

## **Anabolic-androgenic steroids – muscle and man**

### **What are anabolic-androgenic steroids?**

Testosterone is a steroid hormone synthesised in the human body from cholesterol. In the adult male it regulates muscle protein building, sexual functions, red blood cell maturation, plasma lipids, bone metabolism and brain functions regarding knowledge and awareness. The discovery of testosterone in 1935 has given rise to the production of anabolic-androgenic steroids (AAS) which are synthetic derivatives of testosterone. These compounds are modified to enhance the anabolic, that means muscle building, and minimise the androgenic effects. Androgenic means the influence on the male sex characteristics.

After oral intake, testosterone is absorbed from the small intestines and rapidly degraded in the liver, mostly to inactive compounds. Therefore, synthetic anabolic steroids are modified not only to alter the relative anabolic-androgenic potency, but also to slow the rate of inactivation and change the pattern of degradation.

Alkylated derivatives of testosterone are relatively resistant to hepatic degradation which makes them especially suitable for oral intake. Commonly used are stanozolol, danazol, fluoxymesterone, methyltestosterone, methandrostenolone, oxandrolone and oxymetholone. Esterification makes the hormone more soluble in the lipid vesicles used for injection. This slows the release of the steroid into the circulation. Examples of these AAS are nandrolone decanoate, boldenone, trenbolone, methenolone and testosterone enanthate.

### **Action of anabolic-androgenic steroids**

The growth of skeletal muscle induced by testosterone reaches a plateau once the normal physiological concentration is exceeded. Some say that the effect of excessive doses of testosterone on muscle is due less to its androgen action but rather to a blockage of the effects of the so called glucocorticosteroids. These are hormones that stimulate glucose synthesis by breaking down proteins. According to one theory, the high doses of anabolic steroids used by athletes inhibit this break down of muscle protein finally leading to a muscle-building effect.

### **Dangers of using anabolic-androgenic steroids**

The trade-off for any desired effect of AAS is the myriad of adverse side-effects that jeopardise health. In general, oral AAS have more adverse effects than injected AAS. The above mentioned alkylated AAS have potentially more adverse affects, particularly to the liver. One of the problems with sportsmen, in particular strength athletes and bodybuilders, is the “stacking” routine of intake:the use of oral and injected AAS at the same time in doses that may be up to 40 times the recommended dose for therapeutic purpose in medicine. The frequency and severity of side-effects varies with the type of drug, dosage, duration of use as

well as the individual sensitivity and response. The potential adverse effects of AAS can be divided into five main categories:

Heart and vessels: Chronic use of AAS reduces the amount of high-density lipoprotein (HDL) which are also called "good" or heart protecting lipids in the blood. Since HDL binds cholesterol, reduced HDL levels are associated with arteriosclerosis.

Liver: Oral AAS appear to exert a more severe adverse effect on the liver than injected AAS. Nevertheless, lesions of the liver have been reported after injections of nortestosterone. Patients who received anabolic steroids as a treatment for different diseases for prolonged periods showed impaired liver function.

Hormones and reproduction: Intake of AAS may reduce testosterone levels in males and thereby influences the development of spermatid cells, leading to a severe decrease of fertility. Sperm count declines of up to 73% or even azoospermia, which means a complete absence of sperm cells, when high doses of anabolic steroids were taken for long periods of time. In-depth interviews with 110 AAS users revealed that 56% of the males reported testicular atrophy and 62% of the females had menstrual irregularities. In addition, long-term use of steroids can lead to growth of mammary tissue in men.

Psychological: Increased testosterone levels are associated with masculine behaviour, aggressiveness and increased sexual desire. These have led to overt violence or even criminal behaviour outside the training environment. Other side-effects of AAS are euphoria, confusion, sleeping disorders, anxiety, paranoia and hallucinations.

Tendon injuries: Case reports have linked tendon rupture with AAS abuse. It has been suggested that AAS may alter collagen structure. Or, that the rapid strength gains of skeletal muscle are not matched by the more slowly-adapting, less well nourished tendon structures, making them the weak link in the chain.

### **Anabolic-androgenic steroids in sports**

Athletes actually "cycle" on and off AAS. This involves switching from one AAS to another to avoid developing tolerance. They also "stack" AAS, meaning they take lower doses of several different steroids at the same time supposedly to activate different steroid receptors. The scientific basis for stacking is highly questionable.

AAS are effective in enhancing athletic performance. They produce the desired anabolic effects, provided an athlete also consumes adequate protein and exercises intensely. The extent

to which muscle mass, strength and fat-free mass increase differs according to the respective study design, drug choice, training practices, nutrition intake and other factors.

### **Testing for anabolic-androgenic steroids**

The World Anti-Doping Agency's (WADA) 2006 list of substance classes and methods that athletes are forbidden to use during competition and training includes two types of steroids:

1. Typically exogenous steroids, e.g. boldenone, danazol, fluoxymesterone, metenolone, nandrolone, stanozolol, trenbolone.
2. Typically endogenous steroids, e.g. androstenediol, androstendione, dehydroepiandrosterone (DHEA), dihydrotestosterone (DHT), testosterone and related substances.

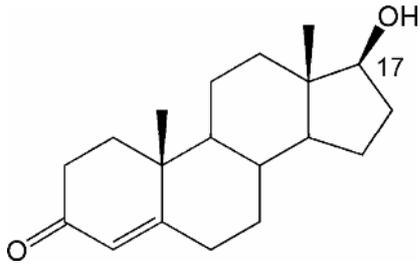
Testing for anabolic agents in the urine was implemented during the 1976 Montreal Olympic Games. Today, most anti-doping laboratories use a solid phase extraction of the urine sample followed by chemical modifications prior to gas chromatography-mass spectrometry (GC-MS).

The detection of exogenous substances means identifying the parent compound or at least one degradation product. Nevertheless, with substances that are produced endogenously such as testosterone, this alone cannot be an offence. To make it even more difficult, a cut-off value for testosterone concentration cannot be defined because urinary concentrations considerably differ between and within individuals and also vary with time.

The intake of testosterone, however, causes characteristic changes in the pattern of steroids in the urine. The ratio of testosterone to epitestosterone (T/E) helps to detect testosterone abuse: Epitestosterone is a minor product of testosterone degradation and does not increase after testosterone intake. The resulting effect from abuse is an increase in the T/E ratio. Among athletes, the ratio is generally less than 2.0. The rules of the International Olympic Committee define a T/E ratio greater than 6.0 constitutes as an offence unless there is evidence that it is due to natural condition or disease, e.g. low epitestosterone excretion or an androgen-producing tumour. Before the sample is declared positive, a longitudinal study, either as a comparison with previous values, or an analysis of several additional urine samples over a short period of time should be done. This may help in discriminating a naturally elevated T/E ratio from an elevated ratio due to manipulation.

According to WADA in 2004, urine samples should be submitted to isotopic ratio mass spectrometry (IRMS) if the T/E is greater than or equal to 4.0 and testosterone, testosterone metabolites, epitestosterone and DHEA concentrations are greater than the fixed cut-off values.

Even if such a longitudinal study gives valuable information on a potential steroid abuse, there is a lack of definitive proof for the exogenous application of natural steroids. A multiple step analysis, the gas chromatography/combustion/isotope-ratio-mass-spectrometry, GC/C/IRMS, can differentiate between natural steroids produced within and those produced outside the body. If the IRMS study does not readily indicate exogenous administration, the result should be reported as inconclusive and necessitate further longitudinal studies.



**Figure 1.** The molecular structure of testosterone