Anabolic Steroids, Athletic Drug Testing, and the Olympic Games

The Centennial Olympic Games will be held this month in Atlanta. During the 16 days of athletic competition, a small group of laboratorians will be doing their part to ensure the integrity of sport. Since 1972, state-of-the-art analytical methods have been used to test for the presence of compounds that could enhance the athletic performance of the participating competitors. Summaries of the experiences at several international competitions have been published in this journal [1–3].

The International Olympic Committee (IOC) now tests for stimulants, narcotic analgesics, anabolic agents, diuretics, peptide hormones, and other pharmacological agents. Statistics from the IOC show that anabolic steroids continue to account for more than half of all positive test results. Testing for anabolic steroids by radioimmunoassay began at the 1976 Montreal Olympic Games. Because of the cross-reactivity of the numerous endogenous and exogenous steroid metabolites, however, this approach was found untenable. At the Pan American Games in Caracas in 1983, Manfred Donike and his colleagues from Cologne, Germany, instituted gas chromatography–mass spectrometry (GC–MS) screening and confirmation, and this analytical approach has been used ever since. Now, in Atlanta, sector mass spectrometers will for the first time at an international athletic competition be used in conjunction with quadrupole mass filters for screening all samples. The higher mass resolution and greater sensitivity of the sector instruments should improve limits of detection. Again, the Cologne laboratory was a leader in this application of technology to sports testing.

Beyond the application of newer and more sophisticated technology, however, is selection of the appropriate steroid metabolites to monitor. The athletic drug testing laboratories are continually seeking better ways to test for steroids for longer periods after administration. Although the contributions of other laboratories to this area should not be minimized, the efforts of Donike and his colleagues in the Cologne laboratory have provided the foundation of anabolic steroid testing. Through the use of both metabolic excretion studies and chemical synthesis to verify the structure of proposed metabolites, they have generated an enormous amount of data on the metabolic patterns observed after administration of steroids. Research in this area spans a large portion of the pharmacology and metabolism drug spectrum, including phase I and phase II metabolism. An understanding of not only the metabolic patterns but also the effects of agents used to potentially manipulate metabolism and excretion is necessary for accurate interpretation of the analytical results.

Recently, the athletic drug testing community suffered a serious loss with the untimely death of Donike in August 1995. He had made many contributions to drug analysis in general as well as testing in sport. He synthesized N-methyl-trimethylsilyl trifluoroacetamide (MSTFA), which is widely used for derivatization of drugs for GC analysis. He also described selective derivatization of amine and hydroxyl groups on the same molecule (e.g., ephedrine), using O-silylation and N-trifluoroacetylation. Before Prof. Donike’s death, Wilhelm Schänzer had agreed to work with him to help prepare a review of anabolic steroid metabolism for publication, if possible, at the time of the Atlanta Olympic Games. This issue of Clinical Chemistry presents an outstanding summary of the present state of knowledge of anabolic steroid metabolism and a fine tribute from Dr. Schänzer to his former mentor [4].

Although the ability to detect exogenous steroids has improved, the use of endogenous steroids, such as testosterone and dihydrotestosterone, to improve athletic performance continues to pose a challenge to the laboratories. The finding of an abnormal concentration of an endogenous steroid is usually not enough evidence to presume an exogenous application of the substance. The ratio of testosterone to epitestosterone, its 17α-epimer, has been a useful index for detection of testosterone abuse. Measurement of the patterns of other endogenous steroids can also be used to evaluate external manipulation of the athlete’s endocrine system. The principle of individual reference ranges has also been utilized in athletic testing. Sequential testing of individuals over time has shown that the testosterone:epitestosterone ratio is quite consistent within an individual. Recent publications have also described the application of gas chromatography/combustion/isotope ratio mass spectrometry to evaluate the source of the testosterone. If the 13C content of the testosterone does not match that of its metabolic precursors, exogenous administration would seem a logical explanation. Although this kind of testing continues to be challenging, progress is being made.

One might ask, Why test at all? Three important considerations are involved. First, there should be a concern for the health of the athletes. Athletes who feel compelled to use drugs to be able to compete will do so, potentially to their physical detriment. The high doses of drug sometimes used combined with the stress of competition can make the health risks even higher. As recently as 1994, a body builder died after nonmedical use of a diuretic. Second, fair competition among athletes on a level playing field is the Olympic spirit. Perhaps the most poignant commentary on the unfairness of competition with drug-enhanced athletes comes from the book The Hundred Yard Lie, in which the author stated, “. . . the game of football, as we know it, has become unplayable. No one should have to play against a creature like him” [5]. Moreover, a minority of athletes apparently view testing as just another competition: “The game . . . is to constantly be one up on the testers” [6]. For those motivated to win at any cost, there seems to be no alternative to drug testing.

Finally, administration of anabolic steroids to prepubescent adolescents has medical implications far beyond those for an adult. The detection of anabolic steroids in the urine of two teen-age female athletes in 1996 should be a matter of concern for health professionals. A study by the Canadian Centre for Drug-Free Sport has identified several risk factors for teen-age athletes in deciding to use performance-enhancing drugs, including the perceptions that these compounds will not harm anyone and that their use is widespread among competitors. An effective drug detection program should be one weapon in the fight against drug use.
Drug testing at the Atlanta Olympic Games will be based on scientific research, as documented by Schänzer [4], sophisticated instrumentation, and highly trained laboratory professionals. The purpose of the testing is to assure that the Gold Medal hangs around the neck of an athlete as a reward for hard work and athletic skill, not pharmaceutical manipulation.

References

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