

# Anabolic Steroids

## Background

1. Definition
  - Anabolic androgenic steroids (AAS) are a type of performance enhancing drug (PED)
2. General info
  - PED
    - Any substance taken in non-pharmacologic doses specifically for improving sports performance<sup>1</sup>
  - Use at all levels of competitive athletics is banned<sup>2</sup>
  - AAS include
    - Methyltestosterone, nandrolone, stanozolol, testosterone, androstenedione, DHT, DHEA, clenbuterol, selective estrogen receptor modulators
  - PEDs have been used since Greeks competed in ancient Olympics<sup>3</sup>
  - Testosterone
    - First synthesized in the 1930's
    - Introduced to sporting arena in 1940's and 1950's<sup>2</sup>
  - International Olympic Committee (IOC)
    - Founded in 1960's administers anti-doping tests to create equal and fair competition among athletes<sup>3</sup>
  - "Prohibited List" of substances is available from World Anti-Doping Agency
    - <http://www.wada-ama.org/>
  - AAS-schedule III controlled substances
  - AAS non-prescription use is illegal
    - Punishable as a felony

## Pathophysiology

1. Pathology of AAS use
  - Believed to exert effects by
    - Binding androgen receptors
    - Stimulating production of RNA
    - Increasing protein synthesis
  - Anti-catabolic effects
    - Improve utilization of protein
    - Inhibit catabolic effect of glucocorticoids
  - May lead to gains in strength by
    - Increasing aggressiveness
    - Inducing euphoria
    - Decreased sense of fatigue during training allowing a higher intensity and longer duration of training
  - Precise effects on athletes are unknown
    - Clinical effects determined by
      - Type and concentrations of androgen receptors in target organ
      - Enzymes controlling steroid metabolism in a given organ

- Extrapolated from side effects of therapeutic drug dosages
    - Potential direct/indirect effects enhancing sport performance
      - Generic anabolic effect
        - Muscle hypertrophy
        - Weight gain with subsequent increased strength, power, speed, endurance, aggressiveness<sup>3</sup>
        - Most profound effects noted with<sup>4</sup>
          - High doses used by individuals who trained heavily prior to use
          - Continued training during use
          - Maintaining diet adequate in calories and protein
        - Demonstrated increase in maximal single lift strength
          - Strength gains lost after cessation of drug
        - Aerobic and endurance activities are not enhanced
      - Various side effects<sup>3</sup>
        - Hypertension
        - Myocardial damage
        - Hepatoma formation
        - Psychosis
        - Prostate hypertrophy
        - Female virilization
        - Uterine atrophy
        - Addiction
2. Incidence, prevalence
  - No data available on prevalence of AAS use in adult athletes
    - 46% of all athletes use a variation of performance enhancing supplements<sup>5</sup>
    - National collegiate sport level anabolic agent use is 8%<sup>2</sup>
    - 4-11% of male and up to 3.3% of female high school students use AAS<sup>6</sup>
3. Risk factors
  - AAS use most common in
    - Males
    - Non-Caucasians
    - More common in middle school than high-school<sup>2</sup>
    - Both male and female adolescents who participate in weight-related sports
  - Female AAS users are less likely to play school-sponsored team sports<sup>7</sup>
  - Female adolescent athletes reporting AAS use are more likely to be clinically depressed (OR 4.13), and have a marked increase in additional health-harming behaviors<sup>7</sup> including increased past 30-day use of
    - Alcohol (OR 8.83)
    - Cigarettes (OR 5.14)
    - Cocaine (OR 10.78)
    - Diet pills (OR 4.86)
    - Marijuana (OR 7.91)
    - More likely to carry a weapon (OR 7.54)
    - More likely to have had sex before age 13 (OR 2.90)

#### 4. Morbidity / mortality

- Presumptive morbidity linked to side effects of AAS use
- Mortality rate unknown

### **Diagnostics**

#### 1. History

- AAS user must be identified with a reliable history to identify those at risk<sup>1</sup>
- AAS users
  - Athletes involved in weight-related sports demanding high degrees of strength, power, size, speed
- Sports such as gymnastics, wrestling, football, baseball, weight-training, and bodybuilding have highest prevalence of AAS use<sup>1</sup>
- Adolescents not involved in sports but being intimidated or bullied may use AAS to appear stronger or to defend themselves<sup>1</sup>
- Male AAS users report higher rates of depressed mood, poorer self-esteem, and attempted suicide<sup>2</sup>

#### 2. Physical exam

- Most adolescent AAS users do not have any distinguishing physical findings<sup>1</sup>
- Height, weight, BMI, body composition, degree of muscularity should be examined/compared to previous measurements
- In individuals who discontinue AAS use, size and strength often diminish dramatically
- Elevated blood pressure
- Males (often irreversible)
  - Acne
  - Male-pattern baldness
  - Gynecomastia (irreversible)
  - Testicular atrophy
  - Severe striae
- Females
  - Acne
  - Male-pattern baldness
  - Hirsutism
  - Clitoral hypertrophy (irreversible)
  - Deepening of voice
- Needle marks on the skin/skin abscesses may be evident<sup>1</sup>
- Long term AAS users often exhibit many characteristics of classic addiction
  - Cravings, difficulty in ceasing steroid use, denial, withdrawal symptoms<sup>2</sup>
- Withdrawal symptoms similar to those seen with alcohol and opioid withdrawal such as
  - Diaphoresis, myalgias, nausea, elevations in blood pressure, tachycardia, major depression<sup>6</sup>

3. Diagnostic testing
  - Laboratory evaluation
    - Several agencies regulate the use of banned substances including
      - World Anti-doping Agency (WADA)
      - US Anti-Doping Agency (USADA)
      - NCAA
      - High school drug testing programs
    - Drug testing for exogenous substances using gas chromatography with mass spectrometry may be used-limited value/availability<sup>1</sup>
    - Urine testing is available for AAS detection
    - Liver function tests can be elevated 2-3 times normal range
      - Usually return to baseline within several weeks of discontinuation<sup>6</sup>
    - Lipid profile may show decreased HDL/increased LDL
    - Additional testing
      - Hepatitis B, hepatitis C, HIV, basic metabolic panel<sup>1</sup>
  - Diagnostic imaging
    - No imaging indicated
      - Hepatocellular adenomas have been associated with high-dose/ long term AAS use
    - Ultrasound may be used to detect liver masses in AAS users with abnormal LFTs or suspicious signs/symptoms<sup>6</sup>

### **Differential Diagnosis**

1. Acromegaly
2. Congenital adrenal hyperplasia
3. Secondary amenorrhea
4. Body dysmorphic disorder
5. Klinefelter's syndrome
6. Adrenal tumor
7. Polycystic ovarian syndrome

### **Therapeutics**

1. Counseling and education programs to help AAS users to stop
2. Prevention programs directed at high risk groups

### **Follow-Up**

1. Return to office
  - Screen for risk factors during routine visits
    - Counsel to promote prevention
  - If risk factors present, consider regular follow-up for counseling and education
  - Established or former AAS users should have laboratory monitoring and imaging according to associated signs and symptoms
2. Refer to specialist
  - Endocrinologist depending on laboratory findings and persistent signs and symptoms<sup>2</sup>
  - Severe or recurrent male gynecomastia

- Raging acne resistant to usual therapies
  - Athletic adolescent females with 2° amenorrhea
  - Unusual tendon injuries
  - New onset type-2 diabetes in an athlete
  - Sexual aggression
  - Aberrant rage behaviors
  - Psychiatrist in the event of withdrawal symptoms or evidence of major depression
  - Consider GI referral if persistent liver function abnormalities
3. Admit to hospital
- Life-threatening withdrawal symptoms, psychotic events, evidence of major depression, suicide risks, or risks of harm to others

### **Prevention**

1. The Adolescents Training and Learning to Avoid Steroids (ATLAS) program is a formalized AAS abuse prevention program for male athletes
  - In a cohort study, ATLAS resulted in significantly lower intentions to use ( $P < 0.05$ ) and actual use ( $P < 0.04$ ) of AAS in adolescent male athletes<sup>9</sup>
2. The Athletes Targeting Healthy Exercise and Nutrition Alternatives (ATHENA) program is a formalized substance abuse and disordered eating prevention program for adolescent female athletes
  - In 1 prospective controlled trial ATHENA resulted in significantly less ongoing and new use of diet pills and less new use of athletic-enhancing substances ( $P < 0.05$ )<sup>11</sup>
3. Random drug testing may be considered a prevention strategy, but only 13% of schools test athletes, and of these schools only 29% specifically test for AAS<sup>6</sup>
  - Random school drug testing in athletes compared to non-athletes may result in reduction in past 30-day use of illicit drugs and PEDs ( $p < 0.05$ ) but increased drug use risk factors ( $p < 0.05$ ) including norms of use and poor attitudes toward efficacy of drug testing and the school (cohort,  $n = 783$ )<sup>12</sup>
  - The Student Athlete Testing Using Random Notification (SATURN) study surveyed students in a drug and alcohol testing program which also tested for AAS in half the samples (RCT,  $n = 1396$ )
  - Surveyed students
    - Had less belief in their own athletic competence ( $p < 0.001$ )
    - Believed less in the benefits of testing ( $p < 0.05$ )
    - Believed that authorities were less opposed to drug use ( $p < 0.001$ )
    - Believed less that testing was a reason not to use drugs ( $p < 0.01$ )
4. Physician sponsored prevention interventions are directed at individual patient encounters
  - Acknowledge both benefits and risks of AAS use
  - Recommending a sports nutritionist may help adolescents make better food choices to optimize their health and performance<sup>1</sup>
  - Provide alternatives to adolescent athletes' athletic goals
  - Pediatric strength training for 8 year olds is endorsed by the American College of Sports Medicine as a safe and effective method of increasing baseline strength and improving athletic performance<sup>7</sup>

- "Scare tactics" by the primary physician strategy has been shown to weaken physician credibility and even encourage use<sup>6</sup>
- 5. Anti-anabolic steroid literature is readily accessible and can be used as a tool by physicians
  - Less effective than formalized team-centered prevention programs such as ATLAS and ATHENA

### **Patient Education**

1. [www.familydoctor.org](http://www.familydoctor.org): Steroid use
2. <http://familydoctor.org/online/famdocen/home/children/parents/parents-teens/steroids.html>

### **References**

1. Holland-Hall, Cynthia. Performance-Enhancing Substances: Is Your Adolescent Patient Using? *Pediatric Clinics of North America* 2007; 54:651-662.
2. Carpenter, Paul. Performance-Enhancing Drugs in Sport. *Endocrinology and Metabolism Clinics in North America* 2007; 36: 481-495.
3. Botre F, Pavan A. Enhancement Drugs and the Athlete. *Neurologic Clinics* 2008; 26: 149-167.
4. Bhasin S, Storer TW, Berman N, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength on normal men. *N Engl J Med* 1996;335:1 – 7.
5. Luigi, Luigi Di. Supplements and the Endocrine System in Athletes. *Clinics in Sports Medicine* 2008; 27:131-151.
6. Kerr J, Congeni J. Anabolic-Androgenic Steroids: Use and Abuse in Pediatric Patients. *Pediatric Clinics of North America* 2007; 54:771-785.
7. American Academy of Pediatrics Committee on Sports Medicine and Fitness. Policy statement: use of performance-enhancing substances. *Pediatrics* 2005;1151-1158.
8. Elliot D, Cheong J, Moe E, et al. Cross-sectional Study of Female Students Reporting Anabolic Steroid Use. *Archives of Pediatrics and Adolescent Medicine* 2007; 161:572-577.
9. Veralino M, Eisenberg M, Story M, et al. Participation in Weight-Related Sports is associated with Higher Use of Unhealthy Weight-Control Behaviors and Steroid Use. *Journal of the American Dietetic Association* 2007; 107:434-440.
10. Goldberg L, Mackinnon D, Elliot D, et al. The Adolescents Training and Learning to Avoid Steroids Program-Preventing Drug Use and Promoting Health Behaviors. *Archives of Pediatrics and Adolescent Medicine* 2000; 154:332-338.
11. Elliot D, Goldberg L, Moe E, et al. Preventing Substance Use and Disordered Eating- Initial Outcomes of the ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternatives) Program. *Archives of Pediatrics and Adolescent Medicine* 2004; 158:1043-1049.
12. Goldberg L, Elliot DL, MacKinnon DP, Moe EL, Kuehl KS, Nohre L. Drug testing athletes to prevent substance abuse: Background and pilot study results of the SATURN (Student Athlete Testing Using Random Notification) study, *J Adolesc Health* 2003; 32: 16–25.

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