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A REVIEW ON PERFORMANCE ENHANCING DRUGS IN ATHLETES

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ABSTRACT

Drug abuse occurs in all sports and at most levels of competition. Athletic life may lead to drug abuse for a number of reasons, including for performance enhancement, to self-treat otherwise untreated mental illness, and to deal with stressors, such as pressure to perform, injuries, physical pain, and retirement from sport. This review examines the history of doping in athletes, the effects of different classes of substances used for doping, detection of drug use and treatment of affected athletes. Doping goes back to ancient times, prior to the development of organized sports. Performance-enhancing drugs have continued to evolve, with "advances" in doping strategies driven by improved drug testing detection methods and advances in scientific research that can lead to the discovery and use of substances that may later be banned. Many sports organizations have come to ban the use of performance-enhancing drugs and have very strict consequences for people caught using them. There is variable evidence for the performance-enhancing effects and side effects of the various substances that are used for doping. Drug abuse in athletes should be addressed with preventive measures, education, motivational interviewing, and, when indicated, pharmacologic interventions.

KEY WORDS: doping; athletes; steroids,; drug abuse; mental illness

INTRODUCTION

PEDs are pharmacologic agents that athletes and nonathlete weightlifters use to enhance performance. The term doping refers to the use of PEDs in competitive sports. For the purpose of this statement, we define nonathlete weightlifters as individuals whose goal is to become leaner and more muscular, often simply for personal appearance, and not to participate in formal sports competitions.[1] Drug abuse in the athlete population may involve doping in an effort to gain a competitive advantage. Alternatively, it may involve use of substances such as alcohol or marijuana without the intent of performance enhancement, since athletes may develop substance use disorders just as any nonathlete may.[2]

Athletes may turn to substances to cope with numerous stressors, including pressure to perform, injuries, physical pain, and retirement from a life of sport (which happens much earlier than retirement from most other careers).[3] Additionally, athletes may be significantly less likely to receive treatment for underlying mental illnesses suchas depression. Athletes receive comprehensive treatment and rehabilitation for physical injuries, but this may be less often the case for mental illness, because of their sometimes viewing mental illness as a sign of weakness.[4] Untreated mental illness is often associated with substance use, perhaps in an effort to self-treat. Alternatively, substances of abuse may cause mental illness.[5]

Since the last decades of the last millennium, it has shown a growing interest for the issue of health. Health promotion passes through good nutrition and a way of living adequate aimed to achieve the "welfare".[6,7] Numerous studies have demonstrated the positive effects of playing sport the psychological and social benefits of playing true sport.[8] Further, numerous studies have demonstrated the positive effects of playing sport on academic success, in large part because of the positive influence of identity formation and emotional development.[9]

There are several categories of PEDs that are currently popular among nonathletic weightlifters and athletes. Lean mass builders, the most frequently used PEDs, are generally promyogenic (anabolic) drugs that increase muscle mass or reduce fat mass. By far the most prevalent illicit drugs in this category are AASs, which are the primary focus of this report. Among non-athlete weightlifters, the use of AASs represents a higher proportion of overall PED use than that of all other categories of PEDs combined.[10,11]

DRUGS IN SPORT FOR PERFORMANCE ENHANCING

The use of performance enhancing drugs in the modern Olympics is on record as early as the games of the third Olympiad, when Thomas Hicks won the marathon after receiving an injection of strychnine in the middle of the race.[12] The first official ban on ‘‘stimulating substances’’ by a sporting organization was introduced by the International Amateur Athletic Federation in 1928.[13] Using drugs to cheat in sport is not new, but it is becoming more effective. In 1976, the East German swimming team won 11 out of 13 Olympic events, and later sued the government for giving them anabolic steroids.[14] Yet despite the health risks, and despite the regulating bodies’ attempts to eliminate drugs from sport, the use of illegal substances is widely known to be rife. It hardly raises an eyebrow now when some famous athlete fails a dope test.[14]

In 1992, Vicky Rabinowicz interviewed small groups of athletes. She found that Olympic athletes, in general, believed that most successful athletes were using banned substances.[15] Much of the writing on the use of drugs in sport is focused on this kind of anecdotal evidence. There is very little rigorous, objective evidence because the athletes are doing something that is taboo, illegal, and sometimes highly dangerous. The anecdotal picture tells us that our attempts to eliminate drugs

from sport have failed. In the absence of good evidence, we need an analytical argument to determine what we should do.[16]

PERFORMANCE-ENHANCING EFFECTS OF SUBSTANCES USED BY ATHLETES

There is a research base demonstrating that many doping agents are in fact performance-enhancing. However, some substances (eg, selective androgen receptor modulators, antiestrogens, and aromatase inhibitors), used in an effort to enhance performance, have little data to back up their effectiveness for such a purpose. There are many risks involved with the use of PEDs. Some are immediate and some take longer to appear. All may be associated with poor academic performance, physical and emotional changes, illness and harm to the body, as well as, in some cases, the potential for addiction.[17,18]

AASs are the most commonly used PEDs, with testosterone, boldenone, and trenbolone being the most frequently detected drugs among illicit PED users in the United States (Figure 4). Although boldenone is a veterinary steroid not approved for human use, this fact has not diminished its popularity among illicit AAS users. In the small subgroup of PED users who are elite athletes, WADA most commonly detects testosterone, stanozolol, and nandrolone, and the highest prevalence of positive tests occur in bodybuilding, power lifting, weightlifting, boxing, and kickboxing.[18]

- **Anabolic Steroids**

Anabolic steroids are the most commonly used of all PEDs. They are synthetic versions of testosterone and are used to increase muscle mass. Certain steroid precursors are also used, marketed under names such as “andro” and DHEA (dehydroepiandrosterone). Most are illegal without a prescription, but DHEA can still be purchased over the counter. Anabolic steroids are what are most often in the news with regard to professional athletes. There are several side effects associated with use of anabolic steroids. Mood swings, referred to as “roid rage,” are common. They can also cause acne, headaches, hair loss, nausea, and bloating, and women may notice a deepening of their voice. There may be joint pain, due to weakening of the tendons, bowel problems, and depression. In men, there may be decreased sperm count, decreased testicular size, and gynecomastia. In women, amenorrhea is common. With continued use, anabolic steroids cause
an increased risk of liver and kidney disease, stroke, blood clots, and heart disease, as well as the risks associated with injection and needle use, if that is the method of administration.[18,19]

- **Androgens**

Androgens include exogenous testosterone, synthetic androgens (eg, danazol, nandrolone, stanozolol), androgen precursors (eg, androstenedione, dehydroepiandrosterone), selective androgen receptor modulators, and other forms of androgen stimulation. The latter categories of substances have been used by athletes in an attempt to increase endogenous testosterone in a way that may circumvent the ban enforced on natural or synthetic androgens by WADA.[20]

Amounts of testosterone above those normally found in the human body have been shown to increase muscle strength and mass. For example, a representative randomized, double-blind study involved 43 men being randomized to four different groups: testosterone enanthate 600 mg once per week with strength training exercise; placebo with strength training exercise; testosterone enanthate 600 mg once per week with no exercise; and placebo with no exercise. This was a critical study in demonstrating that administration of testosterone increased muscle strength and fat-free mass in all recipients, and even moreso in those who exercised.[21] A second study from the same investigators 5 years later further demonstrated a dose–response relationship between testosterone and strength.[22] Another double-blind trial of exogenous testosterone involved 61 males randomized to five different doses of testosterone enanthate, ranging from 25 mg to 600 mg, along with treatment with a gonadotropin-releasing hormone agonist to suppress endogenous testosterone secretion. That study demonstrated findings similar to the previous one, in showing a dose-dependent increase in leg power and leg press strength, which correlated with serum total testosterone concentrations.[23]

- **Human Growth Hormone**

Human growth hormone (HGH) is used by physicians to treat medical problems, but it is also used illegally as a PED. It mimics the effects of anabolic steroids by increasing muscle mass. When used without medical supervision, it is not without side effects. These include joint pain, muscle pain and weakness, fluid retention, hyperlipidemia, and the development of carpal tunnel syndrome. With long term use, there is a risk for development of diabetes, abnormal organ growth,
hardening of the arteries, hypertension, and acromegaly.[24] One of the more serious problems associated with HGH is that, despite being illegal to use for performance enhancement, it is still readily available and rather easy to obtain online.[24]

- **Diuretics**

These substances act on the kidneys in various ways to increase urine output. Many are available by prescription only, but when used for performance enhancement, they are usually obtained over the counter. Two common uses are to decrease weight in order to compete in a different weight class or to dilute a urine sample and mask the presence of anabolic steroids. When used without medical supervision, side effects may include dizziness, dehydration, and hypotension.[19]

- **Amphetamines/Stimulants**

This is a broad category, including medications such as those used to treat attention deficit disorder and cough medicine such as dextromethorphan (DXM). Stimulants are generally used to increase energy and alertness, increase blood flow to muscles, and fight fatigue, and they were the second most commonly used PED in 2012.[17] Side effects include abnormal heart rhythm, palpitations, tremors, and insomnia. DXM is readily available over the counter and can have serious side effects, depending on the amount used. Side effects include confusion, dizziness, double or blurred vision, rapid heartbeat, loss of motor control, and hallucinations. Because of other

ingredients it contains, like acetaminophen, when taken in large amounts, there is risk of liver damage. Caffeine and energy drinks are included in the category of stimulants as well. The risks of taking a non prescribed medication seem obvious, but the risks associated with energy drinks are often overlooked. However, even energy drinks can be abused.[25] Not only are they consumed in large quantities, but some may contain substances that are banned by various sports agencies. The content and purity is not always known. Nor do we know the long-term effect of a large amount of energy drink consumption on the developing brain of an adolescent. The potential harmful effects of energy drinks are so great that the American Academy of Pediatrics (AAP) issued a position statement recommending that adolescents abstain from them completely.[26] Energy drinks contain varying amounts of caffeine, guarana, taurine, glucuronolactone, and ginseng, among other substances that have little or no nutritional value, and may possibly present a health risk. They have not been thoroughly evaluated by the Food and Drug Administration for purity, safety, and how they interact with other substances.[27] In 2011, energy drinks had the largest share of the beverage market, with sales totaling over $9 billion, with adolescents and young adults accounting for $2.3 billion of those sales.[28]

METHODS TO INCREASE OXYGEN TRANSPORT

Substances athletes use to increase oxygen transport include blood transfusions, erythropoiesis-stimulating agents such as recombinant human erythropoietin and darbepoetin alfa, hypoxia mimetics that stimulate endogenous erythropoietin production such as desferrioxamine and cobalt, and artificial oxygen carriers.[29] Transfusions and erythropoiesis-stimulating agents have been shown to increase aerobic power and physical exercise tolerance. However, the ergogenic effects of the other agents are debatable.[29]

OTHER RECREATIONAL DRUGS

Other recreational drugs that may be used in an attempt to enhance performance include alcohol, cannabinoids, narcotics, and nicotine.[30] WADA does not currently ban nicotine but bans cannabinoids and narcotics. Alcohol is banned in six sports during competition only. All of these substances may be used by athletes to reduce anxiety, which may be a form of performance enhancement, but we found little research looking at actual performance enhancement from these agents. Narcotics are used to decrease pain while practicing or playing. Nicotine may enhance weight loss and improve attention.[31]

THE SPIRIT OF SPORT

So is cheating here to stay? Drugs are against the rules. But we define the rules of sport. If we made drugs legal and freely available, there would be no cheating. The World Anti-Doping Agency code declares a drug illegal if it is performance enhancing, if it is a health risk, or if it violates the ‘‘spirit of sport’’.[32] They define this spirit as follows. The spirit of sport is the celebration of the human spirit, body, and mind, and is characterised by the following values: ethics, fair play and honesty, health, excellence in performance, character and education, fun and joy, teamwork, dedication and commitment, respect for rules and laws, respect for self and other participants, courage, community and solidarity.[33] Human sport is different from sports involving other animals, such as horse

or dog racing. Humans are not horses or dogs. We make choices and exercise our own judgment. We choose what kind of training to use and how to run our race. We can display courage, determination, and wisdom. We are not flogged by a jockey on our back but drive ourselves. It is this judgment that competitors exercise when they choose diet, training, and whether to take drugs. We can choose what kind of competitor to be, not just through training, but through biological manipulation. Human sport is different from animal sport because it is creative. Far from being against the spirit of sport, biological manipulation embodies the human spirit—the capacity to improve ourselves on the basis of reason and judgment. When we exercise our reason, we do what only humans do.[34,35]

NONDRUG PERFORMANCE-ENHANCING MEASURES

Gene doping is a concerning potential method of nondrug performance enhancement and is banned by WADA. The potential to directly affect strength and endurance through gene manipulation has been demonstrated in laboratory mice, but no human athletes thus far have been found to be using this method.[36] Additionally, athletes may legally attempt to improve physical performance in a number of nondrug ways. These have varying degrees of research into their effectiveness and safety, and include hypoxia induction techniques.[37] For example, athletes may train at high altitudes, which can result in erythrocytosis. Some studies suggest that a high–low method of sleeping at high altitude followed by training at low altitude is a better training strategy than training or sleeping at either high or low altitudes alone.[38] Some athletes have tried sleeping at simulated high altitude by using low oxygen tents. Athletes may also make dietary changes to try to increase hemoglobin levels.[39,40]

ASSOCIATION OF PED USE WITH OTHER HIGH-RISK BEHAVIORS

Athletes and nonathlete weightlifters that use PEDs often engage in other high-risk health behaviors. In addition to the risks associated with concomitant use of other drugs such as alcohol and opiates with AASs,[41] users of high doses of AAS may be more susceptible to rage, antisocial and violent behaviors, and suicidality. Sharing of needles and other paraphernalia and unprotected sex may increase the risk of infections such as hepatitis and HIV.[42] The use of PEDs, especially in conjunction with analgesics or stimulants, may allow athletes to engage in extremely high-intensity exercise, increasing the risk of musculoskeletal injuries.[43]

DETECTION

Given the mounting evidence of adverse effects related to PED use, there is strong justification for the need to improve methods for detecting illicit PED use and eliminating abuse by both athletes and nonathletes, despite occasional arguments by some authors that PEDs be explicitly allowed in athletic competitions.[44,45] Some of the adverse effects seen in patients who use AASs may include infertility, gynecomastia, sexual dysfunction, hair loss, acne, muscular appearance, and testicular atrophy. Some indicators that might suggest AAS use are increased hemoglobin and hematocrit; suppressed LH, FSH, and testosterone levels; low high-density lipoprotein cholesterol, and low sperm density. Mass spectrometry- based tests (available in many commercial laboratories) can detect AASs in urine. Testosterone abuse is more difficult to detect, but high testosterone, in association with

suppressed LH and FSH levels, should raise suspicion of testosterone abuse. A T/E ratio of more than 4 can confirm testosterone abuse, although it is rarely necessary to check testosterone levels in the clinical setting. Often direct questioning will result in an admission by a patient that he or she is using AASs.[46]

In 1982, Donike and coworkers[47] first reported a method for detecting testosterone abuse. They based their method on the fact that exogenously administered testosterone is predominantly excreted in the urine as the glucuronide conjugate. By determining the T/E ratio, they eliminated the influence of urine density variations. Genetic differences in testosterone metabolism can alter the T/E ratio and result in a false-negative test.[48] A test based on gas chromatography/combustion/isotope ratio mass spectrometry can detect the difference in 13C/12C ratios (CIRs) in endogenous and exogenous testosterone.[49]

Two tests have been developed for the detection of rhGH: a direct method that measures variants of GH produced by the pituitary gland[50] and a biomarkers method based on the GH-induced release of IGF-1 and the N-terminal propeptide of procollagen type III (P-III-NP).[51] In the variants or isoforms test, one immunoassay detects primarily pituitary isoforms of GH including the 22-kDa isoform, oligomers of the 22-kDa isoform, and some other isoforms. The second immunoassay primarily detects the monomeric 22-kDa GH found in rhGH preparations.[52] When a subject receives GH, it increases the concentration measured by the second assay and suppresses the pituitary forms, decreasing the concentration. The result is a dramatic increase in the ratio of the 2 assays (recombinant/ pituitary).[52]

TREATMENT OF AFFECTED ATHLETES, INCLUDING COUNSELING AND PSYCHIATRIC SUPPORT

The first level of addressing the problem of drug abuse by athletes is prevention.[30] Drug screening is used in higher-level athletics both to deter athletes from using drugs and to punish and offer opportunities for rehabilitation to those who are found to have done so. Didactic education is another method aimed at prevention.[53] On the one hand, some authors and clinicians feel that among the most effective preventive strategies for drug abuse in sports is frequent, accurate, very closely observed, truly random urine drug testing.[30,54] However, some view drug testing as ineffective at preventing use of PEDs.[55] The argument for the latter is that these interventions target doping behavior rather than athlete attitudes. Athletes ultimately focus on their performance, and thus may view doping as rational behavior.[54] Moreover, knowledge of the potentially dangerous consequences from doping imparted via didactic education does not necessarily dissuade athletes. For example, in 1997, Bamberger and Yaeger surveyed 198 Olympic athletes. When asked if they would use PEDs under the hypothetical conditions of knowing they would not be caught and knowing their use would result in victory, 195 of 198 responded “yes”. Moreover, if the caveat was added that they would die within 5 years, 61% of the athletes still said they would use them.[56]

There is little research available to guide counseling and psychiatric approaches to treatment of athletes who abuse drugs.[55] However, motivational interviewing approaches have been suggested for athletes with drug abuse or

doping problems, since athletes may often present in the precontemplation stage of change.[30] Important elements of motivational interviewing include:[55]

- Clinician empathy
- Developing discrepancies between where the athlete wants to go in life after sport and the impact that continued use of the substance might have on those goals. During this process, the provider helps athletes to clarify conflict among their values, motives, interest, and behaviors.
- Rolling with resistance. When resistance inevitably occurs, providers should avoid arguing with athletes, as that can exacerbate resistance to change. The provider may "agree to disagree" on certain points with some athletes. Providers may propose or "wonder about" certain alternative viewpoints or actions, but they do not impose or insist upon them.
- Encouragement of self-efficacy. Athletes may need to shift their viewpoint from one of being willing to do whatever it takes to win, to acknowledging that they would use PEDs only if ultimately incapable of succeeding without them (with the hope that athletes will never get to that point).

If an athlete is physically dependent on a drug, then additional strategies may be needed. These may include pharmacologic interventions such as naltrexone, acamprosate, or disulfiram for alcohol dependence, or buprenorphine for opiate dependence.[30] Additionally, providers should assess for comorbid mental illness, since co-occurrence of physical dependence and mental illness is commonplace. Any underlying mental illness should be treated. A recent review paper on the epidemiology of mental illness in athletes noted that some mental illnesses such as depression are probably as common in athletes as nonathletes.[57] Twelve-step facilitation, cognitive behavioral therapy, and network therapy are also approaches that may be helpful for athletes who are abusing drugs, although studies are preliminary.[30,58]

TAKING ACTION AGAINST PED USE

Before you can take action against a problem, you must first know how to recognize it. Anyone who works with adolescents, particularly those involved with sports, should know the signs of PED use.[59] First, look for changes in school performance. Use of PED generally causes grades to drop, as preoccupation with body image and athletic performance increases. Second, look for personality changes, such as mood swings that go beyond those of a normal teenager. Sometimes there is aggression, anger, and frequent loss of temper. There may be problems getting along with friends and family and a tendency to isolate. Watch for a change in how the teen spends his or her time. Often, they suddenly spend all of their time at the gym, obsessed with working out and preoccupied with body image.[59]

The school nurse is in the ideal position to observe for any of the physical, social, and emotional changes previously mentioned. Besides observation, the school nurse can play a vital role in educating students about the dangers of PED use. Education can be carried out on a one-to-one basis, or in groups, and is best coordinated with

athletic coaching staff. Educating against the use of performance enhancers may also open the door to a discussion about other illicit drugs. The latter is a very important aspect of adolescent health teaching and substance abuse prevention.[60]

CONCLUSION

Welfare of the athlete must be our primary concern. If a drug does not expose an athlete to excessive risk, we should allow it even if it enhances performance. We have two choices: to vainly try to turn the clock back, or to rethink who we are and what sport is, and to make a new 21st century Olympics. Not a super-Olympics but a more human Olympics. Our crusade against drugs in sport has failed. Rather than fearing drugs in sport, we should embrace them.

In 1998, the president of the International Olympic Committee, Juan- Antonio Samaranch, suggested that athletes be allowed to use non-harmful performance enhancing drugs.44 This view makes sense only if, by not using drugs, we are assured that athletes are not being harmed. Performance enhancement is not against the spirit of sport; it is the spirit of sport. To choose to be better is to be human. Athletes should be the given this choice. Their welfare should be paramount. But taking drugs is not necessarily cheating. The legalisation of drugs in sport may be fairer and safer.

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