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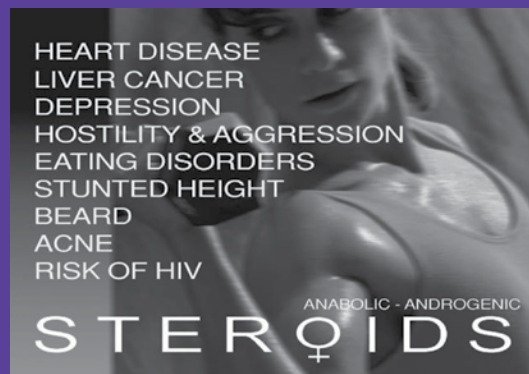
NIDA NOTES

NATIONAL INSTITUTE
ON DRUG ABUSE

Articles That Address



ANABOLIC STERIODS ABUSE



U.S. Department of Health and Human Services
National Institutes of Health
National Institute on Drug Abuse

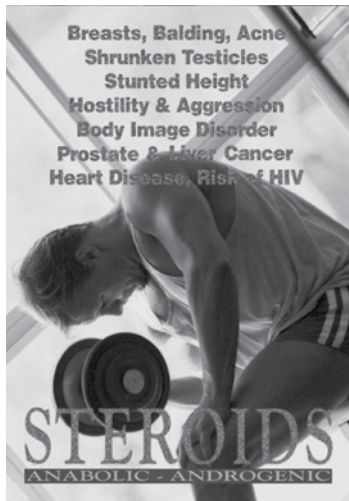
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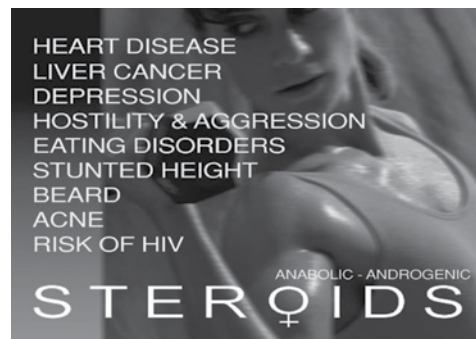
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NOTES**

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STERIODS
ABUSE**



**U.S. Department of Health and Human Services
National Institutes of Health
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Introduction

The National Institute on Drug Abuse (NIDA) supports most of the world's research on drug abuse and addiction. NIDA-funded research enables scientists to apply the most advanced techniques available to the study of every aspect of drug abuse, including:

- genetic and social determinants of vulnerability and response to drugs;
- short- and long-term effects of drugs on the brain, including addiction;
- other health and social impacts of drug abuse, including infectious diseases and economic costs;
- development and testing of medication and behavioral treatments for abuse and addiction; and
- development and evaluation of effective messages to deter young people, in particular, from abusing drugs.

Included in this document are selections of topic-specific articles reprinted from NIDA's research newsletter, *NIDA NOTES*. Six times per year, *NIDA NOTES* reports on important highlights from NIDA-sponsored research, in a format that specialists and lay readers alike can read and put to use. Selections like the current one are intended to remind regular *NIDA NOTES* readers and inform other readers of important research discoveries during the periods they cover.

We hope the information contained here answers your needs and interests. To subscribe to *NIDA NOTES* and for further information on NIDA's drug abuse and addiction research, please visit our Web site at www.drugabuse.gov.

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Study Links Anabolic Steroids to Brain Changes in Adolescent Female Mice

Exposure may promote aggression in girls.

By Carl Sherman, *NIDA NOTES* Contributing Writer

Anabolic androgenic steroid (AAS) abuse, once largely limited to elite athletes, has spread to a wider population that includes adolescents along with adults, and girls as well as boys. While the psychological and behavioral consequences of AAS use presumably reflect its impact on a number of brain areas, a NIDA-funded study at Dartmouth Medical School has identified one neurobiological effect that has potentially important implications for the emotional stability and well-being of adolescent girls in particular.

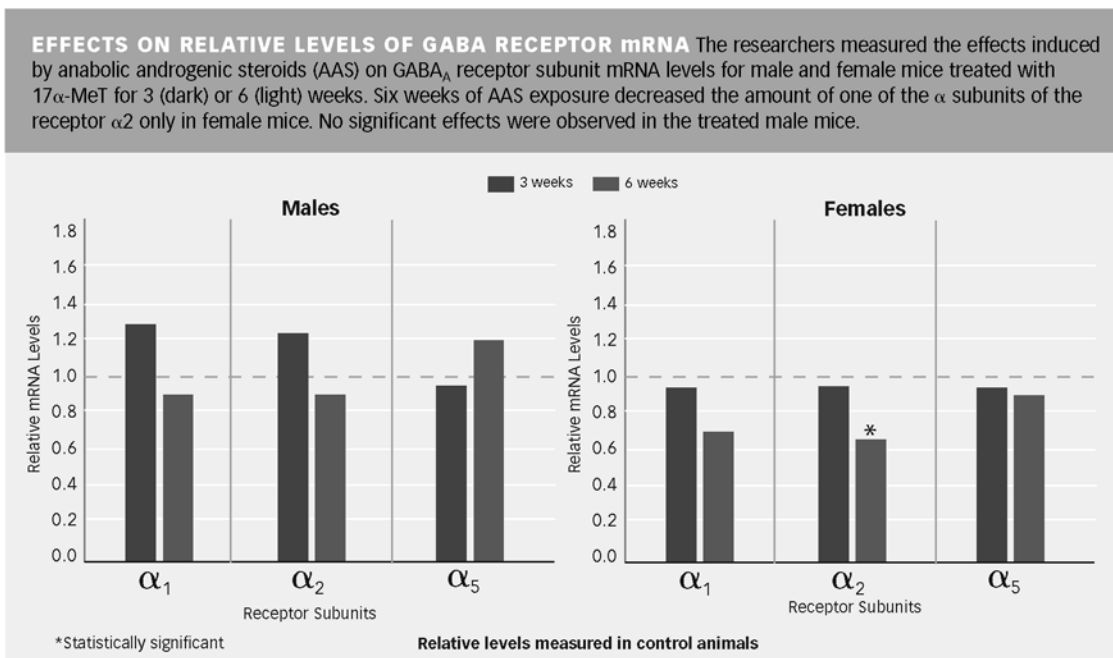
Principal investigator Dr. Leslie Henderson and colleagues studied the effect of the AAS, 17 α -methyltestosterone (17 α -MeT), on the activity of the neurotransmitter gamma-aminobutyric acid (GABA) in adolescent mice. Loosely speaking, GABA acts as a calming agent throughout the nervous system: It dampens activity of the neurons to which they are connected. Specifically, the researchers focused on the steroid's impact on GABA functioning in the medial preoptic area (MPOA) of the basal forebrain, a region that participates in the regulation of sexual behavior, anxiety, and aggression. They found that in female, but not male, animals the AAS interfered with GABA transmission in the area. Theoretically, this effect would reduce GABA's inhibitory influence and thus potentially contribute to the excessive emotions and behaviors seen in AAS abuse. Various studies have linked increased anxiety and aggression, and both increased and decreased libido to AAS use.

"The GABA system isn't the only target for the effects of AAS, but it is likely an important one,"

Dr. Henderson says. "Going into the experiment, we assumed we'd see an anabolic steroid effect on the GABA system in the MPOA and expected there would be differences between males and females." This area of the brain, particularly the cluster of neurons within it called the medial preoptic nucleus (MPN), is structurally different in the sexes.

Drug Targets Receptors

The researchers injected mice with a solution of 17 α -MeT in sesame oil, in doses (7.5 mg/kg/d) that would correspond to those taken by humans who are abusing the drug heavily. They injected a control group of mice with the sesame oil vehicle alone. The researchers examined brain tissue from half the mice in each group after 3 weeks of treatment and from the other half after 6 weeks. They focused on the subunits that make up GABA type A receptors (GABA_A) in cells of the MPN and on the way that AAS exposure affected the function of these receptors. Each receptor contains five of these subunits, proteins that determine the receptor's sensitivity to drugs and hormones.



To test how the reduction in $\alpha 2$ subunit production might affect GABA_A receptor function, the researchers measured the amplitude and frequency of inhibitory postsynaptic currents (IPSCs)—a measure of the receptor’s efficacy in inhibiting the activity of neurons—in the MPN. Here, too, they found sex-based differences that were magnified by AAS. In untreated mice, the IPSCs were smaller in amplitude in females than in males. Female mice that received 3 to 4 weeks of AAS displayed smaller and less frequent currents than controls, suggesting that exposure to the drug had reduced GABA_A receptor function, thereby widening the gender gap. There was no comparable change in males.

The researchers concentrated on the $\alpha 2$ subunit family, which earlier studies had shown that 17 α -MeT alters. Before treatment, levels of messenger RNA (mRNA) for the $\alpha 2$ subunit were lower in female than in male mice in cells of the MPN. After 6 weeks, $\alpha 2$ subunit mRNA—an indicator of the quantity of the subunit being produced—had declined by 37 percent in female mice treated with the AAS compared with controls, but was essentially unchanged in males. When the researchers measured the actual protein that makes up the $\alpha 2$ subunit in female mice, they found a small but significant reduction (8 percent) in the number of neurons containing $\alpha 2$ protein.

Chronic exposure to AAS augmented gender differences in both the structure and function of certain GABA receptors, Dr. Henderson says. “Overall, the effect was to decrease GABA transmission in the MPN of female, but not male, adolescent mice. This would presumably increase the level of activity or change the pattern of activity in postsynaptic neurons of the female mice.”

A Closer Look

How do these neurobiological changes contribute to the behavioral manifestations of AAS abuse? “It could be that an AAS that promotes aggression in males would promote it more in females, or have different effects on the expres-

sion of sexual behaviors, but this is something we are just beginning to explore,” Dr. Henderson says. “What’s more, there are 60 to 100 AAS, and their neurobiological effects are unlikely to be uniform. In time, we may be able to start parsing out whether certain commonly abused steroids are likely to amplify aggression and libido in women or in men while others affect both genders equally.”

Dr. Henderson notes that alterations in GABA_A receptor function could have other important effects as well. “The GABA_A receptor is a major target of many drugs, including alcohol and benzodiazepines. Changing the subunit composition could alter the brain’s sensitivity to these chemicals.”

“Although this is a basic research study, its potential translation to humans, even if speculative, is striking,” says Dr. Pushpa Thadani, formerly of NIDA’s Division of Basic Neuroscience and Behavioral Research. “It demonstrates that AAS exposure in the adolescent period produces gender-specific changes at the molecular level that may be correlated with known behavioral outcomes.”

Although applying findings from this and similar studies in actual interventions remains a distant goal, “these studies advance our understanding of the actions of AAS on the brain and behavior, which can empower us to better educate the lay public on the harmful effects associated with abuse,” Dr. Thadani says. “The research is still in its infancy,” she observes. Other studies, now under way, are seeking to clarify the links between aggression in female mice and AAS-associated neurobiological changes. “When these findings are available, we’ll probably be in a better position to translate this information into the human arena.”

Source

- Penatti, C.A.A., et al. Sex-specific effects of chronic anabolic androgenic steroid treatment on GABA_A receptor expression and function in adolescent mice. *Neuroscience* 135(2):533-543, 2005. **NN**

Steroid Abuse Is a High-Risk Route to the Finish Line

By NIDA Director, Nora D. Volkow, M.D.

Starting last fall, capitalizing on the interest raised by the Winter Olympics in Turin, Italy, NIDA intensified its campaign to warn young people that steroid abuse is a dangerous way to become faster, stronger, and bigger.

Boys and girls who abuse these drugs before reaching their full natural height may prematurely halt bone growth, resulting in permanently shorter stature. Boys and men who abuse steroids risk shrinkage of the testicles, reduced sperm count, infertility, baldness, development of breasts, and an increased risk for prostate cancer. Girls and women are subject to menstrual abnormalities, voice deepening, breast shrinkage, male-pattern baldness, and an increase in sex drive, acne, body hair, and clitoris size. Some of these adverse effects—including breast enlargement in men, menstrual abnormalities in women, and reduced height in both sexes—may be permanent. For both sexes, steroid abuse increases the risk of liver and heart disease, stroke, aggression, and depression. Users of injectable steroids may acquire hepatitis, HIV, and other infections if they use contaminated needles.

In recent animal studies, NIDA-supported researchers tested the effects of chronic exposure to anabolic (muscle-building) and androgenic (masculinizing) steroids on brain circuits that underlie aggression and reproductive behaviors. They found that in mice, a regimen corresponding to chronic human abuse of these drugs reduced levels of the receptor for the neurochemical GABA. Adolescent female



mice were particularly sensitive to the effects of the steroid on GABA, which is critical to the display of female sexual behaviors and is involved in the regulation of hormone release and ovarian maturation.

The need to educate young people about the serious health risks associated with steroids remains urgent. Among American teens, such abuse declined over the past decade, but that encouraging trend shows signs of weakening, especially among younger boys and girls. In 2005, according to the annual NIDA-funded Monitoring the Future (MTF) Survey, the number of high school

seniors reporting steroid abuse dropped significantly, to 1.5 percent, from peak levels of about 2.5 percent just a year before. The rates were unchanged, however, among 10th graders (1.3 percent) and 8th graders (1.1 percent).

NIDA has responded by updating our *Research Report* on Steroids to provide the public with the newest information about steroids and their abuse. The *Research Report* is available on NIDA's Web site at www.drugabuse.gov/ResearchReports/Steroids. A Spanish version is available at www.drugabuse.gov/ResearchReports/Esteroides/Esteroides.html. "Game Plan," a public service announcement that has aired more than 8,000 times in 75 television markets across the United States, reminds young athletes that "quick fixes" can be dangerously deceptive and that cheating is damaging in the long run. NIDA will continue to conduct and publicize research on steroids, and to drive home the point that, ultimately, steroid abuse is a losing strategy. **NN**

ATLAS and ATHENA Prevention Programs Receive First *Sports Illustrated* Champion Award

Two NIDA-supported programs that prevent steroid and drug abuse and promote healthy behavior among high school athletes have been honored with *Sports Illustrated* (*SI*) magazine's first Champion Award. The ATLAS (Athletes Training and Learning to Avoid Steroids) and ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternatives) programs were developed by Dr. Linn Goldberg and Dr. Diane Elliott at the Oregon Health and Science University.

SI President Mark Ford announced the award at a press conference on February 8 in Washington, D.C., and disclosed that over the next year, *SI* will provide \$1 million in support for the programs, including grants to establish *SI* Schools to serve as models demonstrating the program's impact. The magazine also will create a Web site that focuses on science-based nutrition, exercise, and drug prevention for coaches, athletes,



L-R: Dr. Linn Goldberg, Oregon Health and Science University (OHSU); Dr. Elizabeth Robertson, NIDA; Dr. Diane Elliott, and Dr. Esther Moe, also OHSU, at the SI Champion Award ceremony.

and trainers. The *SI* Champion Award will be given annually to a nonprofit organization working for the betterment of sports.

ATLAS and ATHENA are the only prevention programs specifically designated as model curricula in the U.S. Anabolic Steroid Control Act passed by Congress and signed by President Bush in 2004. ATLAS was designed to help male athletes avoid steroid use and develop healthy approaches to training and physical development. ATHENA promotes exercise and nutrition as alternatives to reliance on diet supplements or unhealthy approaches to conditioning and weight control or dieting. Both programs use student athletes as

leaders for team-centered instruction (see "ATHENA Program Reduces Substance Abuse by Girls on High School Sports Teams," *NIDA Notes*, Vol. 20, No. 1). **NN**

NIDA Web Site Addresses Consequences of Steroid Abuse

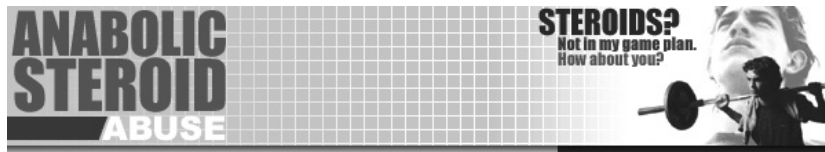
Despite its dangers, anabolic steroid abuse continues as athletes and others attempt to gain competitive advantage and to enhance their musculature, NIDA Director Nora D. Volkow said in recent testimony before the Government Reform Committee in the U.S. House of Representatives. “We are now facing a very damaging message that is becoming pervasive in our society—that bigger is better, and being the best is more important than how you get there.”

Dr. Volkow’s statement is one example of what visitors can find on NIDA’s Web site, <http://www.steroidabuse.gov>, which is devoted to educating the public about the dangers of anabolic steroids. The site provides resources, publications, and links to public service announcements about the consequences of steroid abuse. In the full text of Dr. Volkow’s March 17, 2005, testimony before the Government Reform Committee, she discusses the Institute’s many efforts to find treatments to mitigate the adverse effects of anabolic steroid abuse and to better understand how these substances affect the body and brain.

Anabolic-androgenic steroids are synthetic substances related to male sex hormones. “Anabolic” refers to muscle-building, and “androgenic” refers to these substances’ effect of promoting masculine characteristics such as hair growth or a deepened voice. Steroid drugs are available legally only by prescription to treat conditions that occur when the body produces abnormally low amounts of testosterone, such as delayed puberty and some types of impotence. They are also prescribed to treat body-wasting in patients with AIDS and other diseases that result in loss of lean muscle mass. Abuse of anabolic steroids can lead to serious health problems, some irreversible.

Anabolic steroids differ from other drugs of abuse in that many of their “reinforcing effects” (i.e., those effects that keep a person using a drug) are not experienced immediately or rapidly. The main reasons people abuse steroids are to improve their performance in sports by increasing muscle size and to enhance their appearance by reducing body fat. Although these effects can take months to develop, once they do, they may comprise a strong incentive to continue abuse.

The most recent NIDA-University of Michigan Monitoring the Future survey found that in 2003 and 2004, about 2.5 percent of 12th-graders reported abusing steroids during the past year. This is a peak level among this group, and translates into an estimated 79,000 high school seniors involved with these substances. Meanwhile, the percentage of 12th-graders concerned that steroids might do them harm had fallen to 56 percent from a high of 71 percent



in 1992. When students view drugs as less harmful, their levels of abuse often increase. On the positive side, among 8th-graders, steroid abuse in the past year declined from 1.4 percent in 2003 to 1.1 percent in 2004.

Anabolic steroids are taken orally or injected, typically in “cycles” of weeks or months. Cycling involves taking multiple doses of steroids over a specific period of time, stopping for a period, and starting again. In addition, users often combine (or “stack”) several types of steroids to maximize the substances’ effects while—or so abusers believe—minimizing their negative effects.

“Some percentage of steroid abusers become addicted to the drugs, as evidenced by their continuing to take steroids in spite of seriously adverse medical and behavioral problems,” Dr. Volkow said. “One of the most dangerous consequences is the severe depression that can occur during withdrawal, which, if not recognized and treated properly, can result in suicide weeks after drug discontinuation. Indeed, untreated, depressive symptoms have been known to persist for a year or more after the abuser stops taking the drugs.”

Other consequences of anabolic steroid abuse can include liver and heart disease, stroke, and increased aggression. People who inject anabolic steroids run the added risk of contracting and/or transmitting HIV/AIDS or hepatitis through sharing contaminated needles. In addition, there are some sex-specific side effects:

- For men—shrinking of the testicles, reduced sperm count, infertility, baldness, enlarged breasts, increased risk for prostate cancer.
- For women—growth of facial hair, male-pattern baldness, changes in or cessation of the menstrual cycle, enlargement of the clitoris, deepened voice.
- For adolescents—permanent short stature due to premature cessation of skeletal growth.

NIDA’s Web site also features links to the Institute’s “Game Plan” public service announcements, which encourage young men and women to work with what nature has provided and not to “cheat” by using steroids and thereby expose themselves to the negative side effects associated with these drugs. NIDA released its most recent Game Plan in June 2005. **NN**

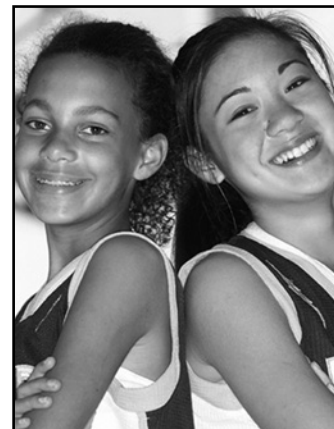
ATHENA Program Reduces Substance Abuse by Girls on High School Sports Teams

By Patrick Zickler, NIDA NOTES Staff Writer

High school girl athletes who participated in a recently evaluated NIDA-supported nutritional and behavioral guidance program were less likely than nonparticipating peers to engage in substance abuse and other high-risk behaviors. Girls on teams that used ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternatives) were less likely than girls on teams that received only printed information to use diet pills or so-called performance-enhancing substances such as steroids, amphetamines, and muscle-building supplements. The ATHENA team members also were less likely to be sexually active and more likely to wear seat belts, and they experienced fewer injuries during the sports season.

In the ATHENA program, developed at the Oregon Health & Science University in Portland by Drs. Diane

Elliott and Linn Goldberg, selected team leaders to receive a 90-minute orientation and then conduct discussion and activity sessions during scheduled team practices. Each team leader works with a squad of approximately six teammates, following a manual that is much like a playbook, with scripts for eight 45-minute sessions dealing with the harmful consequences of substance abuse and other unhealthy behaviors and the beneficial effects of good diet and exercise. Along with providing information, the workbook engages the girls in activities such as critiquing magazine advertising and other



media influences on self-image; classifying various foods according to carbohydrate, fat, and protein content; and determining the best balance of dietary fuels for athletic training and competition. Each ATHENA athlete uses a pocket-sized nutrition and training guide to monitor diet and exercise. Coaches and other staff members receive an orientation to assist the team leaders as timekeepers and facilitators for the sessions.

To evaluate ATHENA, the researchers recruited 40 girls' sports teams in 18 public high schools in northwest Oregon and southwest Washington. Teams from half the schools followed the ATHENA program. The other

ATHENA's Impact on Behavior and Nutrition

	Control Group		Experimental Group	
	Before Intervention	After Intervention	Before Intervention	After Intervention
Nutrition, Exercise Abilities, and Beliefs*				
Tracking protein intake	2.11	2.03	2.16	2.54
Eating more protein in the last 2 months	3.95	3.92	4.19	5.10
Knowing how to lift weights to improve strength	5.48	5.61	5.15	5.92
Self-rating of skill in strength training	5.48	5.61	5.15	5.92
Believing that nutrition affects sport performance	5.75	5.64	6.06	6.01
Additional Health-Influencing Behaviors				
Rode in a car with an alcohol-consuming driver**	0.44	0.42	0.41	0.26
Knowing how to turn down unhealthy weight-loss behaviors*	5.80	5.77	5.91	6.14
No. of sport injuries so could not train in the last 3 months	0.32	0.36	0.32	0.26
Intentions Toward Future Disordered Eating Behaviors and Drug Use*				
Diet pill use	1.74	1.79	1.87	1.62
Vomiting to lose weight	1.66	1.76	1.62	1.57
Tobacco use	1.56	1.79	1.55	1.58
Creatine (muscle-building supplement) use	1.87	1.77	1.72	1.51

Data are significant differences expressed as the mean.

*Scored using a seven-item agreement scale ranging from 1 (strongly disagree) to 7 (strongly agree).

**Scored 0 to 4 for times occurred with 0 indicating none; 1, once; 2, two or three times; 3, four or five times; or 4, six or more times.

High-school girls who participated in the ATHENA curriculum were less likely to engage in drug abuse or other unhealthy behaviors than were girls given printed information about drugs and nutrition.

teams received printed information about eating disorders, substance abuse, and sports nutrition, but did not take part in discussion or group activities. Before the first practice of their sports season and again within 2 weeks after the season ended, each girl filled out a questionnaire about her eating patterns; nutritional awareness; use of diet pills, amphetamines, anabolic steroids, and muscle-building supplements; and other health-related behaviors.

Preseason survey results were essentially the same for girls on ATHENA teams and those in the control group, but in postseason surveys the ATHENA participants reported significant decreases in risky behaviors. According to Dr. Elliott, the control athletes were three times more likely to begin using diet pills and almost twice as likely to begin using other body-shaping substances, including amphetamines, anabolic steroids, and muscle-building supplements, during the season. The use of diet pills went up among control girls, while it fell to approximately half its preseason level among ATHENA girls. ATHENA athletes also were more likely to use seatbelts and less likely to ride in a car with a driver who had been drinking, to believe claims in advertising, or to agree with the statement that men find thin women most attractive.

Adolescent girls experience social and cultural pressure about body image, and they look to each other for role models more than they follow the guidance offered in classrooms, research has shown. The competitive environment of athletic programs may compound the pressure, leading to disordered eating and the use of body-shaping

substances such as steroids, diuretics, laxatives, and even tobacco, Dr. Elliott says. However, the athletic environment can exert positive peer pressure also. The researchers modeled ATHENA's use of sports teams as a forum to promote healthy lifestyles on a similar program they developed for male high school athletes (see "Like ATHENA, ATLAS Targets High School Athletes"). "We found that the team-based approach used in ATLAS [Athletes Training and Learning to Avoid Steroids] produced greater positive change than did a more conventional classroom-style approach," Dr. Elliott says.

"Two features of the ATHENA program are striking," says Dr. Larry Seitz of NIDA's Division of Epidemiology, Services and Prevention Research. "One is the peer-based rather than classroom-based approach, and the other is the effect on a wide spectrum of linked behaviors, from vomiting to induce weight loss to believing nutritional claims in advertising. Improvements like these can help young female athletes make healthier choices throughout life, not just during the sport season."

The Oregon Health & Science University Sports Medicine Web site, www.ohsu.edu/hpsm/index.html, provides more information about ATHENA and ATLAS.

Source

- Elliott, D.L., et al. Preventing substance use and disordered eating: Initial outcomes of the ATHENA program. *Archives of Pediatric and Adolescent Medicine* 158(11):1043-1049, 2004. **NN**

Like ATHENA, ATLAS Targets High School Athletes

ATLAS (Athletes Training and Learning To Avoid Steroids), the result of 5 years of NIDA-supported development, is a program for male high school athletes to help reduce use of anabolic steroids and other sport supplements, alcohol, and other drugs. ATLAS emphasizes the immediate impact of alcohol and other drugs on athletic performance and conditioning rather than potential and abstract long-term effects. An evaluation of the program in 15 high schools showed that, compared with a control group, 1 year after completion of the program, ATLAS-trained students had:

- Half the incidence of new use of anabolic steroids and less intention to use the drugs in the future;
- Less use of alcohol, marijuana, amphetamines, and narcotics;
- Less use of "athletic enhancing" supplements;
- Less likelihood of engaging in hazardous substance abuse behaviors such as drinking and driving;
- Reduced substance abuse risk factors; and
- Improved substance abuse protective factors.



Steroid Abusers May Go On to Abuse Opioids, Too

Recent research findings suggest that men who abuse anabolic-androgenic steroids may begin to abuse heroin or other opioid drugs, such as prescription pain relievers, as well. Dr. Harrison G. Pope, Jr., and his colleagues at Harvard Medical School in Boston reviewed histories of patients at a private drug-abuse treatment facility in New Jersey and found that among 227 men admitted for treatment of opioid addiction in 1999, 21 (9.3 percent) reported that they had used anabolic-androgenic steroids. None of the men had used other illicit drugs prior to their steroid abuse, and most of the men said they were

introduced to opioids through the dealers who supplied them with steroids and through the bodybuilding subculture.

Eighteen of the former steroid users said they had started using opioid drugs to counteract steroid-induced insomnia and irritability; 14 said they used opioids to counteract the depression that accompanied withdrawal from anabolic steroids.

The study was reported in a letter to *The New England Journal of Medicine*. **NN**

Study Provides Additional Evidence That High Steroid Doses Elicit Psychiatric Symptoms in Some Men

By Steven Stocker, NIDA NOTES Contributing Writer

NIDA-supported research has produced additional evidence that high doses of anabolic-androgenic steroids can produce aggressive symptoms in some men. Dr. Harrison Pope and his colleagues at McLean Hospital in Belmont, Massachusetts, compared aggressive reactions in men who received alternate doses of steroids and placebo.

Anabolic-androgenic steroids have been widely, but illegally, available since the 1960s. "Anabolic" refers to steroids' ability to promote tissue growth, while "androgenic" refers to their ability to promote the development of male sexual characteristics. People typically abuse steroids because they boost muscle size, particularly in the chest and shoulders.

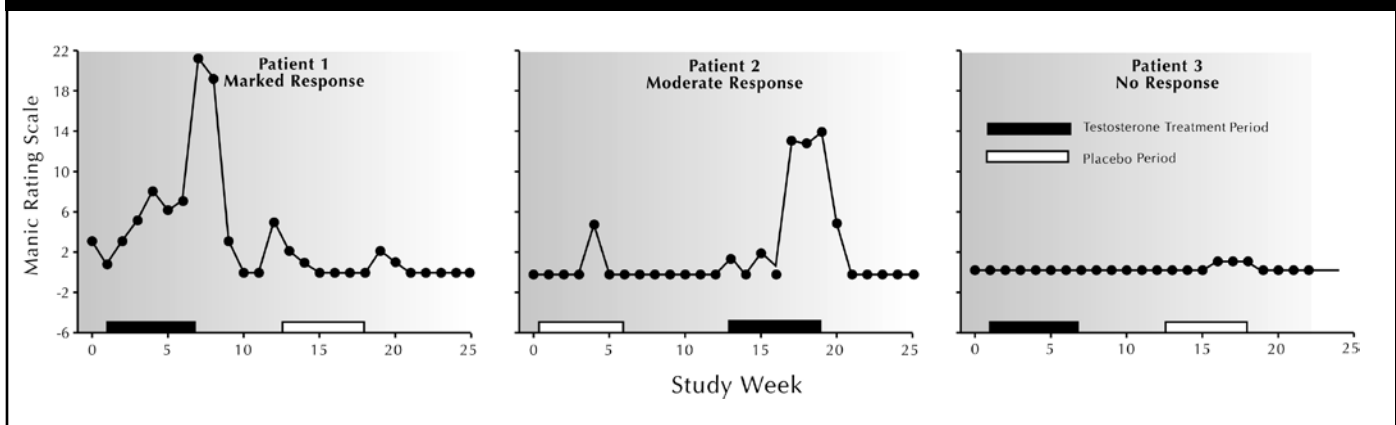
Starting in the late 1980s, evidence began to accumulate that steroids may provoke manic symptoms, such as aggression, euphoria, grandiose beliefs, reckless behavior, and a decreased need for sleep. Reports of violence committed by people who had taken large doses of steroids began to appear in both the scientific literature and the lay press, and in surveys, steroid abusers themselves reported that the drugs prompted them to acts of aggression. However, some scientists questioned the significance of these reports. Perhaps the more aggressive or manic steroid abusers were the ones volunteering for the studies,

critics said. Perhaps abusers were exaggerating the extent of their aggression because they considered aggression to be manly.

The only way to conclusively demonstrate that high steroid doses can provoke aggression and other manic symptoms is to administer high doses to volunteers in double-blind studies in which both the volunteers and the scientists are unaware of who is receiving steroids and who is receiving an inactive substance, or placebo. Three previous double-blind studies have been conducted: one at the University of Oklahoma College of Medicine in Tulsa in 1999; one at the Charles R. Drew University of Medicine and Science in Los Angeles in 1996; and one at the National Institute of Mental Health in Rockville, Maryland, in 1993. Collectively they confirm that high steroid doses can provoke severe aggressive and manic reactions in a minority of men.

The study conducted by Dr. Pope and his colleagues was the most recent and extensive, recruiting 50 men between the ages of 20 and 50. For the first 6 weeks of the study, the investigators gave half of the volunteers weekly injections of the steroid testosterone cypionate in gradually increasing doses. For the next 6 weeks, the

Responses of Three Participants to Testosterone Cypionate Treatment on a Mania Rating Scale



Responses to treatment with testosterone cypionate varied greatly among three study participants. On the Young Mania Rating Scale, a standard scale for rating mania, scores of less than 10 indicated that the participant had minimal psychiatric effects; participants with scores of 10 to 19 were rated moderately manic; and those with scores of 20 or higher were rated markedly manic.

men were given nothing, then for the subsequent 6-week period, they were given injections of a placebo, followed by another 6 weeks of no injections. The other half of the men were treated the same, except they received 6 weeks of placebo injections before receiving 6 weeks of steroid injections. Each time the men came in for their weekly injection, the researchers administered psychological tests to them. In addition, the men kept daily diaries of their psychological symptoms.

Of the 50 men who received all their steroid injections, 42 had only minimal psychiatric reactions to the drugs. However, two men developed prominent manic symptoms, and another six developed moderate symptoms.

“People who responded to the steroid had different combinations of manic symptoms,” says Dr. Pope. “One man had an aggressive outburst at work. Once, when he got cut off in traffic, he followed the person in his car for several miles. The other man with a marked reaction became euphoric and had a decreased need for sleep. Among the moderate responders, one man playing in a college sports competition found himself wanting to beat up his opponent. He said that he had never had such aggressive feelings before in the course of a competition.”

One of the psychological tests given to the volunteers was the Point Subtraction Aggression Paradigm, which has been widely used to measure aggression in alcoholics, drug abusers, adolescents, and other populations. In this test, the volunteers played a computer game in a booth. Each was told that he was playing against a man in another booth, when actually his opponent was a computer. The man could accumulate points by pressing one button on a board and could deprive his “opponent” of points by pressing another button. At the end of the game, accumulated points could be exchanged for money. During the game, the computer provoked the man by randomly depriving him of points. The man’s aggression score consisted of the number of points that he subtracted from his “opponent” in retaliation.

The results showed that the steroid injections significantly increased aggression scores, although, again, most of the men were only minimally affected, while a few showed

substantial aggression. “These aggressive responders would pound on the board and yell and swear at what they thought was their opponent in the neighboring booth, who was, of course, a computer,” says Dr. Pope. “It was quite dramatic.”

Why a few men develop manic reactions to steroids while most do not remains a mystery, Dr. Pope says. Those who reacted with manic symptoms were not more likely to have taken steroids before, to have been a weightlifter, or to have a family history of psychiatric disorder. They also did not differ in various physiological measures, such as the blood level of testosterone following the steroid injections.

“I think that the evidence from this and previous studies indicates that, for unknown reasons, somewhere between 2 and 10 percent of men develop manic behavior and other neuropsychiatric complications from high doses of steroids,” says Dr. Jag Khalsa of NIDA’s Center on AIDS and Other Medical Consequences of Drug Abuse. “These studies were done with 500 and 600 mg per week of steroids, while in actual practice, steroid abusers often take as much as 1,000 or 1,500 mg per week. With these higher doses, the percentage developing manic symptoms is likely to be higher.”

Sources

- Pope, H.G., Jr.; Kouri, E.M.; and Hudson, J.I. Effects of supraphysiologic doses of testosterone on mood and aggression in normal men: A randomized controlled trial. *Archives of General Psychiatry* 57(2):133-140, 2000.
- Pope, H.G., Jr.; Phillips, K.A.; and Olivardia, R. *The Adonis Complex: The Secret Crisis of Male Body Obsession*. New York: The Free Press. 2000.

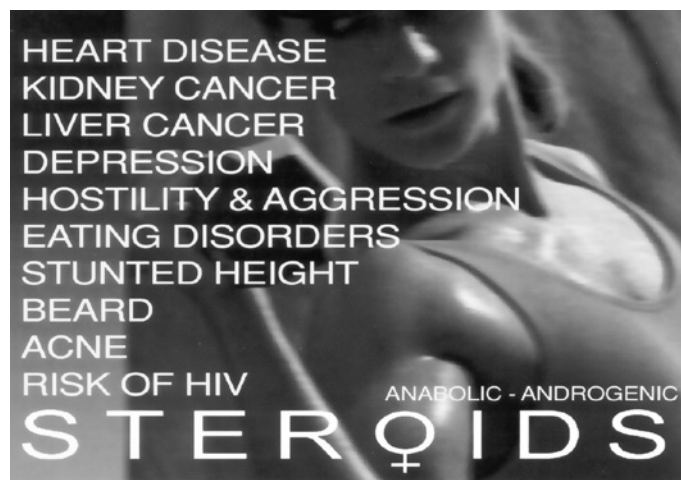
For More Information

For additional information on anabolic steroids and NIDA’s efforts to curtail their use, see “NIDA Initiative Targets Increasing Teen Use of Anabolic Steroids.” NIDA has also created a special Web site, www.steroidabuse.org, that also provides information. **NN**

NIDA Initiative Targets Increasing Teen Use of Anabolic Steroids

By Patrick Zickler, NIDA NOTES Staff Writer

To reverse the rising use of anabolic steroids by high school-age children, NIDA and seven national partners have launched an initiative designed to alert the public about the risks associated with anabolic steroid use.



As part of NIDA's anabolic steroids initiative, the Institute has distributed more than 500,000 "art" cards—colorful postcards with messages about the harmful effects of steroid abuse—in gyms, restaurants, bookstores, and clubs.

"The most recent data from our Monitoring the Future survey tell us that the trends in use of these drugs and in teenagers' attitudes about them are going in the wrong direction," said NIDA Director Dr. Alan I. Leshner at a Washington, D.C., press conference to announce the initiative. "More than a half million 8th- and 10th-grade students are now using these dangerous drugs, and increasing numbers of high school seniors say they don't believe the drugs are risky."

Anabolic steroids are synthetic compounds that mimic the action of the male sex hormone testosterone. The drugs have some medical uses, but they also are abused by some athletes and sports enthusiasts who want

to increase muscle mass and improve performance. Some teens use them because of concern about body image.

In adolescents, anabolic steroid abuse can halt bone growth and has been associated with damage to the heart, kidneys, and liver. In males, steroid abuse can lead to impotence, shrunken testicles, and breast enlargement. In females, the drugs' effects include menstrual irregularities, growth of body hair and loss of scalp hair, a deepened voice, and reduction in breast size. Some of these biological effects are irreversible. Use of anabolic steroids also has been linked to increased and unpredictable levels of aggression in human and animal studies.

NIDA's initiative includes a new Web site—www.steroidabuse.org—that provides science-based information about the risks and prevention of steroid abuse. NIDA has also released an updated Research Report on anabolic steroids as part of the nationwide multimedia initiative. NIDA and its partners will distribute 250,000 copies of a special Community Drug Alert Bulletin on anabolic steroid abuse and will place 500,000 "art cards"—colorful postcards with messages about the harmful effects of steroid abuse—in gyms, bookstores, restaurants, and clubs in Washington, D.C., Los Angeles, Miami, Baltimore, Seattle, and Indianapolis.

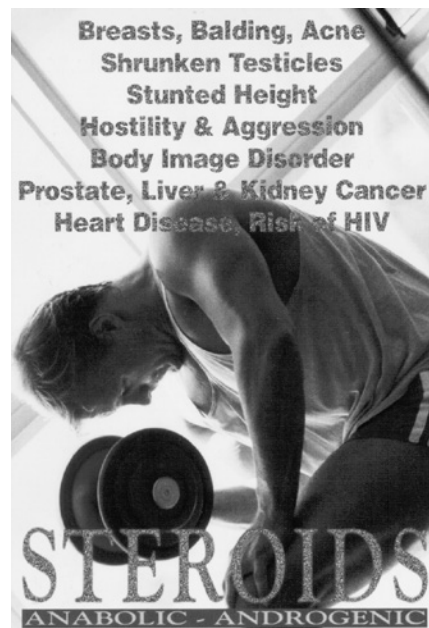
The Institute's partners in the initiative include the National Collegiate Athletic Association, the American Academy of Pediatrics, the American College of Sports Medicine, the National Association of School Nurses, the National Federation of High Schools, International Students in Action, and Dr. Drew Pinsky, a physician who hosts discussions about relationships and sexual behavior on MTV's "Loveline" and the Web site www.drDrew.com.

The press conference announcing the initiative was followed by a scientific session at which NIDA-supported scientists presented summaries of research on anabolic steroids. Dr. Charles Yesalis of Pennsylvania State University discussed the history and social context of steroid use and abuse. Dr. Linn Goldberg and



Dr. Linn Goldberg (left) of Oregon Health Sciences University, explains the Adolescent Training and Learning to Avoid Steroids (ATLAS) program to reporters at a science session following the NIDA press conference.

“More than a half million 8th- and 10th-grade students are now using these dangerous drugs, and increasing numbers of high school seniors say they don’t believe the drugs are risky.”



“Art” cards like this and the one on the previous page help spread the word about the harmful effects of steroids.

Dr. Diane Elliot of the Oregon Health Sciences University in Portland described the Adolescent Training and Learning to Avoid Steroids (ATLAS) program, a science-based prevention program that uses a team-centered approach to educate young male athletes about the risk and protective factors associated with steroid use. The researchers are currently developing a similar program—Athletes Targeting Healthy Exercise and Nutrition Alternatives (ATHENA)—to prevent eating disorders and abuse of steroids and other body-shaping drugs by young women on school-sponsored athletic, dance and drill, and rally teams.

Dr. Harrison Pope of the McLean Hospital in Belmont, Massachusetts, discussed results of a study designed to examine the effects of steroids on mood and increased aggression, a phenomenon referred to as “roid rage.” The research, which involved 56 men who regularly work out at gyms and health clubs, revealed increased aggressive behavior in some participants who received testosterone in dosages smaller than those typically used by athletes or body-builders. Dr. Marilyn McGinnis of Mount Sinai School of Medicine in New York City provided additional

evidence that steroid use can result in aggressive behavior. She described recently completed laboratory studies in which rats with elevated levels of steroids exhibited unprovoked aggression toward passive, nonthreatening rats as well as intensely aggressive responses to provocation.

For More Information

The NIDA *Research Report* “Anabolic Steroid Abuse” and other information about anabolic steroids can be found at the special NIDA Web site: www.steroidabuse.org. **NN**

About Anabolic Steroid Abuse

NIDA has issued an updated research report that summarizes the latest scientific information on anabolic steroids. The eight-page Research Report, *Anabolic Steroid Abuse*, is part of a nationwide education initiative launched by NIDA and several national organizations to counter a significant rise in anabolic steroid abuse among adolescents. Highlights from the report are:

What are anabolic steroids?

Anabolic steroids are synthetic substances related to the male sex hormones, called androgens. They have a number of physiological effects, most notably an anabolic effect that promotes the growth of skeletal muscle and androgenic effects that foster the development of male sexual characteristics. Although the proper term for these compounds is anabolic-androgenic steroids, they commonly are called anabolic steroids.

Anabolic steroids are legally available only by prescription in the United States. Doctors use these drugs to treat delayed puberty, impotence, and body wasting in patients with AIDS and other diseases. Abused steroids most often are obtained from clandestine laboratories, smuggled, or illegally diverted.

What is the scope of steroid abuse?

Steroid abuse is higher among males than females but is growing most rapidly among young women. An estimated 2.7 percent of 8th- and 10th-graders and 2.9 percent of 12th-graders have taken anabolic steroids at least once in their lives, according to the 1999 Monitoring the Future study, a NIDA-funded survey of drug abuse among adolescents. These figures represent increases since 1991 of approximately 50 percent among 8th- and 10th-graders and 38 percent among 12th-graders.

Why do people abuse anabolic steroids?

Abuse of anabolic steroids is motivated in most cases by a desire to build muscles, reduce body fat, and improve sports performance. Abuse is estimated to be very high among competitive bodybuilders and may also be widespread among other athletes. Some men who abuse steroids perceive their own bodies to be small and weak, even if they are large and muscular. Some women who abuse these drugs think they look obese or flabby, even though they are actually lean and muscular. Other

individuals abuse steroids because they are trying to become bigger and stronger to protect themselves from recurrence of physical or sexual assaults.

How are anabolic steroids used?

Anabolic steroids are taken orally as tablets or capsules, by injection into muscles, or as gels or creams that are rubbed into the skin. Doses taken by abusers can be up to 100 times greater than doses used for treating medical conditions.

Anabolic steroids often are taken in combination in a practice called "stacking," in which the abuser mixes oral and/or injectable types of anabolic steroids. Steroid abusers often also "pyramid" stacked compounds in cycles of 6 to 12 weeks, meaning that they gradually increase doses then slowly decrease them to zero. The belief that these practices produce bigger muscles and allow the body to adjust to and recuperate from high doses of steroids has not been substantiated scientifically.

Doses taken by abusers can be up to 100 times greater than doses used for treating medical conditions.

What are the potential health consequences of steroid abuse?

Health consequences associated with anabolic steroid abuse include:

- *Hormonal system disruptions.* Reduced sperm production, shrinking of the testicles, impotence, and irreversible breast enlargement in boys and men. Decreased body fat and breast size, deepening of the voice, growth of excessive body hair, loss of scalp hair, and clitoral enlargement in girls and women.
- *Musculoskeletal system effects.* Premature and permanent termination of growth among adolescents of both sexes.
- *Cardiovascular diseases.* Heart attacks and strokes.
- *Liver diseases.* Potentially fatal cysts and cancer.
- *Skin diseases.* Acne and cysts.
- *Infections.* In injecting steroid abusers, HIV/AIDS, hepatitis B and C, and infective endocarditis, a potentially fatal inflammation of the inner lining of the heart.
- *Behavioral effects.* Increased aggressive behavior, particularly when high doses are taken. Depression, mood swings, fatigue, restlessness, loss of appetite, and reduced sex drive when steroid abuse is stopped. **NN**

Steroid Prevention Program Scores With High School Athletes

By Robert Mathias, *NIDA NOTES* Staff Writer

A NIDA-funded drug abuse prevention program is showing high school football players that they do not need to take anabolic steroids to build powerful muscles and improve athletic performance. By educating student athletes about the harmful effects of anabolic steroids and providing nutrition and weight-training alternatives to steroid use, the program has increased football players' healthy behaviors and reduced their intentions to use steroids.

Until now, anabolic steroids, drugs derived from the male hormone testosterone, have rarely been the focus of drug abuse prevention studies, says Dr. Ro Nemeth-Coslett of NIDA's Division of Epidemiology and Prevention Research. This may be because steroids are not widely abused. Only about 2 percent of 8th, 10th, and 12th grade students have ever used steroids, according to the NIDA-supported Monitoring the Future study for 1996. However, steroid abuse occurs more often among young people who are involved in physical training because anabolic steroids can increase muscle mass, strength, and stamina, Dr. Nemeth-Coslett points out.

Although adolescent boys, particularly those involved in athletics such as football or body building, make up the majority of high school steroid users, national surveys show that adolescent girls also are vulnerable to the lure of steroid use. However, that lure contains a hook—anabolic steroid use can have severe physical and emotional consequences for both males and females. Physical effects can include stunted growth, high blood pressure, and liver tumors. Psychological effects can include wide mood swings that range from episodes of uncontrolled anger and aggressiveness to clinical depression when steroid use is stopped.

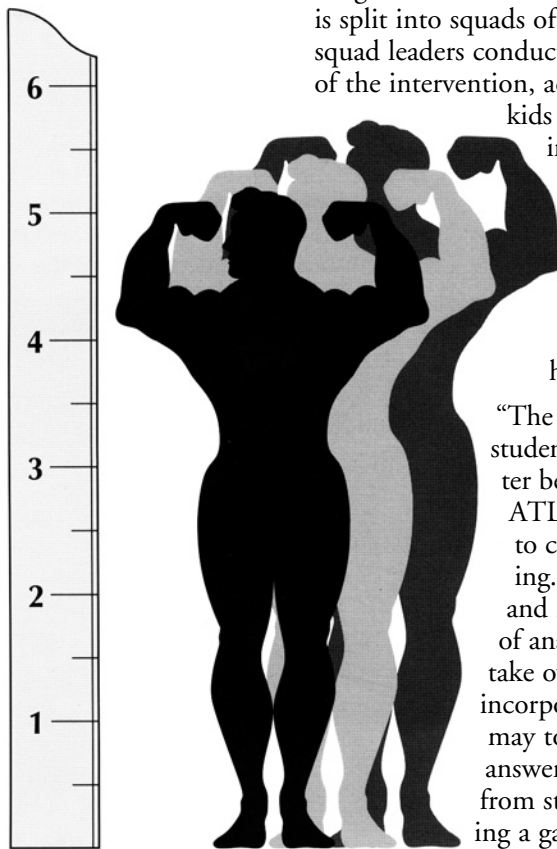
"The Adolescents Training and Learning to Avoid Steroids (ATLAS) program uses a team-oriented educational approach that motivates and empowers student athletes to make the right choices about steroid use," says Dr. Linn Goldberg of Oregon Health Sciences University in Portland, who led the research team that developed and tested the program. The program consists of classroom, weight-training, and parent information components. Together, they give student athletes the knowledge and skills to resist steroid use and achieve their athletic goals in more effective, healthier ways, he says.

In ATLAS's classroom component, football coaches and student leaders conduct seven highly interactive sessions that explore the effects of steroids, the elements of sports nutrition, and strength-training alternatives to steroid use. These classes also hone the athletes' decisionmaking and drug-refusal skills. In a typical session, the football team is split into squads of six or seven students, with student squad leaders conducting the sessions and teaching most of the intervention, according to Dr. Goldberg. "It's

kids talking to kids; that's an important ingredient in our program," he says.

Coaches, who have a substantial influence on these student athletes, also play an important role on the steroid prevention team, Dr. Goldberg says. Coaches introduce topics and wrap up each session, he explains.

"The ATLAS program is voluntary, and students get no credit for it, so it better be entertaining," he says. As a result, ATLAS classroom sessions are designed to combine fun and games and learning. Coaches move from squad to squad and introduce a topic, such as the effects of anabolic steroids. Then squad leaders take over and initiate an action game that incorporates the topic. For example, players may toss a football to each other as they answer questions about problems that stem from steroid use. "Although they are playing a game, each one is paying attention and listening because someone is flipping the ball to them," says Dr. Goldberg. "No one is



Students in the ATLAS program learn that stunted growth and many other harmful effects can result from steroid use.

saying to them, ‘Watch out, steroids cause liver disease, acne, and so forth,’” he notes. “But while they are laughing and having a good time, they are actually watching and learning at every step of the way.”

“Football players are athletes; they like to compete,” Dr. Goldberg notes. Therefore, several games pit squads against each other to try and earn the most points for correct answers about weight training, nutrition, and steroids. In addition to games, “students do mock public service announcements, they do ‘rap,’ they do songs, and they do newspaper articles in the classroom sessions,” he says.

In ATLAS’s weight-training component, research staff members conduct seven hands-on sessions that teach the students proper weight training techniques. These sessions are designed to help student athletes build the muscular strength and agility needed to achieve their athletic goals without using steroids.

In the parent information component, parents participate in an information and discussion session about the program with the ATLAS staff. The staff gives the parents a family sports nutrition guide and encourages them to support and reinforce the antisteroid and nutritional goals of the program at home. Students in the program say their parents are more opposed to steroid use after the intervention and often provide healthier meals at home, according to Dr. Goldberg.

Late last year, Dr. Goldberg reported results of an ongoing study of ATLAS’s effectiveness in preventing steroid use among more than 1,500 football players from 31 high schools in the Portland area. Some 702 football players at randomly selected schools received the 7-week program during football season. Another 804 football players at matched schools served as a control group and received only a standard informational brochure on the dangers of steroid use.

Assessments conducted immediately after the intervention and 1 year later show that, compared with control students, student athletes who participated in the ATLAS program knew more about exercise, nutrition, and the harmful effects of anabolic steroids. ATLAS participants also had an increased sense of personal vulnerability to negative effects of steroids, more unfavorable attitudes toward their own and others’ use of steroids, and reduced intent to use steroids. ATLAS students also showed greater improvement in their nutritional habits than did control students. For example, they were more likely to eat high-protein low-fat meals at school, home, and fast-food restaurants. In addition, ATLAS students were more likely than students who did not participate in the program to use established weight-lifting and strength-conditioning techniques.

“The program’s positive effects flow from changing the student athletes’ attitudes and perceptions about steroids and then changing their nutrition and exercise behaviors,” Dr. Goldberg says. These changes in behavior are reinforced by conducting periodic tests of the athletes’ body composition, strength, and power. “If they are training properly, they are a heck of a lot stronger. So, it’s real positive reinforcement to them,” he says.

“Student athletes who participate in the ATLAS program achieve,” Dr. Goldberg says. The year before they entered the program, the football teams that were randomly assigned to receive the intervention had much worse won-lost records in football than the teams in the control group had, he says. At the end of the first year, the two groups’ records were about the same, but teams in the ATLAS program did slightly better. At the end of the

Adolescent Girls Abuse Steroids, Too

What do anabolic steroids have in common with amphetamines, tobacco, diet pills, laxatives, and anorectics? They all are drugs used by adolescent girls seeking to stay thin, says Dr. Linn Goldberg of Oregon Health Sciences University. The use of these drugs, which often goes hand in hand with eating disorders, is particularly prominent among adolescent girls engaged in athletic activities ranging from track and field, soccer, basketball, and volleyball to school dance and drill teams, Dr. Goldberg says.

Dr. Goldberg and his colleague Dr. Dianne Elliot have been conducting preliminary research, funded by NIDA, to identify risk factors that influence adolescent girls’ use of harmful drugs. Among other things, the researchers have found that many adolescent girls use drugs to maintain thinness, Dr. Goldberg says. National surveys indicate that girls account for about one-third of the high school students who abuse steroids, Dr. Goldberg says. “The primary reason that these girls use steroids is to lose fat and gain lean muscle,” he says.

Dr. Elliot and Dr. Goldberg have already developed an effective steroid prevention program for male high school athletes described beginning on the previous page. Now, they are developing a similar drug abuse prevention program for adolescent girls. In their future research, the researchers hope to test the effectiveness of the intervention in reducing drug use and eating disorders among female athletes in Oregon’s public middle and high schools.

The prevention program gives student athletes the knowledge and skills to resist steroid use and achieve their athletic goals in more effective, healthier ways.

second year, the won-lost records of the ATLAS teams were substantially better than those of the control teams, with some of the ATLAS teams making the playoffs at the end of the season. "I don't know whether these teams' improved performance is due to the ATLAS program," Dr. Goldberg says. "I do know some of those schools hadn't been to the playoffs in 25 years. The data showing improvements in program participants' body composition and muscle mass are consistent with these teams' success," he says.

Source

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For More Information

ATLAS, Oregon Health Sciences University, 3181 S.W. Sam Jackson Park Rd., CB 615, Portland, OR 97201-3098, (503) 494-7900. **NN**

Questions and Answers About Anabolic Steroids

What Are They?

Anabolic steroids are drugs derived from the male hormone testosterone. They promote muscle growth and increase lean body mass. Although anabolic steroids have many approved medical uses, they are abused by some athletes and others seeking to improve performance and physical appearance. These nonmedical uses are illegal and carry many health hazards.

How Are They Used?

Anabolic steroids are taken as pills or injected. Steroid abusers may take hundreds of times more than the medically recommended dose. Users often combine several different types of steroids to boost their effectiveness—a method called stacking. In another method, called cycling, users take steroids for 6 to 12 weeks or more, stop for several weeks, and then start again.

How Many People Use Them?

In 1994, 1,084,000 Americans, or 0.5 percent of the adult population, said that they had used anabolic steroids, according to the Substance Abuse and Mental Health Services Administration's National Household Survey on Drug Abuse. In the 18 to 34 age group, about 1 percent had ever used steroids; for ages 35 and older, that figure went down to 0.2 percent. More men than women had used the drugs: 0.9 percent of men and 0.2 percent of women said they had ever taken steroids.

NIDA's Monitoring the Future study has tracked anabolic steroid use among middle school and high school students in the United States since 1989. From 1989 to 1996, there was a slight, gradual decline in the number of 8th, 10th, and 12th graders who had ever used steroids or used them in the past year. In 1996, 1.8 percent to 2.4 percent of these students had ever used steroids, and 0.9 percent to 1.5 percent had used them in the last year.

How Do People Get Them?

Under Federal law it is illegal to possess or distribute anabolic steroids for nonmedical uses. However, heavy demand has generated a black market with estimated sales of up to \$400 million a year, according to a NIDA Research Report, *Anabolic Steroids: A Threat to Body and Mind*. Anabolic steroids are manufactured legally or ille-

gally outside the United States and smuggled in, usually through the mail; manufactured legally and diverted to the black market; or manufactured illegally in the United States. Many substances sold as anabolic steroids are diluted, contaminated, or simply fake.

What Are the Health Hazards?

Some of the main side effects of anabolic steroid abuse are trembling, severe acne, fluid retention, aching joints, high blood pressure, lower HDL (the "good" form of cholesterol), jaundice, and liver tumors. Also, people who inject steroids with shared needles run the risk of contracting or transmitting hepatitis or HIV, the virus that causes AIDS.

Other side effects include:

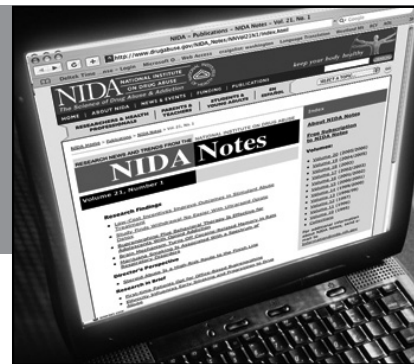
- for men, shrunken testicles, reduced sperm count, impotence, infertility, baldness, development of breasts, difficulty or pain in urinating, and an enlarged prostate;
- for women, growth of facial hair, changes in or cessation of the menstrual cycle, enlargement of the clitoris, deeper voice, and smaller breasts; and
- for adolescents, premature skeletal maturation and accelerated puberty leading to stunted growth.

NIDA-funded studies have shown that steroid abuse can cause wide mood swings including uncontrolled anger and aggressiveness that can lead to violent episodes. Users often become clinically depressed when they stop taking the drugs—a withdrawal symptom that may contribute to dependence. Users also may experience paranoid jealousy, extreme irritability, delusions, and impaired judgment stemming from feelings of invincibility.

Do They Really Work?

Athletes, as well as some coaches, trainers, and physicians, report significant increases in muscle mass, strength, and endurance from steroid use, according to a 1991 NIDA Research Report. In acknowledgment of these effects, the International Olympic Committee has placed 20 anabolic steroids and related compounds on its list of banned drugs. However, no well-controlled studies have documented that the drugs improve agility, skill, cardiovascular capacity, or overall athletic performance. **NN**

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