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Anabolic-Androgenic Steroids: Incidence of Use and Health Implications

"The use of performance-enhancing drugs like steroids in baseball, football and other sports is dangerous, and it sends the wrong message—that there are shortcuts to accomplishment, and that performance is more important than character."

President George W. Bush, State of the Union address, January 20, 2004

Note from the Editors

In recent months there have been more that a few stories in the national media related to the use of anabolic-androgenic steroids among athletes. Because of this attention, and because steroid abuse is not limited to athletes, the editors felt that the time was right for an issue of the *Research Digest* devoted to steroids. As the reference list for this article attests, Charles Yesalis and Michael Bahrke, the authors of this issue of the *Research Digest*, are widely published experts on steroid use and abuse. Yesalis and Bahrke were charged with presenting the evidence about steroid use, something that they did quite well. The authors were not asked to dwell on the legal and ethical issues associated with the use of steroids. For this reason, the editors wish to make it clear to readers, especially youth who might read this paper, that anabolic-androgenic steroids are illegal drugs when used for performance enhancement and attempting to increase muscle mass. In addition most sports organizations, including the Olympics, the NCAA, high school athletic groups, and professional sports, ban the use of these substances. These bans are based on the notion that the use of performance-enhancing drugs is not only illegal, but unethical. More importantly, as the authors of this issue point out, there are many negative health consequences associated with the inappropriate use of steroids.

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Guest Authors: Charles E. Yesalis, College of Health and Human Development, Pennsylvania State University, University Park, Pennsylvania.

Michael S. Bahrke, Scientific, Technical and Medical Division, Human Kinetics, Champaign, Illinois.



Co-edited by:
Drs. Charles B. Corbin and
Robert P. Pangrazi,
Arizona State University, and
Dr. Deborah Young,
University of Maryland

Introduction

Testosterone is the primary natural male hormone (produced primarily by the testes). Though testosterone is considered to be the "male" hormone, it is also present in females in lesser amounts. Testosterone has androgenic or masculinizing effects such as growth of facial and body hair and deepening of the voice. In addition, testosterone has anabolic or tissue-building effects such as increases in muscle cell size. Because males produce more testosterone as they mature, both masculinizing and tissue-building changes are observed during adolescence and into adulthood. Tissue building is increased in females as well, but not to the same extent as for males.

By 1935, testosterone had been isolated and chemically characterized, and the nature of its anabolic effects elucidated (Kochakian & Yesalis, 2000). Anabolic-androgenic steroids, as discussed in this paper, are synthetic derivatives of testosterone. A pure anabolic steroid has yet to be discovered, but many different forms of derivatives of this drug (with many different names) are now in distribution (See Table 1), all properly referred to as anabolic-androgenic steroids. The more common term "anabolic steroid" is used here for convenience. Related substances include prohormones, such as androstenedione ("Andro") and dehydroepiandrosterone (DHEA), which are steroids in the biosynthesis pathway.

Most commonly, anabolic steroids are taken orally or by intra-muscular injection (See Table 2). More recently, gels and creams are being used by elite athletes as delivery mechanisms in an attempt to circumvent drug testing.

As will be discussed in greater detail later in this paper, as many as one million young people have used steroids even though they are illegal and banned by most sports organizations. Health concerns are the principal reason for prohibiting the sales of anabolic steroids while sporting organizations have banned their use for ethical reasons.

Why do people use anabolic steroids?

There are many different reasons why people choose to use steroids. Use was initially most prevalent among athletes with goals of enhancing performance. However, in recent years use by non-athletes has become more prevalent. Now an increasing number of anabolic steroid users simply want to "look good"—which to many people means being big and muscular.

Table 1. Examples of Anabolic Agents Identified by the 31 IOC/WADA Accredited Laboratories in 2003

Nandrolone Testosterone Stanozolol Methandienone Mesterolone Boldenone Tetrahydrogestrinone (THG) Methyltestosterone Methenolone Oxandrolone Androstenedione (Andro) Clostebol Fluoxymesterone Danazol Oxymetholone DHEĂ Norethandrolone Drostanolone Trenbolone Oxymesterone

Source: World Anti-Doping Agency, http://www.wada-ama.org/en/t1.asp, WADA Statistics, 2003.

The goals of individuals who use anabolic steroids in sport and exercise are dependent on the activity in which they participate. Bodybuilders desire more lean body mass and less body fat. Weight lifters desire to lift the maximum amount of weight possible. Field athletes want to put the shot, or throw the hammer, discus, or javelin, farther than their competitors or holders of previous records. Swimmers and runners hope to be able to perform their frequent, high-intensity, long-duration workouts without physical breakdown. Football players want to increase their lean body mass and strength so they can be successful at the high school, college, or professional level.

Anabolic steroids have traditionally been taken in "cycles," which are episodes of use lasting 6 to 12 weeks or more (Llewellyn, 2000). Athletes often take more than one steroid at a time; this is referred to as "stacking." In an attempt to avoid developing a tolerance to a particular anabolic steroid ("plateauing"), some users stagger their drugs, taking the anabolic steroids in an overlapping pattern, or stop one drug and start another (Duchaine, 1989; Gallaway, 1997). Often steroid users will "pyramid" their administration patterns, moving from a low daily dose at the beginning of the cycle to a higher dose and then tapering down the dose toward the end of their cycle (Grundig & Bachmann, 1995; Wright, 1982). In addition, individuals may use other drugs concurrently with anabolic steroids to counteract the common adverse effects of steroids. These drugs include diuretics, antiestrogens, human chorionic gonadotrophin, and anti-acne medications. This polypharmacy is termed an "array" (Duchaine, 1989). The frequency of concurrent drug use or the frequency or efficacy of each of these administration patterns is poorly documented.

The dosage of anabolic steroids depends on the sport as well as on the particular needs of the athlete. Endurance athletes use steroids primarily for their alleged catabolism-blocking effects, i.e., to forestall the occurrence of "overtraining" (decreased natural testosterone levels, fatigue, muscle atrophy and soreness, etc.) (Friedl, 2000a). These athletes, for the most part, are trying to maintain their testosterone levels in the "normal" range. Thus, they use dosages at or slightly below physiological replacement levels, that is, about 7 mg/day of testosterone (Yen & Jaffe, 1978). Participants in the traditional strength sports, seeking to "bulk up," have generally used dosages that exceed physiological replacement levels by 10 to 100 times or more (Kerr, 1982; Wright, 1982). Administration patterns also vary among athletes within a particular sport, based on each athlete's training goals and response to the drugs, as well as on the biological activity of different anabolic steroids (Kochakian & Yesalis, 2000; Wright, 1982). Women, regardless of sport, are generally thought to use lower dosages of anabolic steroids than men (Elliot & Goldberg, 2000).

While it appears that many *elite* athletes obtain pharmaceutical-grade drugs from medical professionals, the large majority of

anabolic steroid users are not elite athletes and use black market steroids produced by clandestine labs in the United States and by companies outside the U.S. that do not adhere to the rigid industry standards that ensure each dosage form contains a predictable and consistent amount of active ingredient(s) (See Table 3). These products may be contaminated and/or may not be what they are purported to be. Regardless of the source, the use of anabolic steroids for purposes of performance enhancement is illegal and unethical.

How prevalent is anabolic steroid use?

High levels of use of anabolic steroids have been attributed to professional football players, weight

lifters, power lifters, bodybuilders, and throwers in track and field events since the 1960s (Yesalis, Courson, & Wright, 2000). Use by high school athletes was rumored as early as 1959 (Frazier, 1973; Gilbert, 1969a,b,c). However, until the mid-1970s, information on the incidence of non-medical use of steroids was based on anecdotes, testimonials, and rumors (Yesalis & Bahrke, 1995). Although rumors still abound, estimates of the incidence of steroid use are now based on the results of systematic surveys. Surveys of steroid use are categorized here as those of (1) adolescent school-age students, (2) college students, and (3) athletes not falling into categories 1 or 2.

Use among adolescent school-age students

In 1987 the first U.S. national study of anabolic steroid use at

| Tabl Examples of Oral and/or Ir | | nabolic Steroids |
|------------------------------------|--------------|------------------|
| Steroid | Oral* | Injectible** |
| Testosterone cypionate | | X |
| Nandrolone decanoate | | X |
| Stanozolol | X | X |
| Methandienone | X | |
| Mesterolone | X | |
| Boldenone undecylenate | | X |
| Tetrahydrogestrinone (THG) | X | X |
| (may also be a gel or injectible) | | |
| Methyltestosterone | X | |
| Methenolone acetate | \mathbf{X} | |
| Methenolone enanthate | | X |
| Oxandrolone | X | |
| Androstenedione (Andro) | X | |
| Clostebol acetate | X | X |
| Fluoxymesterone | X | |
| Danazol | X | |
| Oxymetholone | X | |
| DHEA | X | |
| Norethandrolone | X | |
| Drostanolone proprionate | X | X |
| Oxymesterone | X | |
| Trenbolone acetate | | X |

^{*}Adverse effects of oral steroids—liver disease, decreased HDL, increased LDL.

Sources: adapted from Llewellyn, W. Anabolics 2000, Aurora, CO: Anabolics.com, Inc., 2000; Grunding, P. and Bachmann, M. World Anabolic Review 1996, Houston, TX: MB Muscle Books, 1995; and Phillips, W.N. Anabolic Reference Guide Sixth Issue, Golden, CO: Mile High Publishing, 1991.

^{**}Adverse effects of injecting anabolic steroids (i.e., "needle sharing"): infections, AIDS, hepatitis.

Table 3. **Sources of Anabolic Steroids Medical Professionals Sports Personnel**

Countries United States Physicians Pharmacists Mexico Russia Veterinarians Poland **Dentists Athletic Trainers** Hungary **Physical Therapists**

Sport Coaches Conditioning Coaches Nutrition Consultants

Spain Italy Greece Canada Netherlands Thailand

Source: Adapted from Bahrke, M.S. and Yesalis, C.E. Performance-Enhancing Substances in Sport and Exercise. Champaign, IL: Human Kinetics, 2002.

the high school level was conducted by Buckley and associates (Buckley et al., 1988). The investigators found that 6.6% of male high school seniors reported having used these drugs. There was no difference in the level of reported steroid use between urban and rural areas, but there was a small, yet significant, difference by size of enrollment: students at larger high schools had a higher rate of reported steroid use. In addition, among the self-reported steroid users, 38% had initiated use before 16 years of age; and more than one-third of the steroid users did not intend to participate in interscholastic sports.

During the early to mid 1990s multiple U.S. local-, state-, and national-level studies confirmed the findings of Buckley et al. (1988), and showed that 4% to 6% (with a range of 3% to 12%) of high school males admit to using anabolic steroids at some time in their life (Yesalis, Barsukiewicz, Kopstein, & Bahrke, 1997). Some of these studies also examined the use of anabolic steroids among high school females, generally showed that 1% to 2% reported having used anabolic steroids (Yesalis, Bahrke, Kopstein, & Barsukiewicz, 2000). Likewise, several of the studies confirmed that substantial percentages of steroid users do not participate in traditional school-sponsored sports.

Since 1991, steroid use by males as measured by U.S. national surveys has generally increased (Grunbaum et al. 2004; Hewitt, Smith-Akin, Higgins, Jenkins, 1998; Johnston, Bachman, O'Malley, & Schulenberg, 2004; Kann, Warren, Harris, Collins, Douglas, et al., 1995; Feyrer-Melk, Corbin, & Lewis, 1994) (Table 4). Furthermore, since 1991, data from these U.S. national surveys point to an increase in anabolic steroid use among adolescent females as well as a sharp drop in the perceived dangers of using steroids (Johnston, Bachman, O'Malley, & Schulenberg, 2004). What is more troubling is the 2003 Youth Risk and Behavior Surveillance

System data (Grunbaum et al. 2004) showed that among 9th- to 12th-grade students (ages 13-19) in public and private high schools in the United States, 6.8% of males and 5.3% of females (up from 4.1% and 2.0% respectively in 1997) had used anabolic steroids at least once in their lives. Based on 2000 Census estimates of high school students, these period prevalence rates translate to well over one million young people in the United States who have used (cycled) anabolic steroids at least once during their lifetime.

We should also note the use of anabolic steroids by adolescents is not limited to the U.S.

(Newman, 1994; Yesalis, Ortner, & Bahrke, 1996). Three Canadian studies (Adalf & Smart, 1992; Canadian Centre for Drug-Free Sport, 1993; Killip & Stennett, 1990), four Swedish surveys (Kindlundh, Isacson, Berglund, & Nyberg, 1999; Nilsson, 1995; Nilsson, Baigi, Marklund, & Fridlund, 2001a & b), two South African investigations (Lambert, Titlestad, & Schwellnus, 1998; Schwellnus, Lambert, & Todd, 1992), one British study (Williamson, 1993), and one Australian investigation (Handelsman & Gupta, 1997) have reported overall prevalence rates for high school-aged students to range between 1.2-5.9% for males and 0.0–1.5% for females. Although these rates are slightly lower, they approximate those reported for the U.S., and reflect the cross-cultural impact of anabolic steroids on performance and physical appearance.

Use among college athletes

Since 1985, Anderson et al. (1985, 1991, 1993) and the National Collegiate Athletic Association (NCAA) (1997, 2001) conducted five surveys of male and female student athletes at selected NCAA member colleges and universities regarding substance abuse, including anabolic steroids. In the five surveys, the heaviest anabolic steroid use (defined as use in the past 12 months) was reported in 1985—4.9% among all athletes. Thereafter, steroid use decreased to its lowest level in 1997 (1.1%); in 2001 the level of use increased to 1.4%. In all five surveys, the pattern of self-reported use was fairly consistent among Division I-III schools. In the 2001 survey, there was no striking difference in anabolic steroid use by race. The level of use in men's sports ranged from 0.2% in swimming to 3.0% in football and a high of 5.0% among water polo participants. In women's sports, self-reported steroid use was highest in lacrosse (1.6%); there were five women's sports that reported no steroid use in the 2001 survey. Of the student athletes who acknowledged use of anabolic steroids, over half reported first using these drugs in junior high or high school. Not surprisingly, the predominant reason (42.7%) given for their use of anabolic steroids was the improvement of athletic performance.

Yesalis, Buckley, Anderson, Wang, Norwig, Ott, Puffer, & Strauss (1990) employed projected response survey techniques with collegiate athletes, using indirect questions. Thus, respondents were asked to estimate the level of their competitors' anabolic steroid use. Over 1600 male and female athletes at five NCAA Division I institutions participated in this study during the 1989-1990 academic year. The mean overall projected rate of any prior use of anabolic steroids across all sports surveyed was 14.7% for male and 5.9% for female athletes. Among men's sports, football showed the highest projected lifetime steroid use rates with 29.3%, followed by track and field events with 20.6%. The greatest projected use rate for women's sports was 16.3% for track and field events. The reported overall projected rate of anabolic steroid use

Table 4. Trends in Lifetime Prevalence of Use of Anabolic Steroids for Eighth, Tenth, and Twelfth Graders

| | | | | | Yea | ar | | | | | | | | |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Grade | 91 | 92 | 93 | 94 | 95 | 96 | 97 | 98 | 99 | 00 | 01 | 02 | 03 | |
| 8th | 1.9 | 1.7 | 1.6 | 2.0 | 2.0 | 1.8 | 1.8 | 2.3 | 2.7 | 3.0 | 2.8 | 2.5 | 2.5 | |
| 10th | 1.8 | 1.7 | 1.7 | 1.8 | 2.0 | 1.8 | 2.0 | 2.0 | 2.7 | 3.5 | 3.5 | 3.5 | 3.0 | |
| 12th | 2.1 | 2.1 | 2.0 | 2.4 | 2.3 | 1.9 | 2.4 | 2.7 | 2.9 | 2.5 | 3.7 | 4.0 | 3.5 | |

Source: Monitoring the Future Study, the University of Michigan.

during the past 12 months was approximately three times greater than the rate obtained from self-reports in the 1991 NCAA survey (NCAA Staff 2001).

The true level of steroid use among athletes probably lies between the lower-bound estimates from self-reports and the upper-bound estimates obtained from the projective response techniques (Yesalis, Buckley, Anderson, Wang, Norwig, Ott, Puffer, & Strauss, 1990). While the response of adolescents to anonymous surveys of drug use is considered generally valid, the results of this projective response study as well as those of other validation studies of elite athletes (Yesalis, Bahrke, Kopstein, & Barsukiewicz, 2000) call into question the validity of surveys of elite athletes and argue that there is a substantial underreporting bias.

Use by Olympic athletes

Track and field event athletes who participated in the 1972 Olympics were surveyed (Silvester, 1973): and 68% of the participants reported prior steroid use, with 61% having used steroids within six months of the Games. In 1975, Ljungqvist surveyed elite Swedish male track and field event athletes and found that 31% admitted prior anabolic steroid use. None of the middle- or long-distance runners admitted to anabolic steroid use, but 75% of the throwers did.

In a survey of 155 U.S. Olympians who participated in the 1992 Winter Games, 80% of the athletes classified steroid use among Olympic competitors as a very serious or somewhat serious problem; just 5% thought that it was not a problem (Pearson & Hansen, 1992). When asked to estimate the level of steroid use in their own sport, 43% of the respondents estimated use by 10% or more of competitors, while 34% estimated use at 1% to 9%. Only 23% of the athletes surveyed believed that there was no steroid use in their sport. In another survey of former Olympians (Pearson, 1994), 75% of the medalists and 63% of the nonmedalists stated that more athletes were using performance-enhancing drugs than when they themselves had competed.

An intensive two-year investigation of doping in Olympic sport conducted for the U.S. Office of National Drug Control Policy concluded that while estimates of the magnitude of the doping epidemic vary widely (from 10% to 90% of athletes), there exists an atmosphere in our society that fosters drug use by athletes:

the high financial stakes for Olympic athletes, corporate sponsors, the TV broadcast and cable industries and sport governing bodies, coupled with the pharmacopoeia of performance-enhancing substances, the athlete's drive to win and the absence of an effective policing mechanism, create an environment that encourages doing anything – including doping – to win (National Center on Addiction and Substance Abuse, 2000: 2).

While testing and education programs have been in effect for some time, new efforts to reduce steroid use have recently been implemented. On October 1, 2000 the U.S. Anti-Doping Agency (USADA) was formed as the independent anti-doping agency for Olympic sports in the United States. It was created as the result of recommendations set forth by the U.S. Olympic Committee's Select Task Force on Externalization. They have full authority for testing, education, and research, as well as adjudication for U.S. Olympic, Pan Am and Paralympic athletes.

Use by Weight Lifters

Weight trainers in three gymnasiums in the Chicago area were

questioned (Frankle, Cicero, & Payne, 1984); 44% reported prior steroid use. In a study of amateur competitive bodybuilders (Tricker, O'Neil, & Cook, 1989), over half of the men and 10% of the women reported that they had used anabolic steroids at some time in their life. In 1993, of the 185 members of gymnasiums and health clubs, 18% of men and 3% of women acknowledged having used or currently using anabolic steroids (Kersey, 1993). In 1988, Yesalis et al. surveyed elite power lifters using both questionnaires and follow-up telephone interviews. One-third of the questionnaire respondents admitted prior anabolic steroid use; however, 55% of those interviewed later by telephone conceded steroid use.

The level of steroid use appears to have increased significantly over the past three decades (Johnston, Bachman, O'Malley, & Schulenberg, 2004; Yesalis, Anderson, Buckley, & Wright, 1990; Yesalis, Kennedy, Kopstein, & Bahrke, 1993.), and is no longer limited to elite athletes or to men. Although higher rates of steroid use are reported by competitive athletes, a significant number of recreational athletes and non-athletes appear to be using these drugs, probably to "improve" their appearance. Looking at elite sport in the 20th Century through the eyes of historians and journalists as well as the athletes themselves, an unmistakable picture emerges of a *sustained* doping pandemic of huge proportions in elite sport (Yesalis & Bahrke, 2003). Of greater concern is that the use of anabolic steroids has cascaded down from the Olympic, professional, and college levels to the high schools and junior high schools, and there are significantly more adolescents using anabolic steroids than elite athletes.

Ergogenic effects: Do anabolic steroids improve performance?

While the vast majority of the athletic community accepts that anabolic steroids enhance exercise capacity and performance (Yesalis, Anderson, Buckley, & Wright, 1990), from 1977 to 1984, the American College of Sports Medicine (1977, 1984) regarded anabolic steroids as ineffective, sending mixed messages to the athletic community concerning the potential of anabolic steroids to enhance performance. As recently as 1992, other scientists (Celotti & Negri-Cesi, 1992) remained skeptical, also reporting that anabolic steroids were ineffective. However, a study by Bhasin and his colleagues in 1996 quelled much of the residual doubt concerning the effectiveness of anabolic steroids in humans. Using a relatively high dose of an anabolic steroid (600 mg/wk of testosterone enanthate for 10 weeks), Bhasin et al. (1996) found a 13 lb (6 kg) weight gain and 48.5 lb (22 kg) improvement in the one-repetition maximum (1-RM) bench press in experienced lifters. The results of the Bhasin study (1996) also suggested additive effects of exercise and steroids, with a bench press improvement of approximately 22 lb (10 kg) produced by exercise or steroid, and 44 lb (20 kg) produced by exercise and steroid.

Thus, anabolic steroids, as a class, produce lean mass gain in normal healthy, adult men with a reciprocal decrease in total body adipose tissue. In addition, a dose response effect has been demonstrated (Forbes, 1985; Herbst and Bhasin, 2004). Typical weight gains are 6.6 to 11 lb (3-5 kg) after several weeks of high-dose steroid use. The effects of steroids on strength performance are mostly seen with experienced weight lifters and when strength training is performed concurrently with the steroid administration. Most studies demonstrating strength gains also demonstrate weight gains.

At least one study has demonstrated a threshold response of body composition to anabolic steroids, as well as variations in response according to type of steroid (Friedl, Dettori, Hannan, Patience, & Plymate, 1991). The mechanisms of action for an

Table 5

Potential Adverse Effects of Anabolic Steroids

| Males |
|---------------------|
| Baldness |
| Prostate changes |
| Gynecomastia |
| Impotence/Sterility |

Females
Breast Shrinkage
Clitoral Enlargement
Increased Facial/Body Hair
Menstrual Irregularities
Premature Hair Loss
Deepened Voice

(Vocal cord thickening)

Acne Aggression

Brittle connective tissue Cardiovascular Disease Cerebrovascular incidents

Both Males and Females

Dependency Headaches Hypertension Liver Disease

Psyche and behavior changes

Short Stature

(Premature growth-plate closure)

Source: Adapted from Bahrke, M.S. and Yesalis, C.E. Performance-Enhancing Substances in Sport and Exercise. Champaign, IL: Human Kinetics, 2002.

effect on muscle mass have been increasingly elucidated and involve multiple mechanisms including increased protein anabolism and differentiation of pluripotent stem cells toward the myogenic lineage (Herbst and Bhasin, 2004). Furthermore, the resultant muscle hypertrophy and regeneration is associated with an increase in myoblast differentiation or the number of satellite cells (Herbst and Bhasin, 2004).

While the ergogenic effects of anabolic steroids have been established, the effects of high doses or prolonged administration of anabolic steroids on physique or physiological capacities have not been documented. Likewise, the residual effects of anabolic steroids on physiological capacities after the termination of use have not been established. Furthermore, results of any dose on physical/physiological capacities or performance in females are unknown.

Although the evidence is incomplete, anabolic steroids may also inhibit or block the catabolic effects of glucocorticoids that are released during intense training (Kuhn, 2002). Theoretically, this anti-catabolic effect would allow athletes to train more frequently and more intensely, and this may be the most important factor concerning the performance-enhancing effects of anabolic steroids. Furthermore, while there is little evidence to support a beneficial role of anabolic steroids in other types of exercise performance such as muscular endurance or aerobic endurance, anabolic steroids increase the number of red blood cells (RBCs). With the anti-catabolic effect and an increase in RBCs, endurance athletes may be able to train more frequently, for longer periods of time, and with greater intensity. In turn, this could produce improved aerobic capacity resulting in quicker running times or in more repetitions of a particular activity.

What are the short- and long-term health effects of anabolic steroid use?

Physical and Physiological Effects

The short-term health effects of anabolic-androgenic steroids have been increasingly studied, and several authors have reviewed the physiological and health effects of these drugs (Friedl, 2000b; Haupt & Rovere, 1984; Lamb, 1984; Wilson, 1988; Wright, 1980) (See Table 5). Although anabolic steroid use has been associated (mainly through case reports) with a number of adverse and even fatal effects, the incidence of serious effects thus far reported has been extremely low (Friedl, 2000b). However, for several decades experts have consistently stated that the long-term health effects of anabolic steroid use

are unknown (Yesalis, Wright, & Bahrke, 1989). Specifically, the long-term health effects as related to type of steroid, dose, frequency of use, age at initiation, and concurrent drug use have not been elucidated. Confounding the assessment of health consequences is the fact that some individuals use large doses of anabolic steroids for prolonged periods of time, while others use therapeutic doses intermittently (Buckley et al., 1988; Duchaine, 1989; Grundig & Bachmann, 1995; Llewellyn, 2000).

Although the role of anabolic steroids in the etiology of various diseases in both animals and humans is still uncertain, steroid use in clinical trials and in laboratory studies has been associated with numerous deleterious

changes in risk factors and in the physiology of various organs and body systems, suggesting potential for subsequent health problems (American College of Sports Medicine, 1984; Kruskemper, 1968; Wright, 1980; Freidl, 2000b). The best-documented effects are those on the liver, serum lipids, and the reproductive system. Other suspected areas of concern include the psyche and behavior, coronary artery disease, cerebrovascular accidents, prostatic changes, and the immune function (Friedl, 2000b).

Steroid use has been related to cardiovascular risk factors. The most important are changes in lipoprotein fraction, increased triglyceride levels and concentrations of several clotting factors, and hyperinsulinism and diminished glucose tolerance (Friedl, 2000b; Glazer, 1991; Haupt & Rovere, 1984; Sullivan, Martinez, Gennis, & Gallagher, 1998; Wright, 1980). It should be noted, however, that although these effects vary significantly between types and doses of anabolic steroids, and between individuals and situations (Kruskemper, 1968), all of the effects have been demonstrated to be fully reversible within several months after cessation of steroid use (Friedl, 2000b; Haupt & Rovere, 1984; Wright, 1980).

Anabolic steroids have been shown to be cardiotoxic in animals (Hartgens, Cherlex, & Kulpers, 2003). In addition, some studies in humans, but not all, have shown that anabolic steroid use is associated with left ventricular (LV) hypertrophy (Karila et al., 2003; Hartgens, Cherlex, & Kulpers, 2003; Urhausen, Albers, & Kindermann, 2004). Furthermore, one study demonstrated that the increases in LV mass persist several years after discontinuation of anabolic steroid use (Urhausen, Albers, & Kindermann, 2004).

Acute thrombotic risk has been linked to steroid use in 17 case reports of nonfatal myocardial infarction and stroke in athletes who were using anabolic steroids (Rockhold, 1993; Wu & Eckardstein, 2003). Although there is no direct evidence anabolic steroids are thrombogenic in humans (Ansell, Tiarks, & Fairchild, 1993), the clinical circumstances of these reports suggest a possible causal relationship. These reports further suggest that, if a causal relationship exists, anabolic steroids could have serious short-term effects.

Liver structure and function have also been altered by administration of anabolic steroids; associated conditions include cholestatic jaundice, peliosis hepatitis, hepatocellular hyperplasia, and hepatocellular adenomas (Dickerman, Pertusi, Zachariah, Dufour, & McConathy, 1999; Soe, Soe, & Gluud, 1992). Peliosis hepatitis is clearly associated with the use of 17-

a-alkylated (oral) anabolic steroids, but with unknown frequency. Hepatic tumors are rare in men (1% to 3%), but nearly half of the discovered tumors rupture, and a larger proportion may remain undetected. In two cases, rupture proved fatal (Friedl, 2000b). It has not been convincingly demonstrated that anabolic steroids can cause, at least with therapeutic doses, the development of hepatocellular carcinomas. In summary, virtually all histological changes in the liver have been associated with the use of 17-a-alkylated (oral) steroids (Friedl, 2000b; Kruskemper, 1968; Wilson, 1988; Wright, 1980); and the cause-and-effect relationship between oral anabolic steroids and these conditions is strengthened by the return of normal blood values and excretory function, the regression of tumors, a general recovery, and a return toward normal liver function after cessation of steroid use (Friedl, 2000b).

The effects of anabolic-androgenic steroids on the male reproductive system include reductions in levels of endogenous testosterone, gonadotrophic hormones, and sex hormone-binding globulin (SHBG); reductions in testicle size, sperm count, and sperm motility; and alterations in sperm morphology (Friedl, 2000b; Wright, 1980). When steroid use is stopped, the testes resume sperm production and sperm quality usually recovers spontaneously within four months. However, the impact of anabolic steroids on spermatogenesis may persist for a year or more (Dohle, Smit, & Weber, 2003).

Anabolic steroids have been associated through case reports with tendon injuries and neuropathies (Friedl, 2000b). While the results of animal studies support a causal association, to date the effects of steroids on musculoskeletal injuries in humans cannot be distinguished from the risks ordinarily faced by strength athletes not using anabolic steroids.

In women, anabolic steroids have been associated with a number of adverse effects, some of which are not reversible upon discontinuation of steroid use (Elliot & Goldberg, 2000). These include menstrual abnormalities; deepening of the voice; shrinkage of the breasts; male-pattern baldness; and an increase in sex drive, acne, body hair, and clitoris size. In addition, women using steroids experience dramatically elevated testosterone levels and lowered levels of SHBG, follicle-stimulating hormone, and thyroid-binding proteins (Elliot & Goldberg, 2000; Malarkey, Strauss, & Leizman, 1991). Premature halting of growth in younger male and female users has not been systematically studied, although such effects have been described in case reports for several decades (Rogol & Yesalis, 1992).

Psychological Effects

Previous and current research studies have documented significant positive relationships between testosterone levels, dominance, and aggressive behavior in various species of animals, including nonhuman primates (Bahrke, Yesalis, & Wright, 1996). Relative to the animal literature, fewer studies have assessed the relationship of endogenous or exogenous androgens to aggression or violent behavior in humans. However, a positive pattern of association between endogenous testosterone levels and aggressive behavior in males has been increasingly established (Bahrke, 2000). Also, while random clinical trials using moderate doses of exogenous testosterone for contraceptive and other purposes reveal few adverse effects on male sexual and aggressive behavior, other investigations and case reports of athletes using higher doses suggest the possibility of affective and psychotic syndromes (some of violent proportions), psychological dependence, and withdrawal symptoms.

While several published reports support a pattern of association

between the use of anabolic steroids by athletes and increased levels of irritability, aggression, personality disturbance, and psychiatric diagnoses, others do not (Bhasin et al., 1996; Millar, 1996; Yates, Perry, MacIndoe, Holman, & Ellingrod, 1999). Only a few prospective, blinded studies documenting aggression and adverse overt behavior resulting from steroid use have been reported (Hannan, Friedl, Zold, Kettler, & Plymate, 1991; Pope, Kouri, & Hudson, 2000; Kouri, Lukas, Pope, & Oliva, 1995; Su et al., 1993). As Bjorkqvist and colleagues (1994) point out, much of the psychological and behavioral effect of steroid intake may be placebo. In a double-blind experiment, human males (n = 27) were given either testosterone, placebo, or no treatment, over a one-week period. The results revealed a significant placebo effect. After treatment, the placebo group scored higher than both the testosterone and the control groups on self-estimated anger, irritation, impulsivity, and frustration. Observer-estimated mood yielded similar results. Anticipation of the aggressiveness related to steroid use may lead to actual violent acts and become, in effect, an excuse for aggression.

Although anabolic steroid dependency may be a problem, its prevalence and symptomatology are difficult to reliably establish based on the existing literature. There is some evidence that testosterone is mildly reinforcing (relative to the classic reinforcers, cocaine and heroin) in male rats and hamsters self-administering (Wood et al., 2004). Brower (2002) in his review found no evidence that anabolic steroids lead to dependence (i.e., meeting the Diagnostic and Statistical Manual of Mental Disorders criteria for dependence) with therapeutic use. However, he noted 165 instances of dependence among weightlifters and bodybuilders using supraphysiologic doses of anabolic steroids.

It is interesting to note that with a million or more steroid users in the United States (Yesalis, Kennedy, Kopstein, & Bahrke, 1993), only an extremely small percentage of users appear to experience mental disturbances that result in clinical treatment. Also, of the few individuals who do experience significant changes, most apparently recover without additional problems when the use of steroids is terminated.

Conclusion

Anabolic steroids are synthetic derivatives of testosterone. They are usually administered orally and by injection. Anabolic steroids are used by athletes to enhance performance and non-athletes to enhance appearance. Strong evidence now exists demonstrating that anabolic steroid use results in increased body weight and muscular strength. There is also an increasing body of evidence that anabolic steroid use is associated with a variety of health problems. While the long-term effects of anabolic steroids remain unclear, the best-documented physiological effects are those on the liver, serum lipids, and the reproductive system. A pattern of association between the use of anabolic steroids and increased levels of irritability, aggression, personality disturbance, dependence, and psychiatric diagnoses has been revealed in a number of reports.

Although anabolic steroids are illegal, and their use is banned by virtually every sport governing body, survey and drug-testing data indicate continued use by competitive athletes at all levels. The fact that the level of steroid use appears to have increased significantly over the past three decades among adolescents, women, and recreational athletes is also of growing concern. The use of anabolic steroids presents an interesting public health challenge. While these drugs are associated with deleterious physical and psychological outcomes, they are being used to achieve what many consider socially desirable ends: being physically attractive and being a winner.

"The use of performance-enhancing drugs like steroids in baseball, football and other sports is dangerous, and it sends the wrong message – that there are shortcuts to accomplishment, and that performance is more important than character."

President George W. Bush, State of the Union address, January 20, 2004

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