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Doping in Sports
Although the definition of doping has been modified over the years, its meaning may be pharmacologically understood as attempts to enhance performance (mainly strength and endurance) in sport by illegal administration of pharmaceuticals or application of prohibited methods (e.g. blood transfusions). Regardless of its individual motivation (e.g. unbounded ambitions, collective chauvinism or excessive financial interest), the doping phenomenon has been increasing in relevance for many years. However, any attempt to describe it from a scientific perspective faces the problem that systematic pharmacological principles are less important than the possible uncovering of its administration in doping control analyses.

Over time, we have seen that some of the early and most potent stimulating agents (e.g. amphetamine) have almost disappeared because relevant dosages are easily detected in doping controls. Instead, alternative and less efficient drugs (e.g. caffeine, modafinil) were used until they appeared on the relevant lists of prohibited substances. In some cases, even untested and unapproved drugs (bromantane, carphedone) were administered to circumvent positive doping controls.

Similarly, the ‘progress’ of doping with anabolic compounds was pharmacologically characterised by a loss of efficacy, which is notably paralleled by performance deterioration in highly ‘doping susceptible’ disciplines (compare world records in shot put). Originally, both injectable and orally administered steroids with high myotrophic potential (stanozolol, nandrolone, metandienone) were abused, resulting in significant gain in muscle mass and performance. Their replacement by lower levels of endogenous steroids could still combine reasonable effects with a moderate risk of discovery. Following further analytical improvements to differentiate endogenous and synthetic steroids (carbon isotope mass spectrometry), the application of mimetics and prohormones became popular. The latter (e.g. androstenedione) were temporarily legally available as ‘nutrition supplements’ and were thus abused in large amounts, although the significance of intended pharmacological effects was not proven. The BALCO affair (Bay Area Laboratory Co-operative), an intentional systematic development of new pharmaceutical analogues of anabolic steroids (tetrahydrogestrinone, THG) for doping
purposes, was certainly intriguing but due to the great effort required and the high risks involved it probably does not represent a general tendency.

Relevant detection time windows differ significantly and have to be seen in relation to the duration of possible performance-enhancing effects. Application of amphetamines, for instance, to stimulate sympathetic and central nervous systems is associated with high therapeutic substance concentrations during the performance and can be easily identified “in-competition”. In contrast, effects of anabolic substances or enhancement of oxygen transport capacity may last longer than the presence of the respective doping agents in the body. Unannounced out-of-competition tests were therefore introduced to specifically search for anabolic substances.

Analytically, the detectability in urine, the main specimen in doping control, and the corresponding detection time windows of relevant compounds are mainly governed by their pharmacokinetics. Detailed knowledge of the biotransformation and excretion kinetics of prohibited compounds is therefore essential in doping control. Quite often, pharmacologically irrelevant terminal metabolites are examined in great detail to enable a long-term detection of steroid abuse.

Recent advances in the development of doping strategies are not restricted to the development of new compounds. Forms of administration are also optimised to avoid the detection of administered substances. Anabolic steroids which were classically administered by intramuscular injection of their esters or taken orally became available as sublingual or buccal tablets and in particular as transdermal gels, enabling an efficient application of low dosages with good bioavailability and moderate detection windows.

Some new developments occurred in the 1990s when cheaper and safer recombinant peptide hormones became available. Erythropoietin (EPO), growth hormone (hGH) and insulin-like growth factor (IGF-1) pose outstanding analytical challenges because of their potentially endogenous nature and their pulsatile biosynthesis. Quantitative analyses are not eligible as proof of administration, and alternative procedures to differentiate the complexity of isoforms (hGH) or glycosylation (EPO) became necessary.

This development from classic – yet highly potent – compounds to new replacement strategies reflects a major challenge in doping control: old compounds and methods are still state-of-the-art and their control needs to be maintained while new analytical procedures must be permanently included. The time lapse between the clinical trials of a new drug with a misuse potential and the introduction of the drug might be used to develop a possible detection strategy. Detection methods for specific androgen receptor modulators (SARMs) have already been developed and the substances are included on the prohibited list even before any preparation is registered.

In addition to potentially performance-enhancing substances, masking agents have been prohibited because compounds influencing their analytical detectability were used. A fascinating facet of the BALCO affair was the documented production of “the cream”, a transdermal testosterone preparation with an in-built fraction of the masking agent epitestosterone to prevent an adverse analytical finding.
Recently, genetic aspects and techniques have gained importance in doping analysis, for instance to understand inter-individual variations (pharmacogenomics of testosterone glucuronidation) or as a diagnostic tool (reporter gene biomarkers). Moreover, the possible abuse of developments in gene therapeutic treatment has revealed a new potential for manipulation (gene doping). The first attempts to detect this are in progress.

The development of doping analysis in human sports has been closely related to the abuse and detection of illegal compounds in animal sports (particularly horse racing), while aspects like the availability of substances, species-related biochemical particularities and specific regulation of the acceptance of medications define their speciality. Similarly, the application of inappropriate dosages of anabolic compounds in bodybuilding and their illegal use in food-producing animals are not fully comparable to situations in sport, but permit useful insights into biotransformation, pathobiochemistry and the appearance of side effects and attempts to treat them.

Finally, doping cannot be properly understood without some knowledge of its legal implications. The abuse of certain compounds is restricted by a trade-off between potential gain (honour, social, money) and risk (costs, sanctions or legal penalties). The classification of potentially harmful doping agents as scheduled compounds, their control and limitation of their availability are therefore also as important as analytical means.

A comprehensive overview of the health risks of doping practices and their side effects would exceed the scope of this volume. However, we chose to include some aspects which have not yet been covered extensively in the literature: the side effects of anabolic-androgenic steroids from a forensic point of view and the risks of steroid abuse observed from a cardiologist’s standpoint.

As early as 1980, the International Association of Athletics Federations (IAAF) initiated an accreditation programme for doping control laboratories, which was later taken over by the International Olympic Committee (IOC) and the World Anti-Doping Agency (WADA). Major concepts of quality assessment in analytical chemistry (e.g. identification criteria in mass spectrometry) originated in this process. The anchoring of quality control in the concepts of the International Organization for Standardization (ISO) provides the documentation of adequate competence. The fact that analytical results are periodically the subject of public contention reflects the high awareness of doping and strong financial interests rather than scientific insufficiencies.
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