

**WPA SECTION REPORT****Doping in sports and its spread to at-risk populations: an international review****DAVID A. BARON<sup>1,2</sup>, DAVID M. MARTIN<sup>1,3</sup>, SAMIR ABOL MAGD<sup>1,4</sup>**<sup>1</sup>WPA Section on Exercise, Psychiatry and Sport<sup>2</sup>Department of Psychiatry, Temple University College of Medicine, Episcopal Campus, 100 East Lehigh Street, Philadelphia, PA 19125, USA<sup>3</sup>Department of Research and Development, JMJ Technologies, Inc., 1785 Allentown Road #185, Lansdale, PA 19446, USA<sup>4</sup>Drug Addiction Prevention and Management Unit, Cairo University, 63 Abdel Asis Al Saud Street, Manial, Cairo, Egypt

*Doping is now a global problem that follows international sporting events worldwide. International sports federations, led by the International Olympic Committee, have for the past half century attempted to stop the spread of this problem, with little effect. It was expected that, with educational programs, testing, and supportive medical treatment, this substance-abusing behavior would decrease. Unfortunately, this has not been the case. In fact, new, more powerful and undetectable doping techniques and substances are now abused by professional athletes, while sophisticated networks of distribution have developed. Professional athletes are often the role models of adolescent and young adult populations, who often mimic their behaviors, including the abuse of drugs. This review of doping within international sports is to inform the international psychiatric community and addiction treatment professionals of the historical basis of doping in sport and its spread to vulnerable athletic and non-athletic populations.*

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The creed of the Olympics states: "The important thing in the games is not winning but taking part. The essential thing is not conquering, but fighting well". As noble a goal as this is, it has little to do with the reality of the modern sports world. Athletes are rewarded for winning at virtually every level of competition. Second place is viewed as the "first loser". A coach's job security is directly related to his team's success, not that they are simply "fighting well". Given this reality, it is not surprising that athletes and coaches will sacrifice and risk a great deal in order to obtain a competitive edge and enhance performance at all costs. Performance enhancement in olympic and professional sport has now become a medical, ethical, and legal problem for modern athletes and athletic organizations. This is primarily due to the amount of money associated with winning in today's sports industry. Multimillion dollar contracts, appearance fees, international endorsement and sports merchandising represent a billion dollar industry that offers today's athletes, their sponsors and entourage previously unheard of financial gains. When Sports Illustrated interviewed a cohort of elite olympic athletes, one of the questions was: "If you were given a performance enhancing substance and you would not be caught and win, would you take it?". 98% of the athletes responded "Yes". The more chilling question was: "If you were given a performance enhancing substance and you would not be caught, win all competitions for 5 years, then die, would you take it?". More than 50% said "Yes" (1).

Athletic performance enhancement can be gained using various diets, training routines and hard work. However, it can and has been achieved since ancient competitions by using a wide variety of physiological, mechanical and pharmacological doping techniques. As prize money and en-

dorsement rewards increased, so did the science and abuse of performance-enhancing techniques. Today no sport is spared the cloud of cheating using illegal performance enhancement. Driven by the millions of dollars now routinely available for winning a sporting event, unethical pharmacists, medical professionals, trainers and sports organizations have worked secretly, and at times without their athletes' consent, to develop sophisticated doping programs where performance is optimized, often at the risk of the athletes' health. Now, these same doping programs are moving out of the professional sports market to our youth and other at-risk populations at alarming rates.

There are several hundred forms of known and potentially more unknown doping substances and techniques abused by professional athletes worldwide. This review will provide a summary of the history of doping in sport, and focus on the most commonly abused substances: anabolic androgenic steroids, human growth hormone (hGH) and erythropoietin (EPO).

**HISTORICAL OVERVIEW OF DOPING**

Performance-enhancing drugs are not unique to modern athletic competition. Mushrooms, plants and mixtures of wine and herbs were used by ancient Greek olympic athletes and Roman gladiators competing in Circus Maximus dating back to 776 BC. Various plants were used for their stimulant effects in speed and endurance events as well as to mask pain, allowing injured athletes to continue competing (2-4).

In the 1904 Olympics, marathon runner Thomas Hicks used a mixture of brandy and strychnine and nearly died.

Mixtures of strychnine, heroin, cocaine, and caffeine were used widely by athletes, and each coach or team developed its own unique secret formulae. This was common practice until heroin and cocaine became available only by prescription in the 1920s. During the 1930s, it was amphetamines that replaced strychnine as the stimulant of choice for athletes. In the 1950s, the Soviet Olympic team first used male hormones to increase strength and power. When the Berlin Wall fell, the East German government's program of performance enhancement by meticulous administration of steroids and other drugs to young athletes was exposed. These well-documented and controlled hormonal doping experiments on adolescent athletes by the East German Sports Medical Service yielded a crop of gold medalists (mostly young females as they responded more dramatically to male hormones). These athletes suffered severe medical abnormalities, including premature death (5).

The world became acutely aware of the extent and benefits of doping in sport when Ben Johnson's gold medal was stripped in the 1988 Seoul Olympics for using the steroid stanozolol. The International Olympic Committee (IOC) medical commission had established a list of prohibited substances in 1967 and introduced anti-doping testing of athletes in the 1972 Munich Games. It was clear at this point that doping did work and, if gone undetected, would win gold medals. East German scientists from the state-run doping programs at Kreischa and Leipzig, who were disgraced in their own country, where now in demand in Asia, former Soviet Block nations and sports organizations worldwide that wanted to promote their status. Doping became so prevalent in Olympic sport that some argued that all records should be discarded or put on hold until all forms of doping could be detected and stopped. Through the 1980s and 1990s, clandestine doping programs spread from sport to sport guided by modern, albeit unethical, pharmacists and sports medicine professionals. In 1999, the IOC organized a World Conference on Doping in Sport in response to a shocking discovery of massive amounts of performance enhancing drugs and paraphernalia by French police at the 1998 Tour de France. It was at this meeting that an independent global agency was founded, the World Anti-Doping Agency (WADA). Its mission was to work independently of the IOC, sports organizations and governments to lead the fight against doping in sport (6).

Despite years of aggressive anti-doping testing by international sports federations such as those for cycling, athletics and soccer, steroid abuse scandals involving high profile athletes continue to be front page news across the globe. Professional sports in the United States are not subject to extensive anti-doping programs, as players' unions and collective bargaining agreements prevented such extensive testing to be put into place. However, they did establish limited anti-doping programs, as the professional sports organizations recognized the potential of doping to harm athletes and their sport. In 1998, when Mark

McGuire, an American baseball player, broke Roger Maris' home run record, it was revealed that he had been taking a supplement containing a precursor to nandrolone, a steroid. At that time Major League Baseball did not ban steroids and did not believe that steroids were a problem within the league. However, subsequent government investigations and former players revealed that steroid abuse was a problem in the League, which resulted in a limited steroid testing program.

In 2003, another significant event in the understanding of the institutional nature of doping occurred. A syringe was anonymously sent to a WADA-accredited laboratory in Los Angeles that contained tetrahydrogestrinone (THG), a "designer" steroid that was not known and not on the current WADA prohibited list, made specifically to avoid detection by modern anti-doping technologies. This led to a series of investigations resulting in the indictment and subsequent conviction of individuals running a performance-enhancing program for professional athletes at the BALCO pharmacy in San Francisco.

In May 2006, Spanish police arrested five people and seized a variety of banned performance-enhancing drugs and blood-doping supplies at a Madrid doping clinic. Here, professional athletes would receive medically-supervised injections of hormones and other performance-enhancing drug regimes. The 40-page police report included a clear paper trail of doping procedures on at least 50 professional cyclists. The report was given to the International Cycling Union, which led to the disqualification of 23 professional cyclists, virtually all the top contenders from the 2006 Tour de France. The final of the 2006 Tour was also tarnished, as the champion, Floyd Landis, was found to have a positive anti-doping test for steroids. Landis was stripped of the championship and discharged from his team. At this writing the result is being challenged by Landis and his legal and medical experts, claiming that the test was invalid since several errors were made in the collection, analysis and reporting of the results.

In a separate investigation in Paris in 2006, 23 individuals were sentenced to 4 years in jail for trafficking a cocktail of amphetamines and other performance-enhancing drugs known as "Belgium Pot" to professional cyclists. Making this problem even more complex, in the June 2006 issue of the *Journal of Applied Physiology*, an article from Stanford University reported that Viagra can be used to increase by approximately 45% the performance of cyclists in high altitudes, suggesting a whole new class of performance-enhancing drugs not restricted to cycling (7). In October of that same year, the cricket world was shocked to learn that two Pakistani fast bowlers, Shoaib Akhtar and Mohammad Asif, tested positive for the steroid nandrolone.

This brief overview suggests not only the historical and institutional nature of doping by athletes, but also the international development of a clandestine and sophisticated distribution network of black market doping programs that follows the modern sports industry. Today perform-

ance-enhancing programs and drugs are not the exclusive province of elite athletes, but have spread to health clubs, high schools and other at-risk populations, creating an over \$1.4 billion US dollar industry that is growing daily as new compounds are synthesized and marketed (8).

## KNOWN DOPING SUBSTANCES AND TECHNIQUES

There are literally hundreds of known doping substances and an equal number of designer, veterinary, and yet to be identified drugs and techniques abused in sports today. The 2006 WADA list of prohibited substances includes the following major categories: anabolic agents (i.e., exogenous anabolic androgenic steroids such as androstendiol, boldenone, closterbol and danazol; endogenous anabolic androgenic steroids such as dihydroxytestosterone and testosterone, and other anabolic agents such as clenbuterol and tibolone); hormones and related substances (i.e., EPO, hGH, insulin-like growth factors, mechano growth factors, gonadotropins, insulin and corticotrophins); beta-2 agonists (i.e., terbutaline, salbutamol, etc.); agents with anti-estrogenic activity (i.e., anastrozole, letrozole, clomiphene, etc.); diuretics (furosemide, hydrochlorothiazide, etc.) and other masking agents (such as epitestosterone, probenecid, plasma expanders, etc.); stimulants (amphetamines, ephedrine, cocaine, etc.); narcotics (morphine, oxycodone, etc.); cannabinoids (marijuana, hashish), and glucocorticosteroids (allowed externally but not internally). WADA also lists prohibited methods, including enhancement of oxygen transfer (blood doping, efaproxial, etc.), chemical and physical manipulation (tampering or substitution of sample) and gene doping. In addition, WADA prohibits alcohol and beta-blockers (in specific sports: archery, billiard, etc.) (6).

Testing for the above list of compounds is technically challenging, expensive and only performed by about 35 WADA-accredited laboratories worldwide. Steroids are still the most detected performance-enhancing drugs by WADA laboratories. However, because of the limitations of laboratory technology and sophistication of doping athletes to avoid detection, they may not be the most abused.

### Anabolic androgenic steroids

Anabolic androgenic steroids are naturally occurring male hormones involved in a wide range of physiological functions. Simply referred to as "steroids", they fall into two categories: endogenous or naturally occurring, like testosterone, and exogenous or synthetic, like danazol.

In 1923 Bob Hoffman formed the famous York Barbell Company in the United States. A dominant figure in US weightlifting, he published the *Strength and Health* magazine and sold health and food supplements in his gym. As a weightlifting coach, his success led to him being named the head coach of the US Olympic weightlifting team. At

the 1954 World Championships in Vienna, he met with a Soviet colleague who told him of a synthetic form of testosterone developed by the Nazis which produced dramatic improvements in strength and power. He and his colleagues contacted Ciba Pharmaceuticals in pursuit of synthetic testosterone. Ciba had conducted a number of studies on the use of synthetic testosterone in pain patients and the physically disabled. This resulted in the development of danazol, which rapidly became a doping substance abused by weightlifters (9).

Although steroids were first reported to be abused in Olympic sports in the 1950s, the abuse of steroids in young male non-Olympic athletes was not reported until the 1980s (10). As demand increased, trafficking steroids at schools and gyms became common and the use of steroids was seen in younger and younger populations (11). Steroid sources included doctors, trainers, friends, the black market and foreign suppliers. In the United States, the Anabolic Steroid Enforcement Act of 1990 brought anabolic steroids under the record-keeping, reporting, security, prescribing, import and controls of the Controlled Substances Act. All manufacturers and distributors of steroids were required to register with the Drug Enforcement Agency. Other countries have similar laws on the manufacture and dispensing of steroids. However, the amount of illegal steroids entering the United States and distributed to athletic and at-risk populations has increased dramatically. It is now estimated to be an over 100 million US dollar black market for steroids in the US alone, with more than 80% manufactured in Mexico. Projecting these figures internationally suggests that the illegal steroid market alone approaches a billion US dollars annually, clearly making it a public health concern, especially for at-risk groups.

The serious side effects of steroids described in the medical literature include liver function abnormalities, liver and kidney tumors, endocrine and reproductive dysfunctions, testicular atrophy, lipid and cardiac effects and psychiatric symptoms (12). These consequences are exaggerated with the common doping practices using ten times or more the recommended medical dose, and multiple drugs or "stacking", e.g., steroids and EPO or hGH. Added to this, a new problem has emerged with the manufacture of "counterfeit" drugs by unregulated pharmacies, which are tainted with impurities, contain no medication, or are potentially harmful. Now, more so than in the past, when an athlete buys performance-enhancing drugs from a friend or at the gym, he will never know exactly what is being bought or taken. Steroids are sold on the internet ranging in price from \$50 to \$200 per regime, depending upon the type of steroid and doping program selected. These black market steroids may or may not contain any medication at all or may contain harmful material. Testing for steroids in urine is available at a few commercial clinical laboratories in the United States and can be obtained in the price range of \$100-\$200/test, depending upon the number of steroids screened.



## Human growth hormone (hGH and rhGH)

hGH is a naturally occurring hormone produced by the anterior pituitary gland and is one of the major hormones influencing growth and development. Harvey Cushing discovered the hormone in 1912 and isolated it from human and monkey cadaver brains in 1956. Two years later it was used to treat dwarfism in children by injection. The unfortunate development of Creutzfeldt-Jakob disease, a degenerative brain disorder, in boys who were treated with cadaver growth hormone led to the discontinuation of all products derived from the human pituitary gland. Because of this ban, the abuse of hGH was rare in sport until the middle to the end of the 1980s. In 1985 Genentech received approval from the US Food and Drug Administration (FDA) to market Protropin for children with growth hormone deficiency. This was the first recombinant DNA form of growth hormone (rhGH) that was safer than cadaver extracts used in the past. Recombinant DNA technology made the production of pharmaceutical grade growth hormone easier and cheaper. Genetically engineered rhGH is now marketed as Nutropin, Humatrope, Genotropin, Norditropin, Saizen, and Tev-Tropin. Most human growth hormone used in medicine and diverted to sports doping is now obtained by recombinant technology, and is simply referred to as hGH (but it may also appear as rhGH or HGH). Unfortunately, cadaver extracts of pituitary hGH may still be in circulation. It has been reported that a Russian coach was arrested and, upon searching his apartment in Moscow, over 1000 cadaver pituitary glands were found preserved in a large container (13). Moreover, the problem of counterfeit drugs also exists with hGH: illegal pharmaceutical manufacturers are now flooding the black market with hGH vials of unknown quality and safety. It is estimated that an eight-week performance enhancement regime of pharmaceutical grade rhGH will cost about \$2000, well out of the range of an adolescent and the majority of weekend athletes. However, the increased trafficking of low cost counterfeit rhGH will create interest and experimentation in these at-risk populations. hGH is marketed on the internet in many forms: pills, drops and aerosol formulations; most are ineffective and shams. The normal route of administration of hGH is injection, posing an additional health risk of infection from non-sterile counterfeit drugs and the risk of HIV and hepatitis transmission caused by shared needles.

Olympic, professional and weekend athletes abuse hGH because of unsubstantiated reports that it is as effective as anabolic steroids with fewer side effects. They often abuse hGH as a steroid substitute to prevent loss of muscle after discontinuing the use of steroids. Ben Johnson admitted to using hGH along with steroids during investigations after his disqualification in Seoul. According to some controlled scientific studies, hGH does not increase muscle strength. Nevertheless, the abuse of hGH in sports is escalating, with large caches of needles and vials of hGH being confiscated at sporting events worldwide. Six months prior to the 2000

Olympic Games, a pharmacy in Sydney was broken into and 1,575 multiple dose vials of hGH were taken while nothing else was touched. Also, on their way to Australia, the Chinese swimming team were detained, as needles, syringes, and vials of hGH were found by customs officials in their baggage.

Using hGH may lead to life-threatening health conditions, especially since some estimates report that athletes who use hGH to enhance performance are taking 10 times the therapeutic dosage. Some reported side effects of hGH are abnormal bone growth, hypertension, cardiovascular disease, cardiomyopathy, glucose intolerance, colonic polyps, decreased life span, and cancer (14).

Since hGH is a naturally-produced hormone and rhGH is similar in structure, testing for doping with rhGH has been a technical challenge only recently solved by WADA-certified laboratories. Routine blood tests for hGH available at clinical laboratories will not differentiate hGH from rhGH and are of no value in determining if an adolescent or weekend athlete is doping.

## Erythropoietin (EPO)

EPO is a naturally occurring hormone produced by the kidney that stimulates red blood cell production in the bone marrow in response to low circulating oxygen levels. It was not until 1977 that it was identified and extracted from human urine. This was concurrent with the development of recombinant DNA technology, and in 1989 Epogen was released in the United States and approved for the treatment of anemia. Procrit was licensed in 1991 for the treatment of chemotherapy-induced anemia. European formulations include Aranesp, Eprex and NeoRecorman.

EPO abuse in sport was believed to start as soon as the drug was available as a replacement for the older, more complex and dangerous doping technique referred to as "blood doping". In this technique an athlete donates his own blood several months before a competition, stores it and transfuses it back into himself prior to competing. This technique is fraught with problems and health risk. EPO accomplishes this same effect by increasing red blood cells, which results in more oxygen in circulation. It was in 1998 at the Tour de France that French customs arrested Willy Voet, a physiotherapist of the Festina cycling team, for the illegal possession of needles, syringes and over 400 bottles containing EPO, hGH, steroids, amphetamines, narcotics and stimulants.

EPO used for medical treatments can cost thousands of US dollars a month and is administered by intravenous or subcutaneous injection. As with steroids and hGH, doping with EPO is often injected in supernormal doses that could cause increased blood viscosity, deep vein and coronary thromboses, cerebral thromboses, pulmonary embolism, arrhythmias, stroke and death. It has been estimated that 20 European cyclists have died since 1987 due to abuse of

EPO, making it one of the most deadly doping agents. The genetically engineered form of EPO is indistinguishable from naturally occurring EPO, making routine blood testing useless to determine if an athlete is doping. At the 2000 Olympic Games in Sydney, the Australian WADA-certified laboratory first launched a sophisticated anti-doping test for EPO that required both urine and a blood sample. Over 300 tests were performed for EPO for the first time in Olympic history and no positives were reported. This could be due to the fact that the technology for the test was new and questions still existed about the assay.

### OTHER AT-RISK POPULATIONS FOR DOPING

Given the above history and current state of knowledge, it is not difficult to understand why there would be over a million abusers of steroids in the United States youth alone. Unlike professional athletes, these at-risk users will not have fame and fortune as a result of using steroids, only the side effects.

Pioneering studies in this area were done by Buckley et al in the early 1980s, when they interviewed 3403 male high school seniors nationwide (10). Their results reported in 1988 indicated that 6.6% of respondents had used steroids and more than two-thirds of the group started using steroids when they were 16 years old or younger. Twenty percent reported that health professionals were the primary source for obtaining steroids and 38% used injectable steroids. Pope et al studied 1,010 college men for use of steroids and also reported their findings in 1988 (15). The study found that only 2% of the respondents reported using steroids. The authors qualified their finding as potentially underestimating the true prevalence of steroid abuse. However, it is interesting to note that this study found that 25% of those reporting using steroids were not athletes. They abused steroids to improve personal appearance, a problem that continues today and is fueled by the media and "anti-aging" marketing. A review of published reports concluded that 3-12% of high school students used steroids, and of the group of abusers about half were adolescent females (16,17).

Contrary to popular belief and supported by Pope's early findings, steroid abuse is not exclusively related to performance enhancement. DuRant et al reported in 1993 that steroid abuse in ninth graders was associated with use of cocaine, injected drugs, alcohol, marijuana, cigarettes and smokeless tobacco (18). They then reviewed the 1991 Centers for Disease Control and Prevention Youth Risk Behavior Survey of over 12,272 male and female public and private high school students, and confirmed the earlier finding that there is an association between steroid abuse and multiple drug abuse. In a later review of the 1997 Centers for Disease Control and Prevention Youth Risk Behavior Survey of 16,262 high school students, Miller et al reported no significant correlation in male or female steroid-abusing

high school students with physical activity, nor were athletic participation or strength conditioning alone associated with lifetime steroid abuse (19). Rather, they found that athletic participation was less of a factor than behavior problems such as substance abuse, fighting, binge drinking, tobacco use and high risk sexual behavior. They suggested steroid abuse may be part of a much larger syndrome of problem behaviors. In 2002, Irving et al confirmed Miller's report that physical activity was not associated with steroid abuse. This group shed light on the fact that male and female adolescent steroid abuse may also be associated with unhealthy attitudes and behaviors to lose, gain or control weight and body shape (11). Clancy and Yates reported that steroid abusers may have a unique set of clinical differences and are distinct from other drug abusers (20). Bahrke et al associated a number of personal high-risk behaviors and other factors with a partially developed profile of an adolescent anabolic steroid abuser (21).

What has become evident is that not only high school and weekend athletes are potential steroid abusers. Steroid abuse may also include a wider population of non-athletes who have behavioral problems and may experiment with these now easily available performance-enhancing drugs. Their motivation may not be athletic enhancement, but rather cosmetic and body shaping purposes. To maintain youthful appearances, weekend athletes may experiment with hormones encouraged by "anti-aging" marketing, while adolescent females desirous of the long, lean female media images of "adult women" may use steroids and hGH to reduce fat and increase muscle tone (22).

### DISCUSSION

Modern sports and the media's misplaced fixation on fame, fortune and winning at all costs have unintentionally created a growing market for doping substances. These substances, once only abused by elite athletes, are clearly spreading into our schools and health clubs worldwide. They are being accepted by a whole new generation of young customers who see reports daily in the newspapers of sports icons accused of abusing drugs only to continue playing, breaking records and claiming fortunes. These same performance-enhancing drugs are also abused by adolescents and weekend athletes and non-athletes who have wider behavioral and health risk problems. In addition, these drugs are now being abused by male and female adolescents for cosmetic purposes in an attempt to achieve the "cut" and sexy look promoted by the media. Continuing educational programs developed for these at-risk populations by national olympic organizations and athletic federations are important first steps to curb these dangerous behaviors (23-25). Testing for performance-enhancing drugs in high schools as a means of early detection, intervention and prevention is now being launched in New Jersey, with other states following their lead. Medical profes-

sionals, teachers, coaches and sports organizations must all be made aware of this continuing problem in our adolescent and at-risk populations and contribute to its solution by open, honest discussion. Most importantly, professional athletes must serve as role models and spokesmen for drug-free sport and lifestyle. This position must be actively supported by the media, owners of teams and international sports federations by providing consistent leadership and advocacy of anti-doping programs in sport, regardless of costs and consequences. Accepting the magnitude of doping in at-risk populations and developing education, prevention and treatment programs is the only way we can prevent the continuing spread of the abuse of doping in sport and its spread into the most fragile groups in our society, our youth and at-risk populations.

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