Androgen-Androgenic Steroids, the Athlete, and Mortality

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Use of performance-enhancing substances is widespread among men and women athletes and body builders, professional or amateur, adolescent or adult. Many of these substances are illegal or have adverse effects. This article describes the action and effects of androgenic and growth hormones, their legality, their potential for abuse, and their impact on mortality.

CASE REPORT

The proposed insured is a 25-year-old semi-professional football player and lifeguard who is applying for $500,000 of term insurance. The applicant has no recorded medical or legal problems. The insurance exam reveals a height of 5’11” and weight of 225 lb. The heart rate was 58 beats per minute and the average blood pressure was 138/94 mm Hg. The insurance lab included a total cholesterol of 250 mg/dl, an high density lipoprotein (HDL) of 11 mg/dl, an low density lipoprotein (LDL) of 179 mg/dl, and a triglyceride of 300 mg/dl. The aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 88 U/L and 122 U/L, respectively. The general agent was impressed with his client’s apparent good health and enclosed a photograph to support his opinion; the photo is represented in the illustration given in the Figure. The medical underwriter was also impressed with the picture. She requested an APS.

The APS included the following information about the proposed insured. Since the age of 15, he has had an interest in body building. Over a 5-year period, there were a few notations of his having small testicles and gynecomastia. This prompted the physician’s ordering prolactin and testosterone levels; these were normal and low normal, respectively. Over the past 12 months, his 3 recorded blood pressures averaged 146/92 mm Hg. Other lab data included an AST and ALT of 80 U/L and 102 U/L, respectively. Two years prior to the application date, an entry was made referencing an emergency room visit. He was evaluated for complaints of slurred speech and problems using his right arm for a period of 15 minutes. He was released without a specific diagnosis. On one occasion, the physician pointedly ask the proposed insured if he used any anabolic steroids. He said,
"No." The APS also mentions a "rocky" marriage 3 years before his divorce.
A motor vehicle record was obtained. There were driving while under the influence and resisting arrest charges 4 years prior to the application date.

**DISCUSSION**

Athletes strive for competitive advantages. The "winning at all costs" feeds the demand for ergogenic drugs. A poll of 198 current or aspiring US Olympians produced data stating that 98% of them would take a banned performance-enhancing substance if they were guaranteed to win and not get caught. This same group of athletes said in the survey that they would be willing to risk death from taking undetectable substances if they thought that doing so would enable them to win every competition over a 5-year period. Even a previously "clean" athlete is likely to cave in as his/her opponents use drugs to improve their performances. Given our competitive environment, underground chemists, suppliers, detection-avoidance advisors, and "improved" drugs that are harder to detect, the anabolic-androgenic steroids (AASs) will be a part of our athletic and body-building cultures. In one survey, 70% of athletes stated that access to illegal substances was not difficult. There is a lack of fear of adverse effects. The individual who abuses an anabolic steroid combined with additional nonsteroidal substances like human growth hormone or clenbuterol is likely to have previously used cocaine, injectable drugs, alcohol, marijuana, or shared needles.

Anabolic steroids improve muscle protein formation, and they may lessen the rate of muscle tissue breakdown. These changes increase muscle mass and strength. They also help the individual recover from exercise more quickly, which allows them to intensely train. In addition to improving their performance, athletes have other reasons for taking AASs. They may get pressure from peers, coaches, trainers, and even physicians. One's psychological makeup may lead him/her down this same path in a quest to look better. Many of the substances are legal and are easy to use.

Two thirds of steroid abusers began using them when they were younger than 17. About 75% of the 1 million steroid abusers are thought to be in high school. The other steroid abusers not in high school are generally about 25 years old. Body builders at athletic clubs are about this same age while more men abuse steroids than do women, abuse among women is rising. The "weekend" warrior is the more common user of steroids, compared with professional and elite athletes. Athletes not attending school and nonathletes represent a significant portion of the steroid user population.

Among adolescents, 5–11% of boys and up to 2.5% of girls self-report using anabolic steroids. The 1991 National Household Survey on Drug Abuse study is one of the largest cross-sectional studies of people aged 12 years and older who used AASs. That data suggests that more than 1 million current or former AAS users exists in the United States, and more than half of the lifetime user population is 26 years or older. Age 18 is the me-
COTLAR—ANDROGEN-ANDROGENIC STEROIDS AND MORTALITY

dian age of the individual's first usage of AASs. It is estimated that about 15% of community weight trainers and 30–75% of body builders, elite athletes, and professional athletes use AASs.

Anabolic steroids are veterinary or human agents of androgenic-anabolic steroidal hormones and synthetic testosterone-like products. Anabolic-androgenic steroids are natural and synthetic compounds that have a similar structure to cholesterol. Illicitly used anabolic-androgenic steroids include nandrolone (Deca-Durabolin), stanozolol (Winstrol), methenolone (Primobolan), tibolone (Lival), and oxandrolone. Some of the other agents that are used also for medical reasons are testosterone cypionate, enanthate, undecanoate, and dihydrotestosterone (Transdermal).

Dehydroepiandrosterone (DHEA), a precursor to testosterone, stimulates protein anabolism to build muscle and increase strength. The US Food and Drug Administration banned DHEA in 1996. Androstenedione, "andro," is legal for sale as a nutritional supplement. It increases blood levels of testosterone. This agent increases energy, heightens sexual arousal and function, and enhances recovery and growth from exercise. Androstenedione also has many of the same side effects as anabolic steroids. Norandrostenediol is a more potent steroid than androstenedione. This supplement substantially increases muscle size, strength, and fat loss. Its half-life is 3 weeks; androstenedione's half-life lasts is a few hours. It, too, has many of the same side effects as anabolic steroids. The National Football League (NFL), National Collegiate Athletic Association (NCAA), and the International Olympic Committee (IOC) have banned norandrostenediol.

Human growth hormone (HGH) is a family of structurally related proteins that promote the normal growth and maturation process. Although it has no androgenic effects, many athletes feel that HGH increases muscle mass, reduces recovery time between workouts, and increases strength. Because of its many dangerous side effects, the US Olympic Committee and the NCAA have banned it.

Cycling is a common way to use AASs. The user alternates taking steroids with abstinence over 1–3-month periods. This allows the endocrine system to recuperate and it lessens the chance of detection. Case reports, surveys, and studies show that athletes take steroids in very large amounts (100–1000-fold excess), far exceeding the recommended dosages for legitimate medical purposes. For example, the therapeutic dose of testosterone is 5–10 mg per day. Those abusing it may use doses as high as 300 mg. Athletes report taking up to 20 times the therapeutic dose of human growth hormone, hoping that they will gain some of the effects of anabolic steroids. Another characteristic of AAS usage is the user's taking an average of 5 AASs, by injection and orally, together; this is called stacking the pyramid. How one stacks or cycles depends on who the "mentor" is or what Internet sources tell him. Thus, there is little uniformity in pattern. Today's youth use greater dosages of AASs by as much as 35% compared with athletes in past years. Since most anabolic steroid abusers purchase their drugs on the black market, the quantity and quality of what they take is highly variable. In addition to the Internet, veterinary steroids are another source of supply of AASs for athletes.

Some argue that the extent of long-term complications is questionable because steroids have been used for 50 years and there has been no striking morbidity attached to its use. Unfortunately, there have been few studies on the long-term complications of androgen-androgenic steroid use. Many of the following reported side effects are from case studies.

In those taking 17-alpha-alkylated androgens, there may be high serum concentrations of liver enzymes and cholestatic jaundice. Benign and malignant liver tumors and peliosis hepatis have been seen, although rarely. Endocrine effects include decreased production of luteinizing (LH) hormone, follicle-stimulating hormone (FSH), and testosterone. In males, this results in testicular atrophy, decreases in sperm production, sterility, gyne-
comastia, hypertension, and baldness. Women may have virilization (facial and body hirsutism, male pattern baldness, hoarseness, and clitoral enlargement), menstrual irregularities, and decreased breast size. Both men and women may have acne, altered glucose tolerance, and hyperinsulinism. Catastrophic side effects may be due to thrombotic complications of stroke and acute myocardial infarction. Other cardiovascular side effects include hypertension, cardiac hypertrophy, myocarditis, increased LDL, decreased HDL cholesterol, changes in triglyceride concentrations, and coagulation abnormalities.5 Neurologic problems include transient ischemic attacks (TIAs), cerebrovascular hemorrhage, and intracranial hypertension. Erythrocytosis, tendon ruptures, premature growth cessation in adolescent and premature prostatic hypertrophy are other possible side effects.6 There are studies that link AAS usage with psychiatric symptoms and syndromes in adults. Anabolic steroid abuse is associated with depression, mania, psychosis, delirium, paranoia, aggressiveness, suicides, and homicides.7 There are studies that compare steroid users while they are taking the AASs to when they are not and studies that look at athletes who use these agents compared with those who do not. Consistent differences between these groups are degrees of hostility, aggression, and manic-like symptoms; those taking the steroids have greater psychiatric changes. Studies support the statement that the greater the dose of the steroid, the more pronounced the psychopathology, particularly mood disorders. In the preadolescent boy, androgen use may be linked to conduct disorder (CD) and inappropriate sexual behavior.8 Dependence and euphoria may follow androgen use. Withdrawal symptoms following cessation of AASs include mood swings, depression, fatigue, violent behavior, rages, and craving for steroids. Thus, after one discontinues these drugs, rage behavior may occur.9 A risk factor for steroid use and abuse is personality disorders. A relationship between anabolic use and certain types of personality psychopathology has been reported. Anabolic steroid users and weightlifters compared with controls seem to have a higher prevalence of histrionic, narcissistic, antisocial, and borderline personality traits. More than weight-lifter controls, steroid users have greater pathologic exhibitionism, entitlement, exploitativeness, and antisocial personality traits, and they have lower empathy ratings.10 Psychological changes may occur on a continuum according to duration, dosing, and individual tolerances. Early effects are those of mood and euphoria. The individual exhibits confidence, energy, and self-esteem. The athlete is able to work through pain and fatigue and requires less sleep. Libido wanes, while uncomfortable feelings of irritability, agitation, and irritability emerge. Either with higher doses or prolonged usage of steroids, the individual has less inhibition and lacks judgment.11 More extreme progression of aggressive behavior includes violent and antisocial behavior and rage behavior. This “roid rage” results in property damage, self-injury (often through reckless driving), assaults, domestic violence, child abuse, suicide, and murder.9 Men more prone to these rages are generally young. Often, they come from caring families, have no prior trouble with the law nor have drug-related problems, and, prior to using AASs, were not known to be aggressive. Regardless of the extent of the antisocial behavior that develops, they typically do not feel remorse after the rage. Domestic violence is prevalent enough in this group to support the self-help group, Anabolic Steroid Wives Association.12 Prisoners with histories of violent crime during their adolescences have higher levels of testosterone than do prisoners who lack a violent history.13 In 1990, the US Congress enacted the Anabolic Steroids Control Act. It requires that anabolic steroids be added to Schedule III of the Controlled Substances Act.3 This law puts AASs in the same basket with other controlled substances such as amphetamines, barbiturates, and narcotics. Those who buy these agents on the black market and are caught possessing them without a prescription will suffer criminal penalties. Those
caught trafficking or possessing illegal steroids with the intent to distribute are given more severe penalties.\textsuperscript{14}

Inappropriate use of androgens might be suspected in several instances. An athlete who competes is at a relatively high risk of abusing AASs. Physical and laboratory clues are men with small testes, low sperm counts, increased hematocrit and hemoglobin values, and low serum sex hormone-binding globulin concentrations. Women may have virilization changes. Depending on the compound being tested, androgens other than testosterone can be detected by gas chromatography and mass spectroscopy if the individual is taking the steroids through the time of testing. One method of detecting exogenous use of testosterone is to determine the ratio of urinary testosterone to its endogenous epimer, epitestosterone. A ratio of greater than 6:1 suggests that the subject is taking exogenous testosterone. Another method looks at the ratio of urinary testosterone to LH; a ratio over 30 suggests that the individual is taking testosterone. Exogenous growth hormone administration can be detected by recording an elevation of the serum ratio of insulin-like growth factor-1 to insulin-like growth factor-binding protein-2.

Statistics on steroid use are difficult to obtain for several reasons. Physicians may be the source of the drugs, sometimes by prescription. Athletes take these substances surreptitiously using elaborate schemes to avoid detection or they use an agent like human growth hormone that cannot be detected by current drug screening. The user may stop the drug for months before a competition. He/she may use a diuretic before the drug testing to dilute the urine in order to disguise the steroid. The athlete often takes several agents simultaneously in an attempt to counter a side effect of one medication with another medication. For example, human chorionic gonadotropin (hCG) might be taken to counteract the effect of the androgen that is also taken that decreases the size of the testicle. Among those athletes taking high doses of hCG, gynecomastia may develop.\textsuperscript{6} To counteract this, the athlete may take Tamoxifen. In a survey of 175 inpatient substance-abuse treatment centers, only 19\% of those facilities that responded to the questionnaire said they had treated at least 1 person using AASs. Only 1\% of admissions to these facilities were for individuals abusing these agents. The treatment directors said in this survey that they rarely encounter patients who acknowledged their problems with AAS abuse.

A “quick death” as a result of an accident is an important consideration in this group. Given the risk taking and impetuous characteristics of many of these individuals, there are numerous opportunities for accidents to occur. Auto accidents, violent behavior, and drownings are a few examples. Other sets of problems that provide quick death opportunities include the commonly associated impairments of depression and substance abuse, criminal activity, and medical problems such as acute vascular events. Delayed death may occur as a consequence of liver disease, heart disease, diabetes, or hypertension.

Underwriting steroid abusers is difficult because the available information affords only a peek at the tip of an iceberg; but only if an iceberg is suspected can one detect AAS abuse. If the suspicion is confirmed, then the individual must be assessed by trying to answer the following questions. What substances is the proposed insured taking? How much of it is being taken? How long has the proposed insured been involved with this activity? Is the acquisition of the substance legal? Are there psychiatric concerns? Is the proposed insured likely to be a risk taker? Is there likely to be abuse of other substances? Does the APS include abnormal lab results that are consistent with steroid abuse? Are there notations in the APS that mention impotence or aggressive behavior? Does the motor vehicle record suggest aggressive driving? Are there any other medical impairments? What is his/her occupation? What is (are) his/her avocation(s)? Has there been any trouble with the law? Does the overall profile of the proposed insured have “quick
death’ potential? A separate questionnaire may be useful in delineating some of these facts.

In the case presented, the proposed insured’s use of AASs was supported by the APS. His profile places his excess mortality in an uninsurable range. Medical underwriting must be cognizant of the medical, laboratory, and social aspects of the applicant who may be abusing androgen-androgenic steroids. After determining that the proposed insured is using these agents, then careful risk assessment must be done to assess his/her individual risk.

Acknowledgment

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REFERENCES

15. Snyder. UpToDate.