinoin (Roaccutane)

Properties

In normal medicine, Isotretinoin is reserved for the treatment of severe, therapy-resistant forms of acne. Given the severe side effects and teratogenicity (damage to unborn life), current treatment guidelines recommend that only doctors experienced using the substance and related substances prescribe it.

The use of Isotretinoin as doping

Isotretinoin is used to prevent acne caused by anabolic steroid use.

Side effects

A large variety of side effects may occur. They include liver and kidney disorders, increased fat levels in the blood, harm to the unborn child and loss of vision (see also Annex D).

Extent of use

Bodybuilder websites indicate that using Isotretinoin during a course of anabolic steroids (to prevent acne) is a normal phenomonen.[82]

3.4 Substances for obtaining a slim and/or muscular physique

Table 3 contains an overview of substances used to obtain a slim and/or muscular physique.

3.4.1 Clenbuterol/beta-sympathicomimetics

Properties

In the Netherlands, this substance is solely available for the treatment of horses with (severe) asthma. It causes airway dilation and also has anabolic properties and[83] and fat-burning properties.[84]

The use of Clenbuterol/beta-sympathicomimetics as doping

Bodybuilders and cyclists use Clenbuterol as doping for the anabolic effects. In the bodybuilding circuit, Clenbuterol is not primarily used for the anabolic effects (more suitable substances are available) but due to the effects on fat metabolism, giving the user a 'taut and dry' look. As a fat reduction drug, a three-week course of tablets is recommended, during which the dosage is slowly increased until side effects occur, after which the course is completed at a slightly lower dose.[88]

Table 3 Substances for obtaining a slim and/or muscular physique.

Substance	Desired effect	Risks	Extent of use
Clenbuterol/beta-sympathicomimetics	Weight loss Looking 'taut and dry'	Arrhythmias, heart attack[83,84]	6.1% of the group 'have used at some point'[28]
Thyroid hormone	Weight loss	Mental restlessness Sleeplessness Arrhythmias, Tremor[48,85]	3.3% of the group 'have used at some point'[28]
Lipostabil	"injecting away" fat build-up	Local symptoms including swelling, bruising and pain[86]	unknown
Synthol	Simulating muscle mass	Injection abscesses, inflammation, embolisms, stroke and myocardial infarction[87]	unknown

Side effects

Various publications report heart attacks in young users of Clenbuterol, sometimes in combination with anabolic steroids.[83,84]

Extent of use

6.1% of the group of ‘have use at some point’ doping users in the general Dutch population have used Clenbuterol/beta-sympathicomimetic hormones as doping.[28]

3.4.2 Thyroid hormone

Properties

Thyroid hormones may counter the effects of decreased thyroid function.

The use of Thyroid hormones as doping

Thyroid hormones are used in sports to stimulate metabolism and thereby lose excess fat. The increase in metabolism also affects (valuable) muscle proteins. If the use of the substance is ceased, the opposite will occur, namely slowed metabolism and increased fat storage. After a period of thyroid hormone use as doping, the body’s own production of thyroid hormone may be decreased for a long time or even permanently lowered or stopped entirely.

Side effects

Side effects are seen in the event of overdose, and if substances are used for the wrong indications, such as overweight. Severe mental distress, sleeplessness, tremors, palpitations and arrhythmias may occur. Long-term use of doses that lead to suppression of the thyroid stimulating hormone (TSH) may lead to bone loss.

Extent of use

3.3% of the group of ‘have use at some point’ doping users in the general Dutch population have used thyroid hormones.

3.4.3 *Lipostabil*

Properties

Lipostabil is an injectable substance with the active ingredient soy lecithin.

The use of Lipostabil as doping

Lipostabil is used for the treatment of stubborn local fat build-up. The substance is injected directly into the problem area.

Side effects

In a limited prospective study among 739 people, other than local symptoms such as bruising, no general effects were noted.[86]

Extent of use

The substance is widely used in aesthetic clinics, but the overall extent of use is unknown.[89]

3.4.4 *Synthol*

Properties

The product Synthol is a collection of MCT (Medium Chain Triglycerides – C8, C10 and C12) combined with a disinfectant (Benzylalcohol) and a local anaesthetic (Lidocaine).

The use of Synthol as doping

The substance is advertised as a lubricant, but the common procedure is to inject Synthol deep into the centre of smaller muscle groups – such as biceps, triceps, shoulders and calves – with the goal of imitating muscle mass. Usually a 1 ml injection is used to begin with. This is repeated daily or every other day for ten days. The amount is then increased to 1.5 to 2 ml per injection for another ten days. If the desired result has not been achieved, the amount is further increased

to 3 ml. At this point, injections are usually stopped, with maybe a brief ‘additional injection’ of 1 or 2 ml right before a competition.

Side effects

There are a number of risks for the user: injection abscesses, inflammation, embolisms, stroke and heart attack.[87] A notorious case is that of professional bodybuilder Milos Sarcev, whose life was endangered a few years back when some of the injected fat entered the bloodstream and almost caused a heart attack.

Extent of use

Injecting the fat deep into the muscles is not uncommon in bodybuilding (www.eigenkracht.nl).[90]

Other substances

Table 4 provides an overview of other substances used.

Table 4. Other:

Substance	Desired effect	Risks	Extent of use
Diuretics	Dilution of prohibited substances thanks to increased urine production.	Heart failure[91]	0.1% of a group of German adolescents[47]
	Weight loss prior to a game to allow entry into a lower weight class. Fluid dispersion after anabolic steroid use (which causes fluid retention)	Hypovolemia Hypotension	
Gene doping	Using genetic technology to promote tissue build-up, for example red blood cells or muscle cells, or certain substances that prevent breakdown	Unknown	Theoretical at this time[92]

3.4.5 Diuretics

Properties

Diuretics increase the excretion of salt and water by limiting resorption in the kidneys.

The use of Diuretics as doping

Diuretics are medicines that increase urine production, and are used for various reasons in (professional) sports. The World Anti-Doping Agency (WADA) placed them on the doping list as substances that are prohibited both during and outside of competitions (in other words, at all times). Diuretics belong to the group of masking substances, although they are also seen as separate doping substances. Diuretics cause an increase in urine production. This decreases the odds of finding illicit substances. As fluid is also excreted, body weight is lowered. This allows users to enter a lower weight class and could improve performance (for example in climbing sports, jockeys, ski long jumpers and gymnasts).

Side effects

Aggressive therapy with diuretics may lead to dehydration and a decrease in circulating volume, leading to symptoms of sleepiness, malaise, orthostatic hypotension (sudden blood pressure drop) and muscle cramps. Medical literature has described a case of a 31-year-old body builder using diuretics who developed a heart attack.[91] He experienced chest pain on stage and collapsed. He was subsequently taken to the emergency department, where it was soon noted he had abnormally high potassium concentrations in his blood.[93] He claimed to have been using anabolic steroids and amphetamines for 5-10 years. Before the competition, he had taken a combined diuretic with – among other things – a potassium-sparing effect. He also regularly took potassium and magnesium tablets.

Extent of use

Research among German adolescents found that 0.1% indicated they had used diuretics in the past year. In a specific group of gym visitors, the percentage was 4.2%.[59]

3.4.6 Gene doping

Properties

The goal of gene doping is to use genetic technology to promote tissue build-up, for example red blood cells or muscle cells, or certain substances that prevent breakdown of these tissues or substances.

The use of gene doping

Results from animal experiments (transgenic mice) show effectiveness. However, there are only a few known potential ‘performance-enhancing’ genes for humans. The most promising substances have local effects and leave behind no or almost no traces in blood or urine.[92,94,95]

Side effects

Insufficient data available at this time.

Extent of use

Although doping authorities are worried about the potential, there is currently no evidence of any use in competitive sports.

Chapter 4

Prevalence and characteristics of doping use in unorganised sports

In the Netherlands, about 2 million people engage in unorganised sports[144]; this is a good thing when it comes to achieving the public health goal of getting more people exercising. How many of these individuals use doping is not an easy question to answer. Doping use largely takes place in an illegal circuit, where secrecy is the norm. Doping users are therefore often referred to as a hidden population; estimates of numbers of users are therefore extremely uncertain.[13]

4.1 Past studies into prevalence of doping use

Various studies have been performed into the prevalence of doping use in unorganised sports. In 2003, the NeCeDo funded a study into the practice of using performance-enhancing substances in gyms and the reasons for doping use. 30% of respondents indicated they had used performance-enhancing substances at some point in the past. However, the NeCeDo report has the following to say about this figure: “This is likely a major overestimation of the number of users among all gym visitors in the Netherlands”.[77]

An exploration of the use of performance-enhancing substances in gyms among youths up to the age of 25 conducted in 1994 showed that about 6% of interviewed gym visitors had used performance-enhancing substances at some point. This percentage is based on regional studies in the Netherlands (the study focused on gyms in Rotterdam and the Eemland region), and cannot be considered an accurate representation of the national situation.[97] However, the same

figure is also listed as an estimate for most European countries.[8,9] According to the previously mentioned study by Koert and Van Kleij, who studied trade in doping substances in the Netherlands in 1998, 35,000 gym and fitness centre visitors were more or less regular users of courses of muscle strengthening or other doping substances.[3,9]

In addition to the listed studies, a National Prevalence Study on Substance Use is performed every four years in the Netherlands, looking at, among other things, performance-enhancing substance use in the general population, ages 15-64. The last study was performed in 2005. This showed that 1.5% (about 150,000 people) had used performance-enhancing substances at some point, and that 0.5% indicated they had used it in the past year.[8,98]

Other studies have shown that about 40,000 people in the Netherlands use doping each year; about 100,000 athletes in this study admitted to having used doping at some point.[8,99-101]

4.1.1 Recent prevalence data and characteristics of doping use

Report 'Performance-enhancing substances in fitness enthusiasts' (2009)

In response to a request from the secretary of state for Health, Welfare and Sport, the Doping Authority recently had TNO perform a new study into the prevalence of doping use in unorganised sports.[96] The study was performed among visitors to fitness centres ages 15 and older, based on two questionnaires: the first questionnaire is based on the so-called classic method in order to allow comparisons with previously performed research into doping use in the Netherlands; the second was based on the randomised response method, which allows correction for socially desirable responses. If doping in unorganised sports is a sensitive subject, as it is in professional sports, it is likely respondents will not answer honestly. 92 fitness centres and 718 fitness enthusiasts participated in the study. The study examined doping use in the past year.

Prevalence of doping use among fitness enthusiasts

The classic method revealed a general prevalence of 0.4%, while the randomised response method yielded a prevalence of 8.2%. In terms of absolute figures, the latter percentage indicates 160,000 people have used doping in the past year. The researchers concluded that the classic method leads to underestimation of general prevalence compared with prevalence figures obtained with a randomised response method, with the latter method being deemed more suitable for deter-

mining doping use prevalence in future studies; if social desirability plays a role, the researchers felt the randomised response method yielded a more reliable and valid estimate of actual doping use prevalence than the classic method did.

Other findings

- *Gender*: over half of the membership at the participating fitness centres were women. The majority of respondents were also female (64%). The study does not provide insight into the percentages of male and female users.
- *Age*: average age was 43 years (range: 15-77).
- *Combined use*: in order to gain insight into the health and lifestyle of respondents, the study asked about drug use. More than 8 out of 10 fitness enthusiasts indicated they had never used drugs, 15% had used drugs to try them out, and 4% regularly uses drugs.

4.1.2 *Report 'Secondary NPO analysis 2005 – performance-enhancing substance use in the general population' (2009)*

Upon request of the Committee who asked for the advisory report before you, the Institute for Lifestyle and Addiction Research (Instituut voor onderzoek naar Leefwijzen en Verslaving, IVO) performed a secondary analysis of the data from the 2005 National Prevalence Study (NPO) on substance use regarding doping use in the general population (Ages 15-64 years).[28]

Prevalence of doping use in the general population

The prevalence of doping use among the general population was 2.1% in 2005 for 'use at some point' and 1.0% for 'use in the past year'.* [98] Further analyses were performed on the group 'use at some point' (with the exception of combined use: those figures are for 'use in the past year').

* The National Prevalence Study on Substance Use used two methods: the CAPI (interview) method and the online panel method. The percentages quoted in Paragraph 4.1 (1.5% use at some point and 0.5% used in the past year) are based on the CAPI method. The percentages quoted in this Paragraph (2.1% use at some point and 1.0% used in the past year) deviate from this, since the secondary analysis used the online panel method. The numbers in the CAPI file were too small for extra analyses on type of doping use and subgroups.

Other findings

- *Gender*: more men than women use doping: 3% and 1.2%, respectively.
- *Age*: usage in groups 15-24 years and 25-44 years for 'use at some point' is roughly the same (±3%). This demonstrates once more that – contrary to what is often claimed – doping use is not primarily restricted to young people.
- *Combined use (past year)*: combined use with many (other) substances (cannabis, cocaine, amphetamines, XTC, LSD, heroin and alcohol) is significantly more common among doping users than among the general population (for cocaine, this figure is 10% vs 1.8%, for cannabis 24.5% vs 10.1%, respectively). This may lead to the conclusion that doping users display higher risk behaviour than the general population.
- *Reasons for use*: 'dealing with fatigue better' is the most common reason for using doping. Additionally, an important reason given – other than wanting to look slimmer/more attractive – was 'becoming stronger'/improving performance. Muscle mass may be associated with both an appearance and performance enhancement aspect; in other words, the categories overlap.
- *Urbanisation*: doping use is more common in urban areas than in rural areas. More stimulants are used in urban areas, while anabolic steroids are common in rural areas.
- *Ethnicity*: when various population groups are compared, 4.9% of non-western immigrants have used doping, while this figure is 3.1% for western immigrants and 1.9% for Dutch natives.
- *Place where substances are obtained*: the places where doping users source their doping substances are diverse. Gyms and fitness centres appear to be – in accordance with past findings – the most important places to contact dealers (36.4%). Other listed sources are the doctor (12.7%), friends/family/acquaintances (32.7%), store/drugstore/smartshop (21.8%) and internet (29.1%). The internet appears to play a key role. This contradicts previous research that showed internet plays a (relatively) minor role in the trade/purchase of doping substances at this time, and is primarily a place to obtain information. The study did predict internet sales would increase.[4,8,13] It was noted that the extent can only be estimated based on shipments that have been intercepted. Given the limited possibilities, any statements on this topic would be speculative.[13]

4.2 Types of substances

The doping substances used within unorganised sports are primarily anabolic steroids, growth hormones, precursors of anabolic steroids, slimming substances such as thyroid hormones and ephedra-containing substances. Additionally, substances are used to counteract the side effects of other substances, such as diuretics.[8]

4.2.1 Report 'Performance-enhancing substances in fitness enthusiasts' (2009)[96]

The recent TNO study found the following data on substance use prevalence (as percentages):

Substance	% use by fitness enthusiasts
Anabolic steroids	1.0
Prohormones	0.8
Substances to counter side effects	1.3
Growth hormones and/or insulin	1.1
Stimulants for weight loss	4.8
Additional substances[a]	2.8

[a] Additional substances include: diuretics, thyroid hormones, clenbuterol and other performance-enhancing substances.

4.2.2 Report 'Secondary NPO analysis 2005 – performance-enhancing substance use in the general population' (2009)[28]

The secondary analysis of the 2005 NPO study showed the following data for 'use at some point' in the general population:

Substance	% use in the 'use at some point' group
Anabolic steroids	22.2%
Growth hormones	6.6%
EPO	3.8%
Thyroid hormones	3.3%
Clenbuterol	6.1%
Stimulants	41.8%
Other	2.4%

Men primarily use anabolic steroids (27.4%) and stimulants (33.6%), women primarily use stimulants (63%). Cultural differences have been noted with regard to the types of substances used.

4.2.3 *Is subdivision by risk desirable?*

Given the – objective – harmful effects of the substances, doping substances may be subdivided into 'heavy' and 'less heavy' doping substances.[11] However, given the risks of substance use in daily practice, the Committee does not feel such a subdivision can be justified. This is because substance use is dangerous for the following reasons:

- Use commonly takes place without medical supervision: the substances in question are often strong medicines that cannot be obtained via the official route (GP, pharmacy). The official medical and pharmaceutical guidelines are therefore not followed, exposing users to additional risk.[8] Users often have no idea which risks they are exposing themselves to by taking high doses and dangerous combinations.[13]
- The quality of illegally traded and used doping substances has been found to be poor. Studies have shown that at least 50-60% of products do not deliver what is claimed on the label. The product contains other comparable substances, or too little or too much of the active substances. In 7% of cases, the product contains no active substance at all.[8] There are numerous fakes on the market, which significantly increase the health risks for users compared with non-medical use of original branded items. Even if the user of fake doping substances were aware of the fakes, he still cannot check whether the claims on the packaging or leaflet correspond to the actual substance. This exposes users to unpredictable health risks.[13]

Chapter 5

Consequences of doping use for disease burden and care consumption

As indicated in the description of substances in Chapter 3, doping use may cause a number of side effects. Based on data from the literature on amounts used, it is likely many side effects and complications may occur. The conditions that may occur are many. The most visible in a literal sense are gynaecomastia (male breast growth) and acne. Additionally, a number of invisible organ disorders may occur. These include heart problems (such as arrhythmias) and liver function disorders. Behavioural abnormalities may also be expected. The incidence of these symptoms and conditions in the Netherlands can be traced using a variety of databases.

In order to assess the extent of consequences of doping use in unorganised sports in the short and long term, the Committee also conducted an exploratory study of various registries containing health data that could provide insight into the nature and extent of substance/medicine use as well as the consequences thereof (Table 5). This exploration showed that data is available on the various conditions, but the degree to which they are caused by doping use remains unclear. This is largely due to the more general nature of the available data registries. Many registries record substances and/or medication use, but not the reason for using a specific substance. All else being equal, this applies for various conditions that are registered. Causal doping use is not specifically recorded. However, there are ways to gain greater insight into the consequences of doping use for disease burden and care consumption. This must be organised project basis. The possibilities are listed in Table 5.

Table 5 Overview of registrations of substance/medicine use along with limitations and possibilities for study.

Database	Description	Limitation	Possibilities
LAREB	The Dutch Pharmacovigilance Centre Lareb is the national reporting point for medicine side effects in the Netherlands. As all reports are collected centrally, Lareb can monitor the safety of medicines in the Netherlands.	Registration only contains incidental reports of doping-related side effects (patients do not report and doctors do not ask).	Separate reporting form on a project basis
LINH	The National Family Medicine Information Network (Landelijk Informatie Netwerk Huisartsenzorg, LINH) includes 89 automated general practices with almost 340,000 registered patients (July 2007). LINH uses data from electronic patient files in these practices to examine conditions, interventions, prescriptions and referrals.	Only registers normal medicines for normal indications. No separate registration item for doping.	Inclusion as a standard question in GP measuring station project
IPCI	The *Integrated Primary Care Information* (IPCI) project is being developed by the Medical Informatics group at the Erasmus University in Rotterdam (MIEUR). Set up in 1989, this project aims to collect primary care data for use in post-marketing surveillance. In the Netherlands, the GP is the gatekeeper and has the optimal position to examine what happens with the population registered with his or her practice. This role allows the use of the IPCI to track the effects of medicine use in the population.	Possible to make claims regarding various disease conditions, does not say anything about frequency of use.	Case-control setup possible, entails additional costs.
SFK	The Pharmaceutical Key Figures Foundation (Stichting Farmaceutische Kengetallen, SFK), analyses medication use for over 1670 of the 1850 public pharmacies in the Netherlands. Together, these pharmacies serve a population of 13.5 million people. The SFK publishes its findings:	No indication data available.	Possible on a project basis, mostly by examining comedication: for example Roaccutane and androgenic anabolic steroids.
GIP	The Drug Information System database maintained by the health care insurance board (CVZ) contains detailed overviews of extramural use of medicines and medical devices in the Netherlands. The GIP database is publicly accessible via the internet. The presented usage figures are macro estimates based on a sample size of roughly 80% of the insured population.	Contains only data for extramural use (prescribed by doctor/specialist) reimbursed within the framework of the Health Care Insurance Act.	-
CBS cause of death statistics	-	Cause of death statistics do not register whether death is acute. No link with clinical data.	-
CBS hospital registration	-	Question too specific	-
NVIC	The National Poisoning Information Centre (NVIC). One of the tasks of the NVIC is a 24-hour telephone service providing information to doctors, veterinarians, pharmacists and government agencies on acute poisoning.	Only if reporting party explicitly mentions doping use.	See text 5.1
Stichting Consument en veiligheid (Consumer Safety Institute)	Consumer Safety Foundation. Registers Accidents and exercise in the Netherlands (OBIN), based on a sample of 11,000 Dutch people.	Currently does not contain a question about doping use.	Possible on a project basis

A separate issue when it comes to gaining insight into the disease burden is caused by a combination of factors. Orientation on the internet and an inventory of available literature reveals that substances are often used at far higher doses than normally used for regular indications, and are often combined with other substances.[102] Add to this that the quality of the substances is far from clear, and you are left with a black box containing – in the Committee's opinion – unacceptable risks, given the nature of most of the substances.

All of this occurs in a subculture where parties with financial interests in substance use also play an advisory role as 'experts'.

The literature contains a multitude of case studies (with fatal endings) concerning doping use, often involving multiple substances at the same time. However, these are case studies, and not figures obtained through controlled research. It must be noted, however, that given the nature of the problems, this is not a field that is particularly suitable for controlled research. What is clear based on Department of Justice data in particular, however, is that doping use does have victims (including deaths).[103]

In order to estimate the actual consequences of doping use on disease burden, the Committee feels it is important to differentiate between short-term and long-term effects.

5.1 Short-term effects

The Committee received a report from the National Poisoning Information Centre (NVIC) on cases involving sports-related substance use. The NVIC has been consulted at least 18 times since 2006 regarding symptoms in patients occurring after substance use during sports. With a single exception, all cases concerned adults, and involved a variety of substances. One case was extremely severe, in which a young woman fell into a coma after taking six Clenbuterol tablets of unknown strength in an attempt to lose weight.

These figures are likely to be a significant underestimation, as it should be noted that these are only the reported cases in which the patient reported it to the doctor, who in turn reported the story to the NVIC. It is known that many users do not report use to their doctor.[104]

Overall, it may be concluded that use of doping substances in unorganised sport causes health damage. Certain forms of doping (such as insulin or diuretics) may even lead to acutely life-threatening situations. It is impossible to make any statements regarding the exact consequences of doping use in terms of prevalence and

incidence of conditions/diseases and possible mortality, effects on quality of life, etc. due to the methodological (registration) problems described above.

5.2 Long-term consequences

No suitable registries are available for determining long-term consequences of doping. Given the nature of the substances and the known short-term effect, long-term consequences are primarily harmful effects on the cardiovascular system, as well as the potential carcinogenic properties of substances.[105]

Based on an inventory of available literature, conditions of kidney, liver, cardiovascular system, skin, tendons and muscles have been described. Additionally, a broad range of psychiatric problems are associated with doping use. These problems include addiction issues as well as influence on mood (depression) and behaviour (aggression). The harmful effect of doping as such is not controversial, but the extent of the damage is unclear.

Chapter 6

Current and future doping policy

As indicated previously, the primary responsibility for combating doping use in unorganised sports lies with the government. The government has the constitutional responsibility to take measure to promote public health. This does not negate the responsibilities gyms and fitness centres have to counter doping use in unorganised sports. Currently, the sector itself is focused on combating doping (see Paragraph 2.3.2). The Committee will comment on possible expansion of activities in Paragraph 7.4.

The way current doping policy is implemented in unorganised sports is described in chapter 2. While manufacturing and trade is addressed through legislation, combating risks of use of doping substances is primarily a preventive endeavour: awareness-raising is used to prevent or reduce risks.

This chapter focuses on doping policy in greater detail: which insights are required in order to develop preventive interventions, and to what degree do existing insights into the context of doping use line up with current policy? While exact data regarding the consequences of doping use in terms of disease burden and care consumption are lacking, the Committee is of the opinion that, given the knowledge of harmfulness of using doping and the potential severity of said harm, it is useful to investigate which current policy items could be modified and/or improved in order to prevent/limit potential unnecessary and undesirable severe individual health damage to users.

6.1 Doping use, enhancement and personal identity

In unorganised sports, doping is primarily used to obtain a muscular and slim physique and improve performance. This ‘improvement’ or perfecting of the own body – using genetic, medical or pharmacological knowledge – is referred to as enhancement in (medical) ethics. Enhancement plays (in addition to dealing with the consequences of aging) an increasingly important role in shaping a certain lifestyle, which the person in question wishes to use to clarify what he feels is important in life, what kind of life he wishes to live, what kind of person he wants to be; in short, it is an expression of his/her personal identity. Our current society gives physical beauty an autonomous status that, in addition to other characteristics, makes a person valuable. The focus also lies on the importance of individuality, personal choice and self-expression, and physical beauty is seen as ‘improving chances’ (in professional life and marriage, for example). Individual beauty seems more valuable now than it ever has been. This explains the increased interest in fitness, dieting and cosmetic surgery.[106-108]

Enhancement may lead to an improvement in personal wellbeing. The question of whether enhancement is valuable, and actually improves wellbeing is often largely subjective. Various aspects also depend on how third parties respond, with the side note that beauty judgements are always relative, and context-related.[106,107]

But to what degree is enhancement not underpinned by the need to adhere to a specific dominant social norm, a pressure 'not to be left behind'? The question is whether it is desirable to allow improvement of one’s own body to be driven by social pressures. To what degree does this imply an autonomous choice? Enhancement may also increase the impression that the ‘outside’ of a person counts more than the ‘inside’.[106]

Additionally, enhancement may lead to health risks that – in case of doping use – may be severe. Knowledge of these risks is important in order to determine whether proportionality exists between the ends and the means. This will need to be considered on an individual basis. People are considered to be capable of determining their own needs and making choices that contribute to their wellbeing. The ruling on whether activities focused on striving for an ideal body or the desired appearance are useful or not, are primarily made by the individual undertaking such activities, unless the person clearly lacks the capacity to make a responsible decision (in other words, if someone is legally incompetent) as may be the case with underage individuals.[106]

From an ethical perspective, whether someone has control over his/her own life and can determine its direction is of great value, as this is the core principle of autonomy.[108] The government should therefore remain neutral with regards to beliefs about personal wellbeing that underpin the use of enhancers.[106] However, the government should at least ensure proper education regarding doping use is given. This allows it to protect (potential) doping users from undesirable and unnecessary harm: if (potential) doping users do not have access to the required information, it may be because they are unaware of the serious risks they are exposing themselves to.

When examining the issue of whether further government involvement with regard to doping use can be justified, the concept of harm is key. Limitation of personal freedom may be justified in order to prevent harm to third parties or society or to prevent severe harm to the individual. In the latter case, this generally applies to individuals unable to represent their own interests: young people or legally incompetent adults that cannot be expected to properly weigh the risks of substance use, leading to potential undesirable and unnecessary harm to their own health.[109]

Given the available data, the Committee does not see any reason to deviate from the substance policies the Dutch government has implemented regarding the use of (other) harmful substances. Prevention, rather than repression lies at the heart of these policies.[11] Submitting gym and fitness centre visitors to mandatory doping checks in order to potentially impose sanctions, as has been proposed in this context[11], would – ignoring various legal and financial pitfalls – in the opinion of the Committee represent an excessive violation of the individual's right to respect for personal privacy, as well as violate the right to physical integrity.

6.2 Development of health-promoting interventions

The goal of preventing doping use in unorganised sports is preventing and/or reducing the risks associated with doping in order to address the undesirable and unnecessary health risks that may occur with doping use. Preventive measures are designed to promote an individual's health. The concept of health can mean different things, and appears to be dependent on factors including age and gender. Insight into what the target groups understand to be 'healthy'' is important if preventive interventions are to succeed.[110] Insights into other factors that play a role in doping use are also important for the development and success of doping policy.

Interventions focused on promoting health behaviour may consist of 1) awareness-raising, 2) facilities, and 3) regulations, checks and sanctions. Awareness-raising aims to enable voluntary changes in behaviour. This contrasts with regulations, sanctions and checks which aim to force healthy behaviour. Facilities are designed to facilitate health-promoting behaviour (examples include availability of low-fat alternatives in company cafeterias, and needle exchange programmes for drug users).[111] The development and introduction of planned preventive interventions requires insight into the health problems in question as well as into the underlying behaviours. The groups in which doping use is most prevalent, incidence figures, substances used and risk behaviours underlying use are described in chapter 4. Chapter 5 outlines that to date, data is lacking that might provide insight into the exact consequences of doping use in terms of prevalence and incidence of conditions/diseases and possible mortality, effects on quality of life, etc. among the groups of users, but that there are ways to gain greater insight.

In addition to insight into the health problem at hand and the underlying behaviour, insight into the determinants of this behaviour is important. There are various types of determinants – determining factors or backgrounds – for health behaviour. Some determinants have a very direct effect on behaviour, others a more indirect one. The following categorisation is used: proximal; distal; and final determinants. Proximal determinants are determinants that are closely related to the studied behaviour and affect it directly: knowledge, attitudes, perceived social norms and skills. Distal determinants are further removed from the behaviour, and affect it more indirectly; concrete examples include the direct social and physical environment of an individual, such as the presence of social networks and availability of facilities. Final determinants are even further removed from the individual: these include political, economic and cultural circumstances an individual lives under.

Interventions for promoting health behaviour often focus on influencing proximal determinants, as these are under the most direct control of an individual, and he/she can be called on them.[111,112]

Determinants central to explaining health behaviour and behavioural change are personal determinants (behaviour intention, attitude, subjective values and social influences, behaviour control, personal values and knowledge) and environmental determinants (the physical, socio-cultural, economic and political environment). Which of the personal and environmental determinants are proximal, distal and final is difficult to determine.[111]

Based on the above insights (health problem/behaviour/determinants), preventive interventions may be developed focused on changing the determinants of

behaviour itself. This primarily concerns determinants most strongly related to behaviour and determinants that are easiest to change.

Subsequently, it is important to implement and disseminate the intervention(s) correctly and subsequently evaluate them in order to assess effectiveness, among other things.[111]

6.3 Determinants of doping use in unorganised sports

In order to gain greater insight into how and via which processes determinants may influence behaviour, various models and theories have been developed which describe a number of determinants and their mutual relationships. For example – in addition to behaviour change phases models and so-called ecological models – there are various models for explaining behaviour that may provide insight into the key determinants of behaviour.[111]

The last study conducted in the Netherlands into determinants of performance-enhancing substance use in fitness centres was in 2003. This study, performed by TNO, found that among respondents, more male than female athletes used performance-enhancing substances. Men indicated they used the substances primarily to strengthen muscles, women used them to lose weight. Additionally, use was more frequently associated with use of other types of drugs, such as XTC or GHB.[77]

The TNO study use the Theory of Planned Behaviour to identify which sociopsychological determinants play an important role in the intention to use doping. The basis of this theory is that behaviour can largely be predicted by intended behaviour, which in turn are defined by three sociopsychological determinants: attitude; social influence; own expectations of effectiveness. Attitude – which may be based on both logical or rational reasoning, but also on deep-rooted habits and more irrational beliefs – is partly formed by expected advantages and disadvantages of behaviour (where a differentiation must be made between short and long-term advantages and disadvantages); social influence refers to, among other things, the normative expectations of important individuals from the social environment, and the tendency to conform to them; own expectations of effectiveness refer to the degree to which someone believes themselves capable of implementing the behaviour in question. Sociopsychological determinants are assumed to have a direct influence on intention to use, while personality traits and demographic characteristics such as gender and age are assumed to have an indirect influence. Personality traits include the degree to which someone is extrovert or introvert; yielding or suspicious; calm or passion-

ate; open/curious or closed/uninterested; reliable/organised or unreliable/chaotic.[77,111]

The study performed showed that among fitness enthusiasts in the sampled population, the following sociopsychological determinants directly influence intention to use doping:

1 A permissive attitude towards doping use (personal values)
2 The expectation that use of these substances has performance benefits
3 The suspicion that others in the direct environment use.

Additionally, relatively frequent visits to the gym appear to have an indirect influence on the intention to use, and past use appears to be an important predictor for future use.

Personal values were found to be the most significant explanation for intention to use performance-enhancing substances. The foundations for these personal attitudes/permissive beliefs may be called into question. They are not always based on sufficient and correct information, and are often not well considered. By addressing the foundations of these attitudes/beliefs in a targeted manner, it may be possible to change them into more well-founded attitudes/beliefs.

Other factors – such as expected changes in health, wellbeing and appearance, influence of the direct social environment, feelings of control when it comes to resisting using performance-enhancing substances, and knowledge about performance-enhancing substances – are also influential, but are subordinate to the above factors according to the authors of the TNO report. Satisfaction with one's own appearance did not correlate significantly with intention to use.

In a recent publication, the research indicate that while the findings from 2003 are in line with previous Dutch research from 1994[97], these findings do not agree with those of an American study among bodybuilders, where intention to use anabolic steroids was found to correlate with dissatisfaction with one's own body. As a possible explanation for this difference, they stated that 1) the American study only involved bodybuilders; 2) there are cultural differences; 3) users initially do want to use performance-enhancing substances due to dissatisfaction with appearance, but at the time of the study are satisfied with their appearance, so no (significant) relationship is found between satisfaction with appearance and intention to use.[113] The previous mentioned study from 1998 into trade in doping substances in the Netherlands did find that striving for the ideal body (as defined in the gym world) defines the choice to use doping. According to the

report, the importance of the desire for a muscular body when deciding whether or not to use doping should not be underestimated.[3]

The 2003 TNO study showed there were differences between users, ex-users and non-users regarding the degree to which various determinants influence their intention to use: the influence of personal values, expected performance advantages, suspected use by others and the number of weekly visits to the gym differs, particularly when comparing non-users to users and ex-users. Non-users have a more restrictive attitude towards the use of performance-enhancing substances than users or ex-users. Users and ex-users think that more people in their environment use than non-users do. Non-users expect less of a performance advantage from the use of performance-enhancing substances, both in terms of expected effect and the importance they give it. Finally, non-users visit the gym less frequently than users and ex-users. There are hardly any or no differences between users, ex-users and non-users in terms of distribution of age, gender, education, school/work situation, ethnicity, living conditions and whether or not they participate in competitive sports. Bodybuilders are overrepresented in the group of users and ex-users.

The study also found that the average level of knowledge regarding the effects of substances is relatively low. Knowledge appears to depend on the substance used. Knowledge about anabolic steroids, growth hormone and diuretics is greater than for clenbuterol, substances that counter side effects of other agents/substances and stimulants. The researchers did indicate that knowledge does not play a significant role in determining behaviour. Users appear to assign advantages to the use of performance-enhancing substances and underestimate the risks. The tendency to trivialise risks leads to permanent use among the majority of users, and according to the researchers, these circumstances are difficult to change. The TNO report indicates that handles for addressing behavioural change will have to look for ways to change personal values regarding use and expected performance advantages of using.[114]

Interviews with doping users conducted as part of a 2005 study into the quality of illegal doping substances revealed a similar picture: users almost all trivialise side effects and consider the risk acceptable relative to the goal they are striving for, namely a muscular and slim body.[8] Research by sociologist Monaghan also leads to this conclusion: anabolic steroid users are convinced that, while use of the substances may cause side effects, this does not have any harmful health effects. Use is justified based on the desired goal. To them, the advantages outweigh the disadvantages.[114]

The recently performed TNO study into the use of performance-enhancing substances among athletes (see 4.2) provided no new information about determinants of doping use in unorganised sports in the Netherlands compared with the 2003 study. The reason for this is that prevalence of doping use is too low to perform an analysis of determinants. The report does mention the results of a literature study. A number of recent international studies into the determinants of doping use identified the following determinants: gender, education level, general substance use (drugs, cigarettes, alcohol, coffee, dietary supplements, intention with regard to doping use), athletic behaviour (yes/no sports, frequency of fitness centre visits, active bodybuilding), body image (desire to lose weight, self-confidence, mental health, anxious behaviour), and social network (knowing of others using these substances, having friends who use doping, and educational choices).

The report also indicates that in future, research into the determinants of use should be uncoupled from prevalence studies, as the participation of a large number of users is important for determinant analysis. Research into determinants should primarily take place in fitness centres where doping use is known to be common.[96]

Looking towards the development of future prevention policies, the Committee underwrites the importance of new research into the determinants of doping use, so that (even) greater insight can be gained into the actual motives that play a role for various groups of doping users. Given that Lechner et al already indicated that every explanatory behaviour model has its specific advantages and limitations, it may be worth examining which model or combination of models is most suitable. One criticism of the Theory of Planned Behaviour is that it only provides minimal room for emotional factors that influence behaviour. The data collection method (questionnaires, in this case) may also affect the outcome.[111]

6.4 Is current doping policy sufficient?

As outlined in chapter 2, Dutch doping policy is characterised by both awareness-raising and measures taken (legislation and regulation). A key role is reserved for the Doping Authority, which focuses among other things on providing education and advice to non-professional athletes (fitness enthusiasts in particular) and their direct environment. The goal of awareness-raising and education is preventing and/or reducing the risks of doping use. To what degree is this educational approach effective and is the desired goal achieved? Unlike preventive measures in which an attempt is made to force (healthy) behaviour, awareness-raising aims to stimulate voluntary healthy behaviour. Another possi-

bility for promoting healthy behaviour is creating facilities with the objective of facilitating healthy behaviour.[111] A successful prevention programme usually requires a combination of various preventive interventions.[115]

Research into the health effects of preventive interventions is scarce, as the interval between intervention and noted effects is often very long. Effects are therefore usually determined based on behavioural change.[115]

6.4.1 *Effectiveness of the 'Eigen Kracht' programme*

Paragraph 2.4.2 describes the scope of the 2004 prevention programme 'Eigen Kracht' (True Strength) developed by the Doping Authority, as well as the ways in which this programme aims to combat doping use among gym and fitness centre visitors. A pilot programme was performed in five fitness centres in 2004-2005. The pilot was evaluated extensively. Based on the positive results of this process and satisfaction assessment, the decision was made to roll the programme out nationally. It is too soon to say anything about the effectiveness of the programme.[116]

The success of preventive interventions requires them to be tailored to address the determinants that influence doping use. The 'Eigen Kracht' programme is based on the 2003 TNO study into the determinants of doping use in unorganised sports (see Paragraph 6.3). Awareness-raising is primarily focused on the people who sit on the fence about using, with the motto 'You perform using your true strength'. They are offered alternatives to doping use to achieve a slim, muscular body. Objective information is also provided regarding the use of doping substances.

In addition to insights into the determinants of doping use by gym visitors in general, the TNO report also shows that the degree to which various determinants influence the decision to use depends on whether individuals are users, ex-users or non-users. The differences are particularly distinct when comparing non-users to users and ex-users. 'Eigen Kracht' currently focuses its awareness-raising and alternatives on doubters. This method is consistent with the findings indicating users find alternative individual activities (nutritional advice, weight-loss programmes, training support) less important than non-users (and ex-users) do. Users and ex-users, on the other hand, feel that providing support for the use of performance-enhancing substances is more important than non-users do.[77] This is partially addressed by the 'Doping info number' that users can call with questions about substance use.

6.4.2 *Effect of legislation and regulations on illegal manufacture and trade*

The illegal manufacture and trade in doping substances is countered using, among other things, the Opium Act and the Medicines Act (see Paragraph 2.4.3). In order to better combat this manufacture and trade, the law was changed in May 2001: the unauthorised delivery of medicines, as well as the preparation, sale, issuing, import, trade in or keeping of stock for purposes of delivery of unregistered medicines was declared an economic crime, along with an increase in maximum sentence and expansion of investigative options for law enforcement.[6,8,13]

An evaluation of this modified law published in 2005 found that the desired effect of this change – improving the methods for dealing with illegal trade and manufacture and doping substances – has partially been achieved. While the number of criminal cases has not increased, the fact the number of doping-related investigations initiated has risen indicates that the Attorney General gives these cases a higher priority. It is unknown to what degree the change in the law has affected the scope of trade and manufacture of doping substances, but interviews with experts indicate that the threat of more severe penalties and the possibility of (more aggressive) investigational means being used has made dealers more careful and made it more difficult for users to obtain doping substances.[9]

6.5 Future doping policy

As indicated by the Committee in Paragraph 6.3, with a view on developing future prevention policy, new research into the determinants of doping use should be performed in order to develop preventive interventions that can be set up in a planned, evidence-based manner. As evidence-based research for intervention development is currently lacking, the Committee will make a number of suggestions for future policy based on parallels with other areas in the following paragraphs. Among other areas, the Committee examined Dutch drugs policy, particularly because of the prevalence of combined use among doping users: the secondary analysis of the data from the 2005 NPO study found that doping users had also used cannabis (24.5%), XTC (10.5%), cocaine (10%) and amphetamines (7%) in the past year (see Paragraph 4.2.2). The Committee is therefore of the opinion that it would be useful to investigate which aspects of that policy may be used as a guide when designing any further preventive interventions for doping.

In its recently published advisory report on Dutch drugs policy, the Drugs Policy Advisory Committee indicated that drugs policy cannot be viewed separately from a broader policy on substances.[109] The Committee underwrites this view and is of the opinion that – in addition to drugs, alcohol and tobacco – doping use should be included, particularly when the above-mentioned combined use is considered.

6.5.1 *Dutch drugs policy: a source of inspiration?*

Dutch drugs policy puts public health interests first. The goal is to prevent and limit the risks of use and the health damage to the user that may arise, as well as preventing and limiting damage to his/her direct environment and to society. In addition to harm reduction (through e.g. methadone provision and combating nuisance), this management-focused policy also works on demand reduction and supply reduction. The demand for drugs is decreased through good prevention and (differentiated) aid; supply reduction is sought through combating organised crime (manufacture and trade).[15,117,118]

Drugs use usually begins in adolescence, making young people a key target group for prevention. The preventive interventions are therefore focused on young people. Other target groups for prevention include: parents and carers of young people; recreational drug users; catering industry entrepreneurs; coffee shop owners; and event organisers.[119]

Most preventive interventions are focused on high-risk groups and are implemented in places where these groups may be found. Awareness-raising is provided primarily at schools, in the nightclub circuit and via youth work. Information about drugs and drug use is also provided via the internet. As with doping use, the Drugs Info Line is available to answer questions in this area. In 2007, the Drugs Info Line set up a chat service to supplement the telephone information, which proved particularly popular among young people.

Various national and local organisations are involved in prevention. The Trimbos institute, which has been assigned the role of Health-Promoting Institute (GBI) in the field of drugs, plays an important role.[119] This institute offers a variety of prevention programmes in the field of drugs (and other stimulants) that are used in parallel with each other; this allows an integrated approach to substance abuse. These tools include mass media awareness-raising campaigns focused on youths and intermediaries.[118]

One of the prevention projects is the DIMS - Drugs Information and Monitoring System. DIMS has two tasks: monitoring and surveillance. Monitoring

aims to discover what is available on the recreational drugs market. Surveillance aims to signal risks to public health. Users can anonymously submit drugs for analysis of composition and dosage at various test sites. This allows them to be informed of potential risks of use. If substances are discovered that represent a direct public health risk, regional or national warning campaigns are initiated (source: www.trimbospreventie.nl).[118] Additionally, so-called 'pre-prevention activities' take place: awareness-raising for and by youths who have followed a training course. They inform and advise their peers on safer use of (party) drugs.[119]

Preventive interventions are also performed at schools: the 'Health School and Stimulants' (Gezonde School en Genotmiddelen) is an educational project that aims to teach young people to use stimulants (drugs, alcohol and tobacco) responsibly. In addition to lessons, the programme includes rules about stimulant use at school, a signalling and support protocol for students with problematic substance abuse and meetings for parents.[119]

In addition to education and awareness-raising, specific measures are taken to combating problems surrounding drug use. For example, coffee shops must meet the AHAY-L criteria: no Advertising, no Hard drugs sales, causes no Annoyance, no access to coffee shops for Youths (under the age of 18) and no sale of Large amounts per transaction. The sale of small amounts of soft drugs in coffee shops is illegal, but in practice is only prosecuted if coffee shops do not adhere to the abovementioned cirteria.[15] Additionally, coffee shop staff is trained to identify early signs of problematic use, and young (ages 18-25) coffee shop visitors are given informational materials about 'sensible' use of cannabis, aid options, etc.[118]

6.5.2 *Is current doping policy sufficiently differentiated?*

Prevention within the context of drug use is focused on various goals and target groups. To what degree is current doping policy sufficiently differentiated? The 'Eigen Kracht' programme currently focuses its awareness-raising and alternatives on doubters, and to a lesser degree to those who (have already decided to) use. Users can contact the Doping Info Line with questions, but as previously mentioned, this group is less interested in information about alternatives for obtaining a slim, muscular physique.[77] A certain group of doping users is currently not reached by current prevention programmes. These users appear to assign advantages to the use of performance-enhancing substances and underestimate the risks. For the majority, this leads to permanent use.

Additionally, the prevention programme – unlike the preventive interventions within the context of drug use – does not specifically target young people. Given that the foundations for healthy lifestyle habits are laid at a young age, prevention of problematic alcohol and drug use targets children and youths. Teens and adolescents experiment with various forms of behaviour. This may include alcohol and drug use.[120] And also the use of doping substances. There are also indications that a split has occurred between younger and older users: younger users of doping substances see it primarily as a way to quickly obtain a muscular body, and are primarily attracted to anabolic steroids in pill form. Older, traditional users prefer injected anabolic steroids. This affects the potential health risks: anabolic steroids taken as tablets are far more harmful for the liver.[8]

Given the above, the Committee is of the opinion that future doping policies should take into account the difference between those who are unsure about using and those who already use. In the first group, prevention should be focused on preventing (initial) use, in the second it should attempt to reduce use and/or limit the risks. Furthermore, findings from the recent TNO study and the secondary analysis of the 2005 NPO study indicated that specific differentiation is important between youths (ages 15-24), the 25-44-year-olds, immigrants (as substance use among non-western immigrants is significantly higher than in the native population) and men/women. Although the TNO report does not provide any hard figures, the assumption is that women primarily use substances for weight loss purposes, and men use them to build muscle mass. This assumption is confirmed by the secondary analysis of the 2005 NPO study data. The Committee is of the opinion that this difference in desired effect of substance use requires a specific approach.

Which preventive measures used in drugs policy could be translated to doping policy and focused on various target groups requires further investigation. The Committee believes the DIMS programme is a potential option for combating the potential risks associated with doping substances. Additionally, gym owners and their staff (like coffee shop staff) could be trained to signal early signs of doping use.

Chapter 7

Conclusions and recommendations

7.1 General

The Committee would like to emphasise the importance of unorganised sports, including fitness training, in terms of the positive contribution that exercise (sports) makes to public health.

In formulating the conclusions and recommendations on doping in unorganised sports, the Committee chose a two-pronged approach. On the one hand, much remains unknown, particularly regarding the prevalence of the consequences of doping use. On the other hand, there are sufficient data on the severity of these consequences not to take a wait-and-see attitude, but to work on prevention and take measures by setting up a research agenda and determining urgency.

Doping substances

The doping substances involved in doping in unorganised sports are described in detail in Chapter 3. The substance properties and additional particulars are described. Many of the substances described are used as medicines in regular medicine. Weighing the risk and nature of side effects against the indication the medicine is prescribed for is standard practice when prescribing medication.

Without reservations, the Committee is of the opinion that standard use of most substances already has the potential for severe side effects. For a number of

the substances discussed, side effects are serious enough for current guidelines to recommend they only be prescribed by experienced specialists. When used for doping purposes, it is common knowledge that the recommended dose (for normal use) is exceeded many times over. The Committee is of the opinion that this entails significant risks. Furthermore, it must be considered that neither the quality or the concentrations are reliable. This creates a black box with unacceptable risks for the user.

7.2 Nature and extent of use

Chapter 4 provides an overview of prevalence and characteristics of doping use in unorganised sports. Recent data (see Paragraph 4.2) has shown that the group is small (recent use among about 8% of gym visitors, and about 1% of the general population) in relative terms (certainly compared to problems such as obesity and smoking), but a significant group in terms of absolute size (about 160,000 were found to have used doping substances in the past year). This group of doping users exhibits high-risk behaviour due to the nature of the substances used, the method of use, and the risk perception among users.

7.3 Consequences for disease burden and care consumption

In order to present the true extent of likely health problems the Committee oriented itself using existing health services data collections. The true nature and extent of these health problems can only partially be mapped out. This has largely to do with the nature and objectives of these data collections. The doping issue is not so large as to make default registration a logical or practical desirable. This issue was present in some degree in practically all databases examined.

Despite the fact that doctors do not immediately ask about substance use, a number of issues is clear. Data from the NVIC shows that it is consulted with some regularity regarding problems caused by doping use. It should be obvious that this is only the tip of the iceberg. After all: not every doctor will immediately associate substance use within the context of sports, and not every victim will mention doping use without being prompted. This causes a large number of cases to go unnoticed.

The literature contains a multitude of case studies (with fatal endings) concerning doping use, often involving multiple substances at the same time. However, these are case studies, and not figures obtained through controlled research. It must be noted, however, that given the nature of the problems, this is not a field that is particularly suitable for controlled research. What is clear based on

Department of Justice data in particular, however, is that doping use does have victims (including deaths).

In order to estimate the actual consequences of doping use, the Committee feels it is important to differentiate between short-term and long-term effects. For both short-term and long-term effects, there are databases that – on a project basis – can provide greater insight into various aspects of doping use in unorganised sports. A separate study will need to be initiated for example via the Netherlands Organisations for Health Research and Development (ZonMw). It goes without saying that this type of research entails costs.

7.4 Proposals for improving current doping policy

The Committee sees a number of potential additions/areas for improvement in current doping policy. The Committee drew inspiration from Dutch drug policy, among other areas (see 6.5). The Committee identifies four general recommendations: 1) a different approach to doubters and users; 2) changing the foundations of permissive beliefs (attitude) about doping use; 3) specifically differentiating between various target groups; and 4) combining interventions focused on demand reduction, harm reduction and supply reduction. This includes attention for combined use with other psychotropic substances (drugs, alcohol).

1 A different approach to doubters and users

The current ‘Eigen Kracht’ (True Strength) awareness-raising programme focuses primarily – by providing information and alternatives – on doubters. Those who have already decided to use require a different approach. This is demonstrated among other things by the fact that users feel providing support for the use of performance-enhancing substances is important; they are less interested in alternative individual activities. For example, in the past users have indicated they would like regular health checks by doctors, and would appreciate a doctor’s supervision in using performance-enhancing substances.[77] The Committee also feels the ‘Eigen Kracht’ should, in addition to existing awareness-raising, focus (more) specifically on individuals who have already decided to use.

2 Changing the foundations of permissive beliefs (attitude) about doping use

The success of preventive interventions requires them to be tailored to address the determinants that influence doping use. The 2003 study into the determinants of doping use found that a permissive attitude about doping use was the best predictor of performance-enhancing substance use.[77] The Committee is of the opinion that it is important to attempt to change the 'foundations' of these permissive beliefs about doping use. Doping users tend to trivialise the side effects and feel the risk is acceptable given the desired goal (see 6.3).

3 Differentiating specifically between various target groups

The Committee is of the opinion that current doping policy is not sufficiently differentiated. The development and implementation of preventive interventions should, in addition to differentiating between doubters and users, be focused more specifically on youths (ages 15-24), the group aged 25-44, immigrants and men/women.

4 Combining interventions focused on demand reduction, harm reduction and supply reduction

Promoting healthy individual behaviour requires an intensive, integrated approach that focuses not only on the individual, but also on the environment; various intervention methods should be used at the same time. Combining various intervention strategies may strengthen the preventive effect.[121]

Current doping policy is primarily focused on demand reduction – in the form of awareness-raising within the context of the 'Eigen Kracht' programme – and supply reduction – using legal measures to combat illegal manufacture and trade. Because of the risk perception among doping users, however, the majority of users are permanent users, which appears difficult to change.[77] The Committee feels it is important to investigate whether, and if so which harm reduction measures can be added to current doping policy in order to limit health harm to doping users. Additionally, the Committee feels it is desirable to further investigate whether effective interventions currently used in other fields (drugs, alcohol, smoking) can be used as part of doping policy; an additional reason for this approach is that combined use of doping and other psychotropic substances is relatively common.

The above general recommendations may be translated into a number of concrete areas for improvement in the areas of awareness-raising and facilities.

Concrete points for improvement

Awareness-raising

1 The Committee is of the opinion that, in order to achieve changes to the foundations of permissive beliefs about doping use, hard, objective evidence is required. Research has shown that the effect of awareness-raising improves when the message is balanced and rational, rather than normative or frightening.[118] Awareness-raising must also focus on the dangers of fakes. Users expose themselves – without being able to make a well-informed choice – to entirely unforeseeable health risks. Education about the existence and dangers of fakes could open the eyes of a large group of users that are currently unaware.[13]
Finally, studies have shown that athletes, doctors, trainers and fitness centres want more information about the risks of (illegal) doping substances.[9]

2 Gym directors and staff should be more closely involved in preventing doping use. The Committee supports the possibilities suggested by the secretary of state to give more attention to doping use in training programmes for gym instructors, and to propose natural alternatives for achieving the desired beauty and performance goals during intake discussions with gym visitors. The Committee also feels the proposed inclusion of a paragraph on doping in the terms and conditions for fitness centres and gyms represents an important implementation of the responsibilities the gym and fitness centre sector has in this area.[11]

3 The Committee is of the opinion that GPs and sports doctors should be more actively involved in preventing doping use. In general, knowledge of doping among doctors is minimal. This means they are unable to (correctly) respond to doping-related medical questions.[8] In 1995, the Association of Sports Medicine (VSG) drafted guidelines regarding sports medical treatment.[122] These guidelines indicate that doctors should reject requests to prescribe doping substances, and that they have the obligation to discourage use of these substances. They do state that the doctor should address the underlying question, because categorical rejection may cause harm. The guidelines do not provide any alternatives to doping use. Although the Royal Dutch Medical Association (KNMG) added the guidelines to its code of conduct in 1996, they were removed again in 2002. Evaluation of the guidelines in 2003 showed that all sports doctors were aware of the guidelines, but only a small

percentage of GPs were. The evaluation report therefore recommended promoting the guidelines better and more extensively among GPs. The recommendation was also made to make guidelines on doping more explicit, as it is unclear to certain doctors what precisely supporting athletes entails.[8,122,123] The Committee endorses all of these recommendations, and sees the development and distribution of an informational brochure for GPs outlining the potential use of doping in amateur sports, recommending referral to a sports doctor as a concrete option, as sports doctors are generally more familiar with the alternatives for doping use than general practitioners.

4 The Committee feels the option of placing banners with health warning on info sites about doping requires further investigation. Because such measures may be counterproductive, this requires careful elaboration and testing.

5 A chat service was added to the Drugs Info Line in 2007, which proved very popular among young people in particular.[118] The Committee feels it is useful to investigate whether such a service may supplement current telephone information provision via the Doping Info Line.

Facilities:

1 As previously indicated, the Committee feels it is important to investigate whether and if so which harm reduction interventions may be added to doping policy in order to limit health harm to doping users. The 2003 TNO study shows that some of the athletes have a desire for programmes (such as health tests) to limit health risks associated with use as much as possible. Users also indicate they would appreciate regular health checks with a doctor. A majority of respondents would like a doctor to support them in the use of performance-enhancing substances.[77] The potential role the Committee sees for doctors in this field is comparable to their role in addiction care. The focus lies with supporting doping users who have great difficulty stopping doping use. The primary goal is to prevent and/or limit as much harm caused by doping use as possible by performing physical examinations. Further research may provide insight to the degree to which such desires may be given form and content. Within this context, the ways the health services could be tailored to cater to doping users could be examined.

2 The Committee feels it is desirable to investigate whether a programme like DIMS (see Paragraph 6.5.1) could be developed/set up in order to combat the risks of doping use in unorganised sports.

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Annexes

Annex **A**

Request for advice

Date of request: 23 April 2008

Letter reference: S/TOP-SP-2841067

I hereby request that you initiate a study into the harmful effects of doping use on health and advise me on this subject.

Reports from the former Netherlands Centre for Doping Issues (NeCeDo) and the subsequently founded Doping Authority in the past years have indicated that doping in sports is likely to be a growing problem in our country. Research figures indicate that about 50,000, people use doping each year.

In addition to organised sports (both professional and amateur), doping use is apparently most prevalent in unorganised sports. In this context, doping may be described as unintended use of authorised or unauthorised medicines in order to obtain a muscular or slim appearance. This includes the use of anabolic steroids, growth hormone, EPO, insulin, thyroid hormone, amphetamines and various other substances. Some athletes also reach out to veterinary medicines such as clenbuterol.

The use of anabolic steroids and stimulants by sport school and fitness centre attendees is particularly worrying. Various descriptions of disease cases in medical literature show that athletes run serious health risks in both short and long term when using doping substances. The health harm may be

caused by (side) effects of the substance itself, the method of use (for example, combined with other medicines), and/or the poor quality of the substances.

Better insight into the nature and extent of the problem, particularly with regard to the chances of severe long-term consequences of using doping substances, is of major importance in evaluating current anti-doping policy, and may provide handholds for adjusting preventive measures in the field, such as targeted awareness-raising.

Given the above, I request that you advise me on the current state of knowledge, paying specific attention to the following points:

1 Which medical, short-term or long-term complaints may develop in athletes using the doping substances referred to? Which substances represent the greatest risks?
2 Can you outline the implications of using these high-risk substances in terms of health risk, disease burden and use of health services (care consumption)?
3 Do existing health monitors provide sufficient insight into the degree in which use of the substances described leads to medical complaints?
4 Given the current state of the field, what is your view regarding improving preventing said health harm?
5 In the event important data is lacking, what are your recommendations regarding further research, as well as involving other new forms of doping (such as gene doping)?

The study is already part of the proposed 2008 working programme (paragraph 3.9) of the Health Council of the Netherlands, defined on 18 September 2007.

I look forward to receiving your advisory report in the spring of 2009 at the latest.
(signed)
The Minister for Health, Welfare and Sport
Dr A. Klink

Annex **B**

The Committee

- Professor M.M. Levi, *chairman*
  Professor of Internal Medicine, Academic Medical Centre, Amsterdam
- Professor P.A.B.M. Smits
  Internal specialist and Pharmacologist, University Medical Centre St Radboud, Nijmegen
- Professor J. Meulenbelt
  Internist, intensivist and toxicologist, Utrecht University Medical Centre, also Head of the National Poisoning Information Centre (NVIC) and affiliated with the Institute for Risk Assessment Sciences
- Professor F.M. Haaijer-Ruskamp
  Professor of clinical pharmacology, Groningen University Medical Centre
- Professor A.J. van der Lely
  Professor of Endocrinology, Erasmus Medical Centre, Rotterdam
- Dr. W. de Ronde
  Endocrinologist, VU University Medical Centre, Amsterdam
- Dr. M. Hilhorst
  Ethicist, Erasmus Medical Centre, Rotterdam
- Professor W.W. van Solinge
  Professor of clinical chemistry and laboratory medicine, Utrecht University Medical Centre

- Professor D. van de Mheen
  Professor of Addiction Research, Erasmus Medical Centre, Rotterdam / IVO Director
- Professor H. Kuipers
  Professor of kinesiology, Maastricht University
- Dr. L.A. van Ginkel
  Analytic laboratory for nutrition and residue research of the RIVM, Bilthoven
- O.M. de Hon, *advisor*
  Doping Authority, Capelle aan den IJssel
- P. de Klerk, *observer*
  Ministry of Health, Welfare and Sports, Sports directorate, The Hague
- M. Koornneef, MA, MPH, *observer*
  Ministry of Health, Welfare and Sports, Sports directorate, The Hague
- L.F. Stultiëns, *scientific secretary* until 1 January 2010
  Health Council of the Netherlands, The Hague
- C.A. Postema, MD PhD, *scientific secretary*
  Health Council of the Netherlands, The Hague

The Health Council and interests

Members of Health Council Committees – which also include the members of the Advisory Council on Health Research (RGO) since 1 February 2008 – are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the President and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the establishment meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **C**

Consulted experts

- Dr. A. Voorschuur, Senior policy advisor at Nefarma
- A. van Nes, Medicines Inspector, Healthcare Inspectorate
- Professor G. J. Kok, Professor of applied psychology, Maastricht University
- A.E. Timmermans, GP, President of the Netherlands Family Medicine Society (NHG)
- Professor N. de Vries, Professor of Health Awareness-raising and Education, Maastricht University
- R. Wouters, Eexecutive Director of Fit!vak, sector organisation for certified sports and exercise centres.

Annex **D**

Overview of substances and health risks

This Annex examines the characteristics of a number of listed substances in greater detail. The substance properties for regular use as medication are displayed, and the text from the CVZ Drug Formulary (Farmacotherapeutisch Kompas) was used as the basis.[48] Subsequently, specific properties leading to use of the substance as doping are examined. The extent of use and implications for health risks, disease burden and care consumption are examined for each substance – insofar as data is available.

D.1 Performance-enhancing substances

Anabolic androgenic steroids

Anabolic androgenic steroids (AAS) can be divided into artificial anabolic steroids such as danazol, nandrolon and stanozolol, and natural steroids that occur in the body, such as testosterone and dihydrotestosterone. Nandrolon (deca-durabolin) and testosterone are registered as medicines in the Netherlands.[48] The number of testosterone users registered with the pharmacy was 11,245 in 2008, the number of nandrolon users registered with the pharmacy is likely to be negligible, although there is no listing in the GIP database. Until recently mesterolon (proviron) was registered for use in the Netherlands, with about 300-400 registered users in 2008.

AAS are suitable for oral use due to the alkalisation of the C 17 site. This does make them hepatotoxic. This side effect does not apply or applies far less to injectable AAS.

Properties

Androgens lead to the development and maintenance of secondary male gender characteristics and male sexual function. They also have an anabolic protein-sparing function. Androgens also inhibit gonadotrophin secretion in the anterior pituitary gland. In peripheral tissues, androgen antagonise oestrogen functions. Due to aromatisation to oestrogens, however, oestrogen effects such as gynaecomastia may occur. When taken orally, testosterone is largely inactivated by the liver. Testosterone undecanonate and the testosterone-derived preparation mesterolone are exceptions: a small amount is absorbed into the lymphatic system from the intestines. At normal doses, mesterolone bioactivity is slightly lower than that of testosterone undecanonate. Testosterone esters are available for intramuscular injection. Testosterone is converted into the active dihydrotestosterone by 5-α-reductase and into oestradiol by enzyme aromatase.

Indications and contraindications

Administration of testosterone is indicated in men in cases of primary hypogonadism (e.g. Klinefelter syndrome) and hypopituitarism. Administration of androgens to the mother during pregnancy may cause genital malformation in a female foetus.

The use of anabolic androgenic steroids as doping

This form of doping was widely implemented by the former East-German government, which lead to the dominance of East-German women in sports.[55,56] Of the many publications on anabolic steroids, only a limited number are of sufficient scientific quality, meaning a double-blind, placebo-controlled method was used.

An additional methodological problem is that many users of anabolic steroids use a variety of drugs in often varying (far too high) doses.[57] Furthermore, some of the substances are sourced on the black market, so no statements can be made regarding their quality. Research has shown that 50-60% of the products do not deliver what is promised on the package.[8]

Hartgens and Kuipers found that use of anabolic steroids increased strength by 5-20% compared to baseline. Weight increases by 2-5 kg thanks to an increase in lean body mass.[16] There appears to be no decrease in fat mass.

Side effects

Short-term use of anabolic steroids can already have negative effects. In general, it may be stated that negative effects are more pronounced in cases of extended use and at higher doses.

There are also clear gender differences: when used by women, the consequences are lasting and generally severe.

In men, the following side effects of anabolic steroid use have been reported: gynaecomastia (possibly due to peripheral conversion into oestrogens), increased libido, priapism, inhibition of spermatogenesis, acne and prostate hyperplasia.

While both men and women are likely to use the same substances, the effects of administration are different in part. The endogenous levels of androgens in women are only a fraction of those found in men. Women therefore experience the anabolic effects of androgen administration at lower doses compared with men. Side effects that are only seen in women are lowered voice, hirsutism, male pattern hair loss, clitoral enlargement, menstrual cycle disruption and involution of breast tissue. The side effects mentioned are largely reversible and, compared with men, occur at relatively low doses.

Administration of androgens to the mother during pregnancy may cause genital malformation in a female foetus.

In children and adolescents, height increase after initial swift growth may stop due to closing of the epiphyseal plates. Early puberty will also occur.

Acne

The occurrence of acne associated with steroid use is known.[17] Acne occurs in about 50% of male users of anabolic steroids.[18] If women receive chronic testosterone treatment, almost all users develop acne on the face and back within 4 months. The new development of acne in adult men and women is an indicator for potential anabolic steroid use. The severity of acne usually decreases during chronic use.

Hair growth

In men, administration of large doses of androgens will only lead to an increase in body hair if body hair is still insufficiently developed due to hypogonadism or young age. The use of high doses of anabolic steroids for months to years may lead to early or faster occurrence of male pattern baldness. Women using testosterone chronically exhibit increased hair growth on arms and legs within 4

months. After 12 months of use, hair growth on abdomen and face has also increased, but not to the same extent seen in men.[124]

Cardiovascular effects

The use of testosterone and other anabolic steroids by men and women is almost without exception associated with a slight decrease in HDL cholesterol.[125] This effect appears to be more prominent for oral administration than for transdermal (patches, gels) or intramuscular administration. This HDL-lowering effect of anabolic steroids may remain weeks after stopping administration.[16] However, there are no signs that physiological substitution of testosterone in hypogonadal men leads to an increased incidence of cardiovascular disease. Despite chronic testosterone use, female-male transsexuals also do not display increased cardiovascular mortality.[126] Fluid retention or elevated blood pressure is seldom seen during substitution therapy.[125] The use of anabolic steroids in pharmacological doses for 2 months had no measurable effect on blood pressure or heart dimensions.[16] A more recent study also found no relationship between heart muscle dimensions and a history of androgen use. However, it did find a correlation between past anabolic steroid use and a subclinically reduced heart function.[127,128] Various case reports have been published on sudden cardiac death in bodybuilders using anabolic steroids.[19, 129] However, it is impossible to state whether this correlation is causal. Autopsy did reveal cardiac hypertrophy, acute cellular necrosis and interstitial myocardial fibrosis.[19]

In addition to sudden cardiac death, multiple publications report on the occurrence of myocardial infarction and arrhythmia associated with anabolic steroid use.[20]

Liver

The use of anabolic steroids has been associated with liver damage. Old, observational research describes elevated transaminase levels in 1/3 of patients using methyltestosterone. Only 1 in 60 patients had a mildly elevated bilirubin concentration, and none were symptomatic.[130] Methyltestosterone-induced cholestatic icterus is rare, but generally develops during the first 4 months of use, and generally follows a benign course if medication use is stopped.[131] Use of methandrostenolone (dianabol) for 6 weeks (100mg per day) did not lead to liver enzyme abnormalities.[132] Liver damage appears to be largely limited to the use of 17 alkylated anabolic steroids. During use of high doses (600mg/week) of intramuscular nandrolon (deca-durabolin, also popular with bodybuilders) for 4 months, no liver enzyme elevations were found.[133] In practice, liver enzyme abnormalities are rarely seen during therapeutic use of testosterone by men and women. In

addition to the above, severe intra-hepatic cholestasis is a known complication.[22] Toxic hepatitis[23] and Peliosis Hepatis - a condition in which a blood-filled cavity forms between the liver parenchyma[21] - have also been described. It is likely that the 17 alkylated androgens may lead to the occurrence of hepatocellular hyperplasia and liver carcinomas.23

Psychiatry

The use of high doses of testosterone for 6 weeks by 56 men showed minimal but measurable effects in 84% of users, 12% exhibited mild hypomania and 4% manifest hypomania.[134] In a cross-over study, the effect of varying doses of testosterone on the male psyche was examined. No or only slight minimal psychosexual changes were noted in these men. 1 of the 42 test subject developed brief manic symptoms while using the highest dose (500mg per week).[135] Anabolic steroids can cause a broad array of psychiatric symptoms. The degree to which these symptoms occur is associated with the severity and extent of use.[27]

Anabolic steroid use is associated with a broad scale of potentially long-lasting psychiatric effects such as addiction syndromes, mood disorders and progression to other forms of substance abuse.[26]

Dependency on anabolic steroids has been described.[25] Taking high doses leads to aggressive and violent behaviour.[136] Twin studies have shown that use of anabolic steroids leads to significant psychological changes. High scores were obtained for aggressiveness, hostility, anxiety and paranoid thoughts.[137]

The presence of psychological symptoms and conflicts due to long-term use of anabolic steroids may contribute to successful suicide attempts in some predisposed individuals.[138]

Rhabdomyolysis

Rhabdomyolysis is a syndrome cause by muscle necrosis, in which cell content is released into the bloodstream. The syndrome may occur following exercise, trauma, immobilisation and muscle diseases, as well as due to a series of toxic substances including anabolic steroids.[139]

Extent of use

Extensive literature is available on the use of anabolic steroids in sports. It is estimated 1 to 3 million inhabitants of the United States have used steroids. An estimated 50,000 - 100,000 of the 9 million inhabitants of Sweden are thought to have used steroids, amounting to about 1% of the population.[31] Other studies in a variety of European countries[32] show steroid use by 1-5% of the population. These figures do not, however, reveal the true risks of long-term use.

A study among 6,000 16 and 17 year-old Swedes using anonymous multiple-choice questionnaires showed that 3.2% of young men had used steroids, but none of the questioned young women had.[16,29,30]

German figures report alarming use among fitness centre attendees, particularly among young people aged 18-26 years.[18]

Another study in Brazil, conducted in 13 gyms among 288 weight lifters, showed a prevalence of 11.1% for current and past use of steroids, and 5.2% for use of other hormones. The most commonly used steroids were nandrolon and stanozolol. The other hormones were gonadotrophin and triiodothyronine. Additionally, other medication use was charted. This revealed a prevalence of 4.2%, and concerned substances including lipostabil, diuretics and veterinary medicines.[59]

Research into doping use among the Dutch population between the ages of 15 and 64 revealed that 1.0% had used doping in the past year. 1% indicates they have used doping at some point. In 22.2% of the cases in this 'used at some point' group, the substance in question was anabolic steroids.[28]

Precursors of anabolic steroids, so-called 'prohormones'

Properties

In order to avoid the side effects of anabolic steroids but continue to reap the benefits, substances that play a role in the formation of anabolic steroids have been marketed.

Androstenedione, 4-androstenediol, 5-androstenediol, 19-norandrostenediol, 19-noradrostenedione and dehydroepiandrosterone (DHEA) are testosterone precursors and are also known as 'Andro' prohormones. There have been aggressive advertising campaigns for these products over the past years. Manufacturers claim these substances increase the serum concentration, leading to an increase in muscle strength and volume, a decrease in body fat and improvement in mood and libido. However, most studies dispute these claims.[60,61]

The use of anabolic androgenic steroids as doping

Manufacturers claim these substances increase the serum concentration, leading to an increase in muscle strength and volume, a decrease in body fat and improvement in mood and libido. However, most studies dispute these claims.[60,61]

Side effects

Various studies with oral Andro show that oestrogen-related hormone levels are abnormally high. Most studies also show a significant drop in high-density lipoproteins, which may be linked to an elevated risk of cardiovascular diseases. In summary, this means the industry's claims remain unsubstantiated, and that the potential long-term effects, particularly due to the influence on blood fat metabolism and oestrogen levels are cause for concern.[33]

In the United States, an appeal from the FDA in 2004 led to the Anabolic Steroid Control Act being passed. This act covers androstenedione and 17 other steroids which – as is the case in the Netherlands – may not be sold without a doctor's prescription. It is worth noting that this development led to the marketing of so-called designer nutritional supplements, containing new 'fantasy steroids', where the question is to what degree the substances are still anabolic steroids.

Extent of use

No precise figures are available on the use of prohormones. What is clear is that many so-called nutritional supplements are used to address assumed vitamin and mineral deficiencies. It is known that these supplements may be polluted by, among other things, prohormones.[63]

Growth hormone

Properties

There are a number of registered medicines available containing growth hormone (somatropin) made using recombinant DNA techniques.

Somatropin is a polypeptide created using recombinant DNA techniques that is analogous to human pituitary growth hormone. It stimulates longitudinal growth in children with growth hormone deficiency. Somatropin also stimulates tissue growth by increasing the number and size of skeletal muscle cells. It also affects carbohydrate metabolism; at higher doses, glucose tolerance may decrease and insulin resistance may develop. Lipolysis in fat cells increases under the influence of growth hormone. Sodium, potassium and phosphor retention occur through stimulation of cell growth, and nitrogen retention occurs due to increased protein synthesis.

Indications

Somatropin is registered for use in a variety of growth disorders. Studies show that administration of high doses of growth hormone during catabolic (postoperative) periods has no benefits whatsoever.

Side effects

In children with insufficient height growth, side effects of somatropin treatment were reported in 10% of cases. In adults, this percentage lies at 30-40%, primarily due to fluid retention. In the event of fluid retention, the dosage should be lowered. In some cases (4%), antibodies against somatropin were formed during treatment. The titre and binding activity of these antibodies proved low, however.[105]

The use of growth hormone as doping

The goal that growth hormone (GH) is primarily used for in sports is its effect on muscle mass. GH does not directly cause muscle growth; it works very indirectly by increasing the potential for protein synthesis, which increases the amount of insulin and anabolic steroids a person can use effectively. Many dosage schedules are used. Muscles may increase in size due to GH administration. The muscle mass in question does not lead to an increase in muscle strength.[34,64] Available research data do suggest an increase in lean body mass. This is countered by decreased stamina and an increase in side effects. Large amounts of anabolic steroids and often insulin need to be used alongside growth hormone in order to see any result; this is not the case for IGF. Growth hormone is also used as an anti-aging substance.

Side effects

A comparative study found higher rates of joint pain and carpal tunnel syndrome (nerve impingement) among growth hormone users.[34] Additionally, soft tissue swelling, breast growth, insulin resistance with an increased risk of diabetes mellitus[35] and extreme growth of hands, feet, nose and jaw (acromegaly) have been described. In a double-blind, placebo-controlled study with supra-physiological amounts of growth hormone. Cittadini found an increase in the relative thickness of the left ventricle of the heart in the growth hormone group.[36]

Extent of use

Growth hormone is used as an anti-aging substance by body builders. The majority of trade with this objective takes place on the black market. This has led to a large number of illegally important combined preparations on the market. In the

Netherlands, 6.6% of the 'have used at some point' group indicated they had used growth hormone.[28] Industry sources suggest that in the United States alone, trade with this purpose yields a turnover of 2 billion dollars per year.[35] Danish research among 702 general practices showed that 182 patients had used doping in the past year, nine of whom had used growth hormone.[39] The high costs limit the use of growth hormone, and anabolic steroids are also more attractive to users.[66]

Insulin-like Growth Factor I

Properties

In doping, Insulin-like Growth Factor I (IGF-I) is often used alongside growth hormone and insulin. IGF-I plays a role in growth hormone effects.

Mecasermine is recombinant human insulin-like growth factor 1 (rhIGF-I). Activation of the IGF-I receptor type 1 in the target tissue, which is homologous with the insulin receptor, leads to tissue growth and changes in carbohydrate and bone/mineral metabolism. Mecasermine is also used for growth disorders in medical practice.

Side effects are commonly reported during normal treatment with mecasermine. In practice, they are rarely a reason to interrupt/terminate treatment. The most common side effects are hypoglycaemia (in about 50%), lipohypertrophy at the injection size, tonsil hypertrophy and adenoid vegetations, headache and intracranial hypertension. Cardiac hypertrophy has also been reported. Due to the potential for complications caused by treatment with mecasermine, additional tests such as fundoscopy and echocardiographic imaging are required. One should also remain alert for symptoms of intracranial hypertension (papillary oedema, vision changes, headache, nausea and/or vomiting), complications associated with hypertrophy of lymphoid tissue and symptoms warning of hip dysplasia or progression of scoliosis (such as limping or pain in hips or knees). The risks of treatment in terms of neoplasia, antibody formation and organ growth require further investigation.

The use of Insulin-Like Growth Factor I (IGF-I) as doping

The increase in IGF-I stimulates conversion of glycogen into glucose and of fats into fatty acids. IGF is more effective than GH in directly causing muscle growth and increasing muscle density. IGF can also be used on its own. Unlike GH, it is

not necessary to also use large amounts of anabolic steroids as well as insulin to achieve results.

Side effects

The use of IGF-I may lead to severe hypoglycaemia.[40]

Extent of use

No precise figures are available on the extent of Insulin-like Growth Factor I (IGF-I) use.

Insulin

Insulin has an effect on carbohydrate, fat and protein metabolism. By combining growth hormone and insulin, users hope to stimulate the production and uptake of proteins.

The effect on carbohydrate metabolism is based on promoting uptake of glucose in liver, muscle and fat tissues. Additionally, insulin inhibits the production of glucose in the liver by inhibiting gluconeogenesis and promotes glycogen creation from glucose. The effect on fat metabolism consists of stimulating lipogenesis. It also inhibits lipolysis and release of free fatty acids from fat tissue. Insulin also promotes protein synthesis.

Side effects

The higher the doses, the higher the risk of (severe) hypoglycaemia. Hypoglycaemia may occur among other things due to overdose, eating too little or too late, alcohol, physical exertion and concurrent use of other medicines. Stimulation of the autonomic nervous system by low blood glucose levels (around 3.3 mmol/l) may lead to so-called adrenergic symptoms such as tremor, perspiration and palpitations. These symptoms warn of impending hypoglycaemia. Further drop of blood glucose concentration (to about 2.7 mmol/l) lead to neuroglycopaenic symptoms including dizziness, blurred vision and concentration difficulties. Awareness of hypoglycaemia decreases if adrenergic warning signs do not occur or only occur at lower blood glucose levels than neuroglycopaenic symptoms.

Atrophy or hypertrophy of subcutaneous fat may occur at frequent injection sites. This is often caused by incorrect injection technique. It can also be prevented by frequently changing injection site.

GH and insulin

In addition to an increase in muscle mass, GH leads to an elevation of blood glucose levels (glucose) and it stimulates the conversion of fats into fatty acids. Insulin, on the other hand, ensures storage of fatty acids, glucose and proteins. By combining GH and insulin, some body builders hope to strengthen the effects. However, there are major risks in doing so. In response to GH administration, the body will automatically make more insulin. If exogenous insulin is also administered, this leads to an abnormally high insulin concentration in the body. This will cause a severe drop in blood sugar levels, endangering the body's energy supply. The brain in particular is endangered, and brain damage or coma may result.[140] The combination of growth hormone and insulin – potentially combined with IGF-I – is commonly used in professional bodybuilding. Studies have been conducted that do not show the assumed anabolic effect.[67]

Extent of use

No precise figures are available on the use of insulin as doping.

Amphetamines, ephedra and amphetamine derivatives (ecstasy)

Properties

Amphetamines are medicines registered for the treatment of ADHD and depression. They are also used as appetite inhibitors in the treatment of weight problems. The street names of the illegal variants are Crystal Meth or Speed. The most important effects of amphetamines are arousal and a suppression of feelings of fatigue. The latter effect in particular led to wide use in sports.

Use of amphetamines as doping

Amphetamines have a performance-enhancing effect during short, explosive bursts of activity. For high-intensity endurance effects such as cycling, they have a performance decreasing effect.[67] For explosive activities such as shot-put and brief exertion like a 100-400 meter sprint, use appears to increase performance by 1-2%.

Side effects

Use is associated with a variety of psychological and physical effects. Euphoria, hyperalertness, emotional hypersensitivity with stress and anger may occur. There are also influences on heart rate, and pupil dilation and blood pressure changes occur.[45] In rare cases, liver disorders and epileptic seizures may occur. Amphetamine dependence may occur quickly, and is apparent in the inability to

sustain normal social and professional activities. In order to experience the same feeling, increasing amounts of the substance must be used. Physically, this may lead to severe weight loss, psychologically to paranoid delusions.

Extent of use

Ample data is available on amphetamine use in general. Less is known about use in unorganised sports. In the 'used at some point' group, 41.8% indicated they used stimulants[28] as well as 2.4% in the recent use group.[46,47]

Erythropoietin

Properties

Erythropoietin is a glycoprotein hormone produced in the kidney that, among other things, stimulates erythropoiesis. Currently, EPO or (long-acting) pegylated erythropoietin variants produced using recombinant DNA techniques are available.

Haematopoietic growth factors can specifically stimulate the production and functional activity of certain types of blood cells. In this way, they play a key role in the regulatory process of blood cell formation. The physiology of these factors has been known for some time; however, therapeutic application only became a possibility when recombinant DNA techniques allowed production on an industrial scale. Currently, the following erythropoiesis-stimulating substances may be identified: darbepoietin, epoietin-α, epoietin-β, epoietin-∂ (Dynepo) and Cera. Erythropoiesis-stimulating substances stimulate erythrocyte production. These substances are produced using recombinant DNA techniques, and immunologically and biologically identical or closely related to human erythropoietin (EPO), a glycoprotein primarily created in the kidney that regulates erythrocyte production in the bone marrow. The amount of erythropoietin produced depends on the relationship between oxygen provision to tissues and oxygen consumption. The EPO system has a feedback mechanism. Oxygen deprivation in tissues leads to increased EPO production and blood concentrations. More red blood cells are created; this lowers oxygen deprivation in tissues and EPO production decreases. Darbepoietin, epoietin-α, epoietin-β, epoietin-∂ (Dynepo) and Cera are available on the market. The protein chain is identical; the difference lies in the composition and position of the carbohydrate section or a link with a PEG molecule.

Darbepoietin has more carbohydrate residues compared with epoietin. This higher carbohydrate content gives it a longer elimination half-life than epoietin,

requiring less frequent administration. The mechanism of action is identical to epoietin.

Methoxypoyethyleneglycol epoietin-β is a continuous erythropoietin receptor activator with slower binding and quicker dissociation compared with erythropoietin. It has a significantly longer elimination half-life than darbepoietin and epoietin. Once titrated, it is administered once per month.

Recently, new, synthetic erythropoietin receptor agonists consisting of small peptides have been marketed (Hematide). These are not Epo analogues, but do bind to the receptor. These molecules have long-lasting effects.

The indication for all forms of erythropoiesis-stimulating substances is a variety of types of anaemia.

The use of Erythropoietin as doping

It has been shown that the use of EPO causes changes in performance comparable to blood doping. Maximum power and the ability to sustain a specific exertion improve significantly within 6 weeks of EPO administration. There may also be a direct effect on muscles.[68]

Extent of use

A Danish study among 702 general practices revealed 182 patients had used doping in the past year.[39] In this group, anabolic steroid use was common, but none of the interviewees had used EPO. EPO use gained widespread attention due to its use by professional cyclists and top athletes.[69]

The death of almost 20 European cyclists in the late 1980s and early 1990s is suspected to be related to EPO use. In 1998, a Tour de France team was removed from the competition due to EPO use, and six other teams left the competition.[70]

In a group of Dutch people who had admitted to using doping at some point, 3.8% indicated they had used EPO.[28] That EPO is also used in unorganised sports may be deduced from the content of a variety of websites.[71,72]

Side effects

The primary side effect of erythropoietic is flu-like symptoms. Blood pressure elevation is sometimes noted. There is also a significant risk of thrombosis.[49] Additionally, there have been reports of sporadically occurring erythrocyte aplasia in patients with chronic renal insufficiency treated with epoietin-α for

months or years. Methoxypoyethyleneglycol epoietin-β may lead to an elevated risk of vascular side effects compared to other epoietins. During sports, particularly in warm weather, this may also lead to an increase in blood cell content (hematocrit), which leads to increased blood viscosity, which ultimately may lead to circulatory problems or even circulatory arrest.[1]

Yohimbe

Properties

Yohimbe is the name for the dried bark of *Pausinystalia yohimbe* or *Corynanthe yohimbe*, a tree native to the tropical forests of West Africa. Double-blind studies have shown that yohimbe works as an aphrodisiac and a potency-increasing substance.[73]

Mechanism of action

Yohimbe's biological activity is primarily caused by yohimbine. Yohimbine is quickly absorbed after oral administration; the maximum plasma concentrations are achieved 10-60 minutes after ingestion. Yohimbine has psychoactive, local anaesthetic, sympathicolytic, pupil dilating, blood vessel dilating (primarily in skin, mucous membranes, genitals) and blood pressure lowering properties. Products prepared from bark are usually only weakly active. The mechanism of action of yohimbine is primarily based on blocking α-adrenergic receptors. These α−adrenergic receptors are mostly found in the smooth muscle tissue of the blood vessels. If these receptors are activated, contraction of smooth muscle tissue and vasoconstriction occur. The α-adrenergic receptor blockers, including yohimbine (=a2-adrenergic receptor blockers) antagonise this vasoconstriction and thereby promote blood flow in the tissues. Yohimbe is also reported to increase sensitivity to stimuli in the area of sacrum.[75]

Yohimbine overdoses have been described. Reported signs of yohimbe intoxication are: saliva flooding, nausea, diarrhoea, elevated heart rate, blood pressure drop or increase, persistent erections, muscle spasms, anxiety, emotional arousal, restlessness, manic behaviour, hallucinations, bronchospasm, disrupted signal transfer in the brain, hypothermia and decreased heart muscle contractility. Excessive use may have hallucinogenic effects.

Interactions

Because yohimbine has MAO-inhibiting activities in-vitro, serious interactions following combined use with certain medicines and foodstuffs cannot be ruled out.[141]

Interactions with medicines

Serotonin plays a role in the genesis of depression, and there are numerous medicines on the market that affect serotonin levels. Examples of medicines that work by influencing serotonin concentrations are tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) and MAO inhibitors. If therapeutic use of such medication is combined with recreational use of hallucinogens and/or herbal MAO inhibitors, severe side effects may occur. The activity of tryptamines may be increased manyfold, and the effects may last longer. Mutual potentiation of effects may lead to the development of serotonin syndrome; this is characterised by severe hypertension, hyperexia (extremely high fever > 42°C) and convulsions.

Interactions with foodstuffs

Combination of (herbal) MAO inhibitors with certain amines, particularly tyramine, may lead to a severe hypertensive crisis. Normally, tyramine is broken down by MAO. A MAO inhibitor causes tyramine build-up. Tyramine absorbed from the gastrointestinal tract combined with MAO-inhibiting activity may shift noradrenalin out of adrenergic neurons. This excretion of noradrenalin may cause severe hypertension with symptoms include headache, vision disorders, chest pain, elevated or lowered heart rate and intracranial bleeding. Nausea, vomiting, perspiration and fever may also occur. Care is required when it comes to eating foods with high tyramine concentrations while using a MAO inhibitor. Products with high amine contents (tyramine and others) are: fermented proteins, meat and yeast extracts, soy products and sour dairy products, certain cheeses (including Camembert, Cheddar and Stilton), red wine, certain alcoholic beverages, heavy beers, chocolates, non-fresh meat and fish products, avocados, overripe bananas and fava beans.[75]

The use of Yohimbe as doping

The promotional text on a pot of Yohimbe makes the following claim: “Yohimbe is known in the athletic world for its positive effect on strengthening muscles. This dietary supplement provides its positive contribution to muscles, joints and the stomach. This formula is particularly recommended for bodybuilding, high-level athletics, weight lifting and fitness.” Research does not support this claim.[74]

Extent of use

No specific data is available on the use of Yohimbe in unorganised sports.

Gamma Hydroxy Buteric Acid (GHB) and similar substances

Properties

Gamma Hydroxy Buteric Acid (GHB) occurs naturally in the body. It is a building block of the neurotransmitter Gamma Amino Buteric Acid (GABA). GHB is converted to water and carbon dioxide by the body's metabolism. No active metabolites are formed. GHB is first converted to succinate semialdehyde by GHD dehydrogenase, which is converted into butane diacid via succinate semialdehyde dehydrogenase (SSADH), which then enters the citric acid cycle and is converted to CO2 and water. It is also oxidized to 3,4-dihydroxybutyrate, which is also converted into CO2 and water by the citric acid cycle.[142]

In the late 80s, GHB gained notoriety as a substance that could stimulate growth hormone production, promote muscle growth and lead to fat tissue breakdown. Body builders in particular started using the substance because of this. In the United States, GHB was sold in health stores until the FDA banned it in 1990.[71,76]

In the illegal circuit, GHB is available as a recreational drug in the form of (white) powder or granules. It is mixed with water before use. GHB is also available as a fluid, but the purity and concentration of these solutions vary greatly. The liquid form of GHB is transparent, has no smell and a salty taste. GHB tablets and capsules are also available.

After ingestion as a fluid, GHB is quickly absorbed from the gastrointestinal system (within 15-30 minutes). GHB absorption decreases by 37% if taken after a fatty meal. GHB undergoes first-pass metabolism, with biological availability at about 25%.

The chemical structure of GHB is highly analogous to neurotransmitters gamma amino buteric acid (GABA) and glutamic acid. GHB is formed from GABA, and occurs naturally in the body. In the brain, where it is found in low concentrations, it has neurotransmitter properties. GHB plays a role in temperature regulation, blood flow and conversion of glucose in the brain, as well as in the initiation of sleep cycles.

GHB administration is thought to decrease the release of dopamine by dopaminergic neurons in the brain, while inducing accumulation thereof by acti-

vating tyrosine hydroxylase. At lower doses, the opposite effect may occur. The feeling of euphoria experiences after recreational use of GHB may be due to the increased dopamine concentration in the brain.

GHB also affects endogenous GABA-ergic and opioid systems, but the precise mechanism of action is not yet entirely understood. The effects may be caused by enzymatic conversion of GHB into GABA (indirect effects) as well as an interaction of GHB with specific GHB receptors (direct effect).

It remains unclear which factors play a role in the natural regulation of GHB concentration in the brain. GABA is the main GHB precursor in the brain, but 1,4-butanediol may be a GHB precursor in liver and brain, and enzyme succinate semialdehyde reductase may play a role in biosynthesis. GHB is also found outside the central nervous system, but the biochemical role of GHB outside the brain has not yet been clarified. Various studies have shown that GHB can limit tissue damage in the event of oxygen deprivation, including during sepsis, blood vessel blockage or shock caused by major blood loss. The fact that most patients recover fully within a few hours of a GHB overdose, while it caused severe respiratory depression for a few hours, may be linked to this.

GHB is used in the treatment of sleeping disorders (narcolepsy) because of its ability to initiate certain sleep cycles and a positive effect on the sleeping patterns of narcolepsy patients. GHB stimulates slow-wave sleep at the cost of sleep stages 1 and 2 without affecting REM sleep. Symptoms that may occur due to narcolepsy (abnormal sleeping tendencies, cataplexy, hallucinations occurring at the beginning of sleep, sleep paralysis and disturbed nightly sleep) are reduced by GHB. The exact neuropharmacological mechanism of action is not entirely clear. Mechanism of action in alcohol addiction therapy: the decrease in the intensity of alcohol withdrawal symptoms after GHB administration is thought to be caused by GHB's analogous effects on the central nervous system. GHB, like alcohol, causes decreased neural activity, which likely stems from an interaction between GHB and the GABAB receptor. GHB’s interaction with dopamine and serotonin release may also play a role.

GHB became popular as a recreational drug, as the substance may cause euphoria and supposedly worked as an aphrodisiac. At higher doses, GHB is used as a sleeping medicine. After an incident in which six people became comatose after using GHB together with alcohol, the substance has been banned in the Netherlands since 1996 unless prescribed as a medication.

In the media, GHB has been associated with sexual abuse, and is known as the date rape drug.

Originally, Gamma Hydroxy Buteric Acid (GHB) was developed as an anaesthetic in the 1960s. It is currently no longer used as such, as it can cause side effects including myoclonia and vomiting, and safer alternatives have been developed.

The use of Gamma Hydroxy Buteric Acid as doping

In the late 80s, GHB gained notoriety as a substance that could stimulate growth hormone production, promote muscle growth and lead to fat tissue breakdown. Body builders in particular started using the substance because of this. In the United States, GHB was sold in health stores until the FDA banned it in 1990.[71,76]

Extent of use

The use of 'smartdrug' GHB appears to be increasing steadily among gym visitors. It is used as an alternative to anabolic steroids and to supplement a course of steroids. In both cases, the assumption is that GHB helps build muscle by stimulating growth hormone release. Australian research found a percentage of 0.5% 'used at some point' and 0.1% 'used in the past year'.[52-54]

D.2 Substances that counteract side effects of other doping substances

Selective Estrogen Receptor Modulators (SERMs)

Properties

Various substances are used to counter the effects of female hormones. The degree to which bodybuilders suffer from oestrogen overdose is not really known, and in part depends on the type of AAS used, specifically aromatisable versus non-aromatisable. A little more is known about which SERMs are used. A few serious studies have been performed, although most are quite dated. Two British studies performed 10 years ago showed that Tamoxifen is the most commonly used SERM. User percentage was 5% in one study and 23% in the other. The Dutch study by de Boer among Dutch professional bodybuilders showed that Tamoxifen and Clomifene were particularly popular.[57] 18% of men used Tamoxifen regularly, and 14% used clomifene.[81] A more recent study by TNO (2003) showed that one-third of anabolic steroid users use substances to counter the side effects. It did not ask which substances were used.

Clomifene

Properties

Clomifene is a non-hormonal ovulation induction substance. It binds with the oestrogen receptor in the thalamus, inhibiting the feedback mechanism that regulates the production of oestrogen. This leads to elevated FSH and LH levels, stimulating sexual organs and possibly leading to ovulation.

Indications and contraindications

Anovular sterility, caused by functional disorders in the hypothalamus-pituitary-ovarium axis, in women with a desire to become pregnant. The substance may not be used in the event of liver insufficiency, icterus and any changes in liver function. It is also contraindicated in unexplained vaginal bleeding, ovarian cysts and primary pituitary or ovarian dysfunction. Oral ovulation-inducing substances must be prescribed by or in consultation with a specialist with experience in this field.

Side effects

Gastrointestinal complaints such as (pressure) tenderness, bloated feeling, rising and enlargement of the ovary. At high doses, ovarian hyperstimulation syndrome may occur. Vision disorders (blurred vision, spots). Sometimes: nausea, vomiting, depression, fatigue, sleeplessness, dizziness, headache, chest pain, excessive menstruation, intermenstrual spotting, weight gain, urticaria and allergic dermatitis, pollakisuria, reversible hair loss, sensitive breasts. Increase in bromosulphalein retention.

Use as doping

Clomifene is used by anabolic steroid users at the end of a course of treatment to stimulate the production of testosterone by the body itself. Clomifene has ‘oestrogen blocking’ functions, meaning: it attaches to receptors that oestrogens can also bind to. This way, Clomifene prevents oestrogens (particularly estradiol) from causing side effects such as fat build-up in the hips and gynaecomastia. The substance may also increase testosterone production. As it also binds to oestrogen receptors in the hypothalamus, it stimulates the pituitary gland to, among other things, release more lutenising hormone. In turn, LH stimulates the testes to produce more testosterone.

Tamoxifen

Tamoxifen primarily has anti-oestrogen effects due to blocking of oestrogen receptors in hormone-sensitive conditions such as breast cancer. Fulvestrant is a selective anti-oestrogen without agonist properties.

Properties

Non-steroid triphenylethylene derivative. It has an anti-oestrogen effect on breast tissue. It also exhibits weak oestrogen effects on endometrium (stimulating endometrium, leading to an elevated risk of endometrial carcinoma), on bone in postmenopausal women (inhibition of bone resorption), and the pituitary and blood lipids (lowering of total and LDL cholesterol). The precise mechanism of action is unknown, and may be due to direct binding with the oestrogen receptor, leading to disruption of RNA transcription and decreased cellular proliferation. The latter is also caused by an influence on growth factors. The affinity natural oestrogens have for the oestrogen receptor is far greater than that of Tamoxifen. In premenopausal women, an increase in oestrogen and progesterone levels occurs; in postmenopausal women, Tamoxifen use does not affect oestrogen levels.

Indications

Palliative treatment of hormone-sensitive tumours such as breast cancers. Tamoxifen may only be prescribed by or following instructions from a specialist with experience with oncology.

Side effects

Most common: hot flushes, nausea and vomiting. Also: vaginal bleeding, pruritus vulvae, irregular periods or amenorrhoea. Uncommon: eye disorders such as cataracts, retinopathy, keratopathy and neuritis optica. Also: depression, headache, dizziness, fatigue, weight gain, hirsutism, alopecia, skin rash (including incidents of erythema multiforme, Stevens-Johnson syndrome and bullous pemphigoid), blood dyscrasia, hypercalcemia and thromboembolic complications. Rarely: hypersensitivity reactions, including angio oedema. Ovarian cysts have been reported in premenopausal women. Pancreatitis and liver function disorders have been reported, as well as – in rare cases – severe liver disorders including cholestasis, hepatitis and fatty liver disease. An increased incidence of endometrial abnormalities, including hyperplasia, polyps and carcinoma have been reported. Fibromyomas of the uterus have been observed. Elevation of triglyceride levels has been reported.

Interactions

The effects of anticoagulants of the coumarin type may be potentiated. When combined with cytotoxic substances, there is an elevated risk of thromboembolic complications.

Overdose

Symptoms: in cases of severe chronic overdose, neurotoxic effects may occur (such as dizziness, tremor, hyperreflexia, respiratory depression, ataxia and convulsions) as well as an increased QT interval on the ECG.

Use as doping

Tamoxifen may in part prevent oestrogen effects. However, it cannot prevent the formation of oestrogens. The use of Tamoxifen is associated with mild side effects of a transient nature, such as hot flushes, nausea and vomiting. In exceptional cases, use may lead to severe side effects.

Tamoxifen is mostly used to counter early gynaecomastia. No good data is available on the incidence of gynaecomastia among anabolic steroid users. In one of the few scientific studies performed in a group of Dutch competitive bodybuilders (116 men in total), over 20% were found to suffer from it.[57] It appears that men who suffered from sensitive and hard nipples and/or breast growth during puberty are at higher risk of gynaecomastia. They are likely more susceptible to it. The effectiveness in terms of countering gynaecomastia displays significant individual variability.

Aromatase inhibitors

Properties

Aromatase inhibitors prevent conversion of androstenedione and testosterone into estrone and estradiol, respectively, by enzyme aromatase in peripheral tissues. Aromatase is present in 60-70% of breast cancers. Aminoglutethimide, anastrozole and letrozole are non-steroidal aromotase inhibitors. Exemestane is a steroidal aromatase inhibitor. Aminoglutethimide is a non-selective aromotase inhibitor that is no longer used for the treatment of breast cancer. It also inhibits other enzymes, inhibiting the synthesis of glucocorticoids, mineralcorticoids and other steroids and leading to adrenal insufficiency. This means substitution therapy with hydrocortisone is required. Anastrozole, exemestane and letrozole are selective aromatase inhibitors that do not require concurrent treatment with hydrocortisone. Aromatase inhibitors are used in the treatment of surgically removable, hormone-sensitive breast cancer (adjuvant use) and the treatment of

no longer surgically removable and/or metastasised hormone-sensitive breast cancer. The major side effect of selective aromatase inhibitors consists of symptoms of oestrogen deprivation. This is also seen with fulvestrant. When progesterones are used, weight gain is the primary effect, and cardiovascular side effects may occur.

Indications

Antihormones are used in regular medical care for the treatment of adrenal adenoma or carcinoma, endometrial carcinoma, prostate carcinoma and breast carcinoma. In breast carcinoma, primary treatment consists of surgical treatment supported by radiotherapy, chemotherapy and/or hormonal therapy. The usefulness of adjuvant therapy with (anti)hormones or chemotherapy has been demonstrated by clinical research. Hormonal therapy is an alternative to chemotherapy, particularly for certain older patients.

Use as doping

Aromatase inhibitors slow the production of oestrogens, as compared to a substance like Tamoxifen which blocks the effect of oestrogen. The effects are largely analogous to those of SERMs: prevention of gynaecomastia and subcutaneous fat build-up, stimulation of endogenous testosterone production. The doses recommended to bodybuilders in underground books are equivalent to those used clinically in women.

Side effects

The key side effect of selective aromatase inhibitors are symptoms of oestrogen deprivation such as hot flushes, headaches, nausea and diarrhoea.

Extent of use

No precise figures are available on the use of aromatase inhibitors such as doping.

Gonadotropic hormones

Two gonadotropic hormones are formed in the anterior pituitary gland: follicle stimulating hormone (FSH) and lutenising hormone (LH). Both hormones are glycolate polypeptides. The effects depend on gender. In men, FSH stimulates the development of seminal tubules (channels in the testicles that produce sperm) and the formation of spermatozoa, while LH stimulates leydig cells to form testo-

sterone. In women, the gonadotrophins have no effect on testosterone production and therefore do not work as doping.

Properties

Human menopausal gonadotrophin (HMG) is prepared from the urine of postmenopausal women. HMG contains roughly equal parts of FSH (follicle-stimulating hormone) and LH (lutenising hormone). It stimulates ovum ripening. FSH and LH created using recombinant DNA techniques are now available, follitropin-α and follitropin-β, and LH, and lutropin-α, respectively. Follitropin-α and follitropin-β are identical with regard to the protein chain, only the glycolisation is different.

Human chorionic gonadotrophin (HCG) is prepared from the urine of pregnant women, and mostly displays LH activity. If it is administered at a suitable moment after treatment with HMG or urofollitropin, it leads to ovulation. Chorionic gonadotrophin alpha is made using recombinant DNA techniques and has the same amino acid sequences as HCG obtained from urine. HCG has limited value as doping for men.

Indications and contraindications

The use of gonadotrophins is gender-dependent.

In men, indications include retentio testis; a course of HCG is given for six weeks (before puberty). Ectopic or retractile testes are not an indication.

A second indication in men is secondary hypogonadism caused by hypopituitarism, but only if restoration of fertility is desired. HCG is used in combination with HMG. These courses must be taken under close sperm count monitoring. Before starting, the partner's fertility must be likely. Sperm count may be restored within six to twelve months. In congenital forms of hypogonadism (Kallmann syndrome), the testicles are so underdeveloped that such treatment courses must be taken for very long periods. If the goal is not restoration of spermatogenesis, the androgenic functions of the testes must be substituted with androgenic hormones, as is the case with primary hypogonadism.

In women, gonadotropic hormones are used in ovulation induction in cases of anovulation or decreased ovulation as well as part of artificial reproductive techniques.

Side effects

In men, high doses may lead to water and salt retention due to excessive androgen production. Incidental cases of gynaecomastia have been reported.

Use of gonadotrophins as doping

As testosterone production drops dramatically after a course of anabolic steroids, human choriogonadotrophin (HCG) is used as doping to stimulate testosterone production. As this does not restore the natural cycle, it merely delays natural production.

Extent of use

No precise figures are available on the use of gonadotropic hormones as doping.

Isotretinoin

Isotretinoin is used to counter anabolic steroid side effects, specifically acne formation.

In normal medicine, Isotretinoin is reserved for the treatment of severe, therapy-resistant forms of acne. Given the severe side effects and teratogenicity, current treatment guidelines recommend that only doctors with experience using systemic retinoids prescribe it.

Properties

Synthetic stereo-isomer of tretinoin (vitamin A acid); the mechanism of action is not entirely understood. It reduces sebaceous gland size, inhibits sebum excretion and has an anti-inflammatory (in the dermis) and anti-euplastic effect. Lowered HDL concentrations have been observed.[143]

Contraindications

Hepatic and renal insufficiency. Hypervitaminosis A. Strongly elevated blood lipid levels. Women of childbearing age, unless pregnancy has been ruled out definitively and adequate contraceptive measures have been taken. Before initiating treatment with Isotretinoin, the doctor must inform women of childbearing age of the potential harm Isotretinoin may cause to the unborn child.

Side effects

Most side effects are dose-dependent and reversible. Very common (>10%): symptoms of hypervitaminosis A, including dry and/or flaking skin (mostly on hand

palms and soles of the feet), dry mucosa (lips, nasal cavity, pharynx, conjunctiva) and conjunctivitis. Also: eye irritation, thinning of the skin, itch, exanthema, dermatitis, chelitis, blepharitis, muscle and joint pain, back pain, thrombosis, elevation of liver enzyme levels, and, particularly in predisposed patients (family history of lipid metabolism disorders, diabetes mellitus, obesity or alcohol abuse), anaemia, elevated erythrocyte sedimentation rate, thrombocytopaenia, elevated triglyceride levels and lowered serum HDL concentrations. Common (1-10%): headache, nasopharyngitis, epistaxis, elevated cholesterol levels, hyperglycaemia, neutropaenia, haematuria, proteinuria. Rare (0.1-1%): allergic skin reactions, anaphylactic reactions, (worsening of) depression, aggression, anxiety, mood changes, (reversible) alopecia. Very rare (0.01-0.1%): acne fulminans, worsening of acne, malaise, nausea, bowel inflammation, gastrointestinal bleeding, hepatitis, pancreatitis, glomerulonephritis, hyperurikaemia, elevated creatinine phosphokinase levels, diabetes mellitus, lymphadenopathy, benign intracranial hypertension (with symptoms of papillary oedema, headache, nausea, vomiting, vision disorders), convulsions, sleepiness, vision disorders, (reversible) clouding of the cornea, cataract, night vision adaptation problems, photophobia, keratitis, loss of hearing, vasculitis, bronchospasm, hoarseness, thinning of hair, hirsutism, hyperpigmentation, hyperhidrosis, nail dystrophia, paronychia, granuloma pygenicum, osteoarthritis, calcinosis, exostosis, early closing of epiphiseal disks, decreased bone density, tendonitis, psychotic reactions, (attempted) suicide, suicidal thoughts, menstrual disorders. In men, gynaecomastia and impotence have been described. Soy oil may cause severe allergic reactions in rare cases.

Interactions

Do not use concurrently with tetracylins due to the danger of benign intracranial hypertension. Avoid concurrent use of vitamin A supplements. Do not use together with low-dose progesterone contraceptive pills (‘mini pill’), because Isotretinoin may decrease the contraceptive effect of the pill. Due to an increase in local irritation, do not use together with keratolytic or exfoliative anti-acne substances.

Warnings and precautions for use

Care is required if there is a history of depression. Before initiating treatment, liver function, (fasting) triglycerides and serum lipids should be checked. Check liver function and triglyceride levels after one month, and then every 3-4 months (triglycerides more frequently if a predisposition exists for hypertriglyceridemia and in cases of (suspected) diabetes mellitus). Check serum lipids after treatment is ended. In the event of vision disorders, the ophthalmologist should be con-

sulted. Patients should be warned that sudden disturbances in night vision adaptation may occur during treatment. In early stages of therapy, a brief worsening of acne may occur. Concurrent exposure to UV radiation should be avoided. Do not donate blood during treatment with Isotertinoin and for one month after stopping, due to the potential risk to the foetus if a pregnant woman receives a transfusion. In women of childbearing age, start treatment on the second or third day of the next normal menstrual cycle. Follow-up appointments should take place every 28 days. They should be given understandable information about preventing pregnancy and use at least one additional contraceptive method, including a barrier method. Avoid aggressive dermabrasion and depilation during and for at least 5-6 months after treatment with Isotretinoin due to the potential for scarring or dermatitis.

Overdose

In the event of acute vitamin A toxicity, characterised by severe headache, nausea or vomiting, sleepiness, irritability and itch, treatment must be stopped. Gastric lavage in the first hour after ingestion of very high doses may be useful.

It has been demonstrated that the total cumulative dose is more important than the daily dose during maintenance treatment; a cumulative dose of 100-200 mg/kg leads to more lasting treatment results.

Prescriptions for women of childbearing age must be limited to 30 days.

Extent of use

Bodybuilder websites indicate that using Isotretinoin during a course of anabolic steroids (to prevent acne) is a normal phenomenon.[82]

D.3 Substances for improving appearance

Clenbuterol/beta-sympathicomimetics

Properties

Clenbuterol is a bronchodilator. In the Netherlands, this substance is solely available for the treatment of horses with (severe) asthma. It is a β2-sympathicomimetic with anabolic[83] and lipolytic properties.[84]

Its function is comparable to that of ephedrine, but the effect lasts longer. Clenbuterol is usually prescribed for a four to six week period.

When β-sympathicomimetics are used as bronchospasmolytics, effects on the cardiovascular system including elevated heart rate, heart-minute volume and vasodilatation are undesirable. The influence on the circulatory system may lead to an increase in blood flow through parts of the lung that ventilate poorly. Although lung ventilation improves under the influence of β-sympathicomimetics, blood flow in poorly ventilated alveoli may increase, leading to worsening of hypoxia (which is often present in obstructive pulmonary disease). Hypoxia also increases the heart's sensitivity to the sympathicomimetic. The maximum available decrease in bronchial obstruction is roughly the same for all sympathicomimetics, although the required dose differs.

For regular athletes with asthma, the WADA has drafted strict criteria on how to deal with these medicines.

Sympathicomimetics with primarily β2-adrenergic activity generally have minimal influence on heart rate and blood pressure. At high doses or following frequent use, these substances also cause tremors of the hands, headache, dizziness and nausea. High doses may also lead to hypokalaemia, tachycardia and arrhythmia. Fewer side effects may be expected from inhalation compared to oral use, as the lower inhaled dose leads to lower blood concentrations and fewer side effects. Myocardial ischemia has been associated with salbutamol. Low doses of ephedrine may lead to sleeplessness, tremors, restlessness and miction disorders in susceptible patients.

The use of Clenbuterol/beta-sympathicomimetics as doping

Clenbuterol is used as doping by, among others, body builders and cyclists for its anabolic effects. In the bodybuilding circuit, Clenbuterol is not primarily used for the anabolic effects (more suitable substances are available) but due to the effects on fat metabolism. The user is looking for a 'taut and dry' look. As a weight loss drug, a three week course of tablets is recommended, during which the dosage is slowly increased until side effects occur, after which the course is completed at a slightly lower dose.[88]

Side effects

Various publications report heart attacks in young users of Clenbuterol, sometimes in combination with anabolic steroids.[83,84]

Extent of use

6.1% of the 'used at some point' group has used Clenbuterol/beta-sympathicomimetic hormones as doping.[28]

Thyroid hormone

Properties
Thyroid hormones can counter the effects of decreased thyroid function.

The use of thyroid hormones as doping
Thyroid hormones are used in sports to stimulate metabolism and thereby lose excess fat. The increase in metabolism also affects (valuable) muscle proteins. If the use of the substance is ceased, the opposite will occur, namely slowed metabolism and increased fat storage. However, the body's own production of thyroid hormone may be decreased for a long time or even permanently lowered or stopped entirely.

Side effects
Side effects are seen in the event of overdose, and if substances are used for the wrong indications, such as overweight. Severe psychological restlessness, sleeplessness, tremors, palpitations and cardiac arrhythmias may occur. Long-term use of doses that lead to suppression of the thyroid stimulating hormone (TSH) may lead to bone loss.

Extent of use
The incidence of hypothyroidism in general practice is 1.2 per 1 000 per year. 3.3% of the 'used at some point' group have used thyroid hormones.

Lipostabil

Properties
Lipostabil is an injectable substance with the active ingredient soy lecithin.

The use of Lipostabil as doping
Lipostabil is used for the treatment of stubborn local fat build-up. The substance is injected directly into the problem area.

Side effects
In a limited prospective study among 739 people, other than local symptoms such as bruising, no generalised effects were noted.[86]

Extent of use

The substance is widely used in aesthetic clinics, but the overall extent of use is unknown.[89]

Synthol

Properties

The product Synthol is a collection of MCT (Medium Chain Triglycerides – C8, C10 and C12) combined with a disinfectant (Benzylalcohol) and a local anaesthetic (Lidocaine).

The use of Synthol as doping

The substance is advertised as a lubricant, but the common procedure is to inject Synthol deep into the centre of smaller muscle groups – such as biceps, triceps, shoulders and calves – with the goal of imitating muscle mass. Usually a 1 ml injection is used to begin with. This is repeated daily or every other day for ten days. The amount is then increased to 1.5 to 2 ml per injection for another ten days. If the desired result has not been achieved, the amount is further increased to 3 ml. At this point, injections are usually stopped, with maybe a brief 'additional injection' of 1 or 2 ml right before a competition.

Side effects

There are a number of risks for the user: injection abscesses, inflammation, embolisms, stroke and heart attack.[87] A notorious case is that of professional bodybuilder Milos Sarcev, whose life was endangered a few years back when some of the injected fat entered the bloodstream and almost caused a heart attack.

Extent of use

Injecting fat deep into the muscle tissue is not uncommon, and has become common practice at the highest levels of competitive bodybuilding (www.eigenkracht.nl).[90]

D.4 Other substances

Diuretics

Properties

Diuretics increase excretion of sodium chloride and water by decreasing resorption in the kidneys. Diuretics are divided into osmotic diuretics, loop diuretics,

thiazide diuretics and potassium-sparing diuretics. They affect different areas of the kidney. Loop diuretics are most relevant to doping. They are discussed in greater detail below.

The indications for various groups of diuretics are: oedema, hypertension, idiopathic calciuria, calcium containing kidney stones, hypercalcaemia and forced diuresis in the event of intoxications.

Side effects

Side effects are generally limited to disruption of water and electrolyte balance.

Decreasing the effects of circulating volume

Aggressive therapy with diuretics may lead to dehydration and a decrease in circulating volume, leading to symptoms of sleepiness, malaise, orthostatic hypotension and muscle cramps. However, these side effects may occur at lower doses in susceptible patients such as the elderly. It is important that the patient drink sufficient fluids when using loop diuretics in particular. However, drinking too much fluid may lead to hyponatraemia (with a risk of brain oedema). Regular monitoring of hydration and electrolytes (particularly sodium and potassium) when using loop diuretics in particular is indicated.

Hypokalaemia

Loop and thiazide diuretics lead to increased exchange of sodium for potassium, leading to increased sodium availability in more distal segments. Hypovolaemia and underlying diseases (heart failure, liver cirrhosis) can increase aldosterone secretion, leading to stimulation of this active co-transport Na+/2Cl-/K+/NH4+. This results in increased potassium loss.

Other effects on water and electrolyte balance

The occurrence of hyponatraemia and hypomagnesaemia may occur during loop or thiazide diuretic use. Hyponatraemia occurs in both, and may have serious side effects Water and electrolyte imbalance.

The increased exchange of Na+/K+ in the distal tubules and collection tubules promotes the local counter transportation of K+/H+. Therefore, intensive use of loop and thiazide diuretics may lead to hypochloremic alkalosis.

Other side effects

Increase in serum lipids. A number of short-term studies found high doses of diuretics were associated with increases in LDL, VLDL, total cholesterol and triglycerides. The degree to which these serum lipids were influenced did differ, however. In long-term studies, the listed negative effects could not be confirmed; no significant elevation of cholesterol levels was seen.

Loop and thiazide diuretics increase uric acid concentrations in the blood, which can trigger attacks of gout in predisposed individuals. If asymptomatic, uric acid elevation does not require treatment. Furosemide and bumetanide are ototoxic, which may manifest as tinnitus, deafness, dizziness and pressure in the ears. In some cases, deafness is not reversible. Ototoxicity is more common following intravenous administration than with oral administration. Ototoxicity may be potentiated by aminoglycosides. Bumetanide appears to be more ototoxic than Furosemide.

Interactions of diuretics

The natriuretic properties of diuretics are inhibited by prostaglandin synthesis inhibitors (NSAIDs). The latter substances also negatively influence glomerular filtration, albeit mildly. However, severe renal insufficiency may occur if dehydration caused by strong acting diuretics is combined with administration of a prostaglandin synthesis inhibitor. This may result in pulmonary oedema and acute heart failure. If a potassium sparing diuretic is used alongside the combination of a diuretic/NSAID, life-threatening hyperkalaemia may occur.

Patients treated with an ACE inhibitor or AT1 antagonist may also develop severe hypokalemia if combined with a potassium-sparing diuretic.

An aldosterone antagonist, combined with a ‘regular’ diuretic and salt restriction, is a strong volume-depleting combination, as it breaks through the natural protective measures; this is not without dangers, particularly at high doses.

Increased resorption in the proximal tubule leads to increased lithium concentrations if diuretics are used.

The use of diuretics as doping

Diuretics are medicines that increase urine production, and are used for various reasons in (professional) sports. The World Anti-Doping Agency (WADA) placed them on the doping list as substances that are prohibited both during and outside of competitions (in other words, at all times). Diuretics belong to the group of masking substances, although they are also seen as separate doping sub-

stances. Diuretics cause an increase in urine production. This decreases the odds of finding illicit substances. As fluid is also excreted, body weight is lowered, which would allow the user to enter a lower weight class or improve performance. An example of the latter would be climbing sports. Jockeys, ski jumpers and gymnasts have also been found using diuretics.

Side effects

Aggressive therapy with diuretics may lead to dehydration and a decrease in circulating volume, leading to symptoms of sleepiness, malaise, orthostatic hypotension and muscle cramps. Medical literature has described a case of a 31 year-old body builder using diuretics who developed a heart attack.[91] He experienced chest pain on stage and collapsed. He was subsequently taken to the emergency department. He had used anabolic steroids and amphetamines for 5-10 years. Before the competition, he had taken a combined diuretic with – among other things – a potassium-sparing effect. He also took potassium and magnesium supplements for his health. At the emergency department, it soon became apparent he had extremely high potassium concentrations in his blood.[93]

Extent of use

Research among German adolescents found that 0.1% indicated they had used diuretics in the past year. In a specific group of gym visitors, the percentage was 4.2%.[59]

Gene doping

Properties

The goal of gene doping is to use genetic technology to promote tissue build-up, for example red blood cells or muscle cells, or certain substances that prevent breakdown of these tissues or substances.

The use of gene doping

Results from animal experiments (transgenic mice) show effectiveness. However, there are only a few known potential ‘performance-enhancing’ genes for humans. The most promising substances have local effects and leave behind no or almost no traces in blood or urine.[92,95]

Side effects

Insufficient data available at this time.

Extent of use

Although doping authorities are worried about the potential, there is currently no evidence of any use in competitive sports.