[Primary Care]

Update on Banned Substances 2013

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Context: Doping has been pervasive throughout the history of athletic competitions and has only recently been regulated by organizations such as the World Anti-Doping Agency (WADA), US Anti-Doping Agency (USADA), and the National Collegiate Athletic Association (NCAA). These regulatory bodies were created to preserve fair play and maintain the safety of the participants. Their updated 2013 lists of banned substances and practices include a variety of drugs and practices that could cause harm to an athlete or give one an unfair competitive advantage.

Evidence Acquisition: Published websites for the WADA, USADA, and NCAA were investigated. These governing bodies update and publish their lists annually.

Results: The WADA, USADA, and NCAA monitor anabolic steroids, hormones, growth factors, β -agonists, hormone and metabolic modulators, masking agents, street drugs, manipulation of blood and blood components, chemical and physical manipulation, gene doping, stimulants, narcotics, glucocorticosteroids, and β -blockers. Some substances may be used by athletes but require formal exemption. The WADA has also recently created a category of nonapproved substances that have yet to be identified to curb athletes from experimenting with new doping agents.

Conclusion: The lists of banned substances and practices per the WADA, USADA, and NCAA are in place to ensure the integrity of sports and maintain safe competition. Health care providers who work with athletes under the jurisdiction of these organizations should review updated lists of banned substances when prescribing medications.

Keywords: banned substances and practices; athletes; updated lists; governing bodies; WADA; USADA; NCAA

The history of doping pervades back to the ancient Greeks and early Olympic competition when fame and fortune were first presented to successful athletes.² Then and now, doping has compromised the safety and health of many athletes.²

The National Collegiate Athletic Association (NCAA) was formed in 1906 with the help of President Theodore Roosevelt in response to aggressive early college football causing many injuries, even deaths, leading to the discontinuation of some collegiate sports programs altogether.⁶ The initial goal of the NCAA was to provide protection for young athletes in injury-prone sports.⁶ During its 1986 and 1990 conventions, the NCAA reaffirmed its position on safety and fairness in sports by starting the NCAA drug-testing program, initially at championship events and then at year-round programs.⁵

As doping became more prevalent and advanced, preserving true sport and fairness developed on an international level. After numerous doping scandals of the late 1990s—most notably in road cycling—the international community of sports came together in 1999 at the First World Conference on Doping in Sport (Lausanne, Switzerland) to discuss the

evolving challenges of doping in sports.²² The World Anti-Doping Agency (WADA) was created with the intent to oversee antidoping policies that would be enforced at an international level, most notably at the Olympics.²² To be eligible, all national and international sports organizations participating in the Olympics were required to accept regulation by the WADA.²²

Once the WADA was established, many countries followed by creating their own antidoping agencies to monitor utilization of the WADA's regulations. The US Anti-Doping Agency (USADA) was founded upon the US Olympic Committee's recommendations to endorse fair play and ensure that athletes would be eligible for international competition.⁷ On October 1, 2000, the USADA was developed and given full authority to establish a comprehensive national antidoping program, including testing, education, research, policy formation, and procedures to ensure fairness in all US-sanctioned events that could qualify an athlete for the Olympics.⁷

The first event monitored by the WADA was the 2000 Summer Olympics, in Sydney, Australia.²² However, full enforcement did not occur until January 1, 2004, after the 2003 Second World Conference on Doping in Sport.^{22,23} The WADA's code

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of antidoping rules provides the framework for all rules and regulations.²³ The code outlines the standards for testing, laboratory regulation, therapeutic use exemptions, and the list of prohibited substances and methods, along with the protection of privacy and personal information policies.²³

Currently, the WADA oversees over 630 sports organizations, including the International Olympic Committee, the International Paralympics Committee, and all Olympic sport international federations.⁴ The WADA updates its list of prohibited substances annually, publishing it every October 1.¹ Categories include substances that are always prohibited, those prohibited in competition, and those prohibited in specific sports. The annually updated list of prohibited substances is enforced on January 1 of each year. The USADA concurrently uses the WADA's list of prohibited substances and implements the new list every January 1.^{16,17}

The NCAA also provides a list of prohibited substances to the student athletes annually.^{5,10} This list is updated by the Committee on Competitive Safeguards and Medical Aspects of Sports: 20 members from law, medicine, administration, and coaching, in addition to student athletes.^{5,11}

BANNED SUBSTANCES

The WADA and USADA ban substances on the basis of 3 criteria¹⁷: the potential to enhance performance, an actual or potential health risk, and whether it violates the spirit of sport.¹⁷ If a substance is banned, the entire class of the substance is usually banned, regardless of whether the specific substance is named with a few exceptions. It is the athlete's personal responsibility to avoid consuming a banned substance.^{10,16}

Always Prohibited

Nonapproved Substances

In the WADA's and USADA's regulations, the nonapproved-substances clause prohibits athletes from using any pharmaceutical substance that is not prohibited by other sections of the prohibited list for the purpose of enhancing performance. This bans all pharmaceuticals in research, veterinary medicine, discontinued and designer medications, and medicines not approved for human therapeutic use that might provide an unfair advantage.¹⁶ This new provision introduced in 2011 provides sanctions for experimental substances before they are banned. Athletes that consume any substance, named or unnamed, that can enhance performance are in violation of the WADA's and USADA's regulations.¹⁶ The NCAA does not have a similar clause at this time.¹⁰

Anabolic Steroids

Exogenous anabolic steroids are banned.^{10,16} The WADA, USADA, and NCAA also ban all endogenous anabolic androgenic steroids used exogenously.^{10,16} Clenbuterol, selective androgen receptor modulators, tibolone, zeranol, and zilpaterol are also prohibited per the WADA and USADA.¹⁶

Peptide Hormones, Growth Factors, and Related Substances

Any form of peptide or hormone that boosts athletic performance by increasing oxygen-carrying capacity or augmenting muscle growth and recovery is prohibited.^{10,16} Banned substances include the following: erythropoiesis-stimulating agents, chorionic gonadotropin and luteinizing hormone (in men), corticotrophins, growth hormone, insulin-like growth factor 1, fibroblast growth factors, hepatocyte growth factor, mechano growth factors, platelet-derived growth factor, vascular-endothelial growth factor, as well as any other growth factor affecting protein synthesis/degradation (ie, muscle, tendon, or ligament), vascularization, energy utilization, regenerative capacity, or fiber-type switching.^{10,16} Platelet-rich plasma is not banned and does not require a therapeutic use exemption under the WADA's and USADA's regulations or per the NCAA.^{10,16}

β₂-Agonists

For the WADA and USADA, all β₂-agonists are banned, including optical isomers, except for salbutamol, formoterol, and salmeterol when taken by inhalation. Salmeterol can be inhaled and does not have a threshold. Salbutamol and formoterol are threshold drugs. Salbutamol is limited to 1600 µg in 24 hours, and formoterol, 54 µg in 24 hours.¹⁶ Inhaled β₂-agonists require a therapeutic use exemption. According to the USADA, albuterol is a threshold drug requiring a concentration no greater than 1600 µg per 24 hours without therapeutic use exemption. Concentrations greater than 1600 µg per 24 hours require a therapeutic use exemption.³ The NCAA bans all types of β₂-agonists unless the athlete has a physician prescription for an inhaled β₂-agonist and a therapeutic use exemption has been completed.^{9,10}

Hormone and Metabolic Modulators

Aromatase inhibitors, selective estrogen receptor modulators, antiestrogenic substances, and agents modifying myostatin function are banned, as are insulins, peroxisome proliferator-activated receptor δ agonists, and PPARδ-AMP-activated protein kinase axis agonists. Insulins can be used with a therapeutic use exemption.^{10,16}

Diuretics and Other Masking Agents

All masking agents are prohibited, including diuretics, desmopressin, and plasma expanders. Banned diuretics include acetazolamide, amiloride, bumetanide, canrenone, chlorthalidone, etacrynic acid, furosemide, indapamide, metolazone, spironolactone, and all thiazides, such as hydrochlorothiazide in addition to triamterene. Diuretics that are not banned but require therapeutic use exemptions include only drospirenone, pamabrom, and topical dorzolamide and brinzolamide for the WADA and USADA.¹⁶ The NCAA bans all forms of diuretics and masking agents.¹⁰ However, any substance that has threshold restriction that is detected in the presence of a diuretic or masking agent must have a therapeutic use exemption.^{10,16}

NCAA Banned Substances

The NCAA restricts caffeine in urine concentrations exceeding 15 µg/mL, as well as all forms of street drugs (heroin, all forms of marijuana, and cocaine). Local or topical anesthetics can be used in competition but only if medically justifiable.^{10,11}

Prohibited Methods

Manipulation of Blood and Blood Components

Any form of blood-doping, autologous, homologous, heterologous, or red cell products is banned. The sequential withdrawal, manipulation, and reinfusion of whole blood into the athlete's body are also banned.^{10,16} Manipulating the uptake, transport, or delivery of oxygen is prohibited, including perfluorochemicals, efaproxiral, and modified hemoglobin products.¹⁶ Supplemental oxygen is not prohibited.¹⁶

Chemical and Physical Manipulation of Body Fluids

Urine substitution or adulteration by chemicals or proteases is banned. Intravenous fluid infusion at rates greater than 50 mL per 6 hours is prohibited, except for hospitalization or clinical investigation.¹⁶ The NCAA does not currently have a policy on the administration of intravenous fluids.¹⁰

Gene Doping

The WADA and USADA prohibit gene manipulation to enhance sports performance.¹⁶ The transfer of nucleic acids or nucleic acid sequences, as well as the use of normal or genetically modified cells that directly or indirectly affect gene expression, is banned.¹⁶ This is not currently banned by the NCAA.¹⁰

Prohibited Substances and Methods in Competition

Unlike those of the WADA and USADA, the NCAA's bans apply during competition and training. The exception to this is tobacco products, which are banned in NCAA sports during competition and practice.^{10,16}

Stimulants

All stimulants are prohibited in competition by the WADA, USADA, and NCAA, including both optical isomers.^{10,16} However, there are exceptions to this rule for each governing body. The topical use of imidazole derivatives and stimulants in the 2013 monitoring program is not prohibited according to the WADA and USADA. Stimulants in the monitoring program for the WADA include caffeine, nicotine, phenylephrine, phenylpropanolamine, pipradol, and synephrine. These medications are not prohibited by the WADA and USADA but are being evaluated for potential abuse.¹⁶ Cathine, ephedrine, methylephedrine, and pseudoephedrine are monitored closely and have threshold limitations but are not currently banned by the WADA and USADA.¹⁶

The NCAA allows athletes to use pseudoephedrine and phenylephrine but restricts the consumption of caffeine. The NCAA prohibits levels of caffeine greater than 15 µg/mL in the urine and considers it a threshold drug.¹⁰ Caffeine was removed

from the WADA list in 2004 because high levels could decrease performance.¹² It is ubiquitous in foods and beverages and is metabolized at different rates, thereby making it a challenging substance to restrict in athletes.^{10,16}

Narcotics

Narcotics in any form are not banned in the NCAA, except for heroin, which is considered a street drug.¹⁰ However, the WADA and USADA prohibit the use of buprenorphine, dextromoramide, diamorphine (heroin), fentanyl and its derivatives, hydromorphone, methadone, morphine, oxycodone, oxymorphone, pentazocine, and pethidine in competition.¹⁶

Cannabinoids

The WADA and USADA prohibit natural and synthetic forms of cannabinoids during competition. The NCAA bans all forms of cannabinoids at all times.^{10,16}

Glucocorticosteroids

Glucocorticosteroids are not currently banned by the NCAA.¹⁰ However, the WADA and USADA ban all glucocorticosteroids during competition when administered via oral, intravenous, intramuscular, or rectal routes, unless a therapeutic use exemption has been approved.¹⁶

Alcohol

Alcohol (ethanol) is prohibited during aeronautic, archery, automobile, karate, motorcycling, and power boating competitions by the WADA and USADA.¹⁶ Testing for alcohol may be performed via blood and breath analysis. The doping hematologic threshold for alcohol is 0.10 g/L.¹⁶ The NCAA prohibits alcohol use during riflery competitions only.¹⁰ It also requires each collegiate institution to have an alcohol policy to guide athletes.^{10,11}

β-Blockers

All forms of β-blockers are banned during competition per the WADA and USADA for the following sports¹⁶: archery (also prohibited out of competition), automobile, billiards (all forms), darts, golf, shooting (also prohibited out of competition), skiing/snowboarding (in ski jumping, freestyle aerials/halfpipe, and snowboard halfpipe/big air). The NCAA bans all forms of β-blockers in riflery competitions.¹⁰

Monitored Substances

The WADA and USADA place pharmacological substances on the monitoring list annually to assess possible abuse. At this time, the monitoring program is assessing 3 classes of medications: stimulants, narcotics, and glucocorticosteroids. Stimulants being monitored throughout 2013 in competition include bupropion, caffeine, nicotine, phenylephrine, phenylpropanolamine, pipradol, synephrine, and pseudoephedrine (< 150 µg/mL). Narcotics that will be monitored in competition include hydrocodone, morphine/

codeine ratios, tapentadol, and tramadol. Glucocorticosteroids will be assessed out of competition only. Many of these 2013 monitored substances were monitored in 2012.^{14,15}

TESTING

The WADA, USADA, and NCAA have similar testing processes. The NCAA primarily uses urine samples, while the WADA and USADA use either blood or urine testing.^{11,18}

Testing Pools

Per the WADA and USADA, an athlete can be tested by a national federation at any time and during any federation-hosted event. The international federation organizes doping control at international events, while national federations organize doping control at national events. The WADA remains the clearinghouse for all testing.^{18,19}

International and national federations determine the balance of in- and out-of-competition testing based on the profile of the athletes. The physical demands of the sport, doping statistics, the history of the sport, training periods, and the competition calendar are all assessed. Testing occurs whenever most appropriate, based on the likelihood of banned substances use.^{18,19}

In-competition testing can take place up to 12 hours before an event, until the event is completed.^{18,19} Athletes must complete a whereabouts form quarterly, detailing where they will train, live, and compete. In addition, they must be available for testing for 60 minutes, daily, from 6 AM to 11 PM. If athletes do not file their whereabouts properly or are not available for testing for the 60-minute slot, they can be penalized.^{18,19}

NCAA athletes must annually consent to drug testing before they begin workouts or competition or before the fourth Monday of classes. There is a 14-day grace period for athletes trying out for a team. Athletes must be informed of the banned drugs at the beginning of each academic year.¹¹ NCAA athletes are eligible for drug testing once they are identified on the official team rosters as division I and II athletes.

Testing Notification

The WADA and USADA have a test distribution plan, which determines the number of in- and out-of-competition drug-testing events.^{18,19} Athletes are notified prior to a test unless the drug test is a “no advance notice” test. The athlete may eat or drink at one’s own risk prior to testing. The athlete’s rights include (1) a representative or interpreter, (2) a sample collection explanation, (3) a delay in reporting for valid reasons, and (4) modifications of the collection process because of disabilities.¹⁹

Athletes must sign a notification form certifying that they have been informed of the drug-testing requirement. If an athlete cannot be located—during, for example, their daily 60-minute period of availability as required by the WADA and USADA—she or he will be notified of a missed test. If an athlete misses a test or fails a whereabouts filing, she or he

is placed on probation for 18 months.^{18,19} Athletes that have a combination of 3 missed tests or whereabouts filing failures will be penalized as if they had a positive drug test.^{18,19}

The NCAA notifies athletes to be tested. If the testing takes place on the college campus, the athletic director, site coordinator, and compliance officer are notified no more than 2 days in advance of the testing. This information remains confidential. However, if testing is to take place off campus during year-round testing, the NCAA drug-testing certified collector or Drug Free Sport representative will notify the athlete of the off-campus testing.¹¹

NCAA athletes may be tested during practice, regular season competition, and championship events. Hosts for championship events are notified before the first day of testing, while institutions competing in the events are not notified in advance. An athlete can request a delay in testing to complete a final event. An institutional representative’s signature is required if the athlete’s testing is to be deferred. The athlete must present within 1 hour after the completion of the event with the institutional representative to certify identification for drug testing.¹¹

Specimen Collection

The WADA’s and USADA’s regulations require that a chaperone or doping control officer be present throughout the collection procedures to validate the sample. If necessary, the doping control officer or chaperone may allow the athlete to hydrate, although the athlete must avoid excessive rehydration since a urine sample must have an appropriate specific gravity. Annexes D and E of the International Standard for Testing (January 2012) provide specific regulations of urine- and blood-sampling procedures, respectively.¹⁹

When urine drug testing occurs, the athlete will remain in control of the collection vessel, as well as its contents, once the code numbers have been recorded. The athlete must provide at least 90 mL of urine. If the urine does not have a specific gravity greater than 1.005, another urine sample will be needed. The urine pH must also be between 4.5 and 7.5.^{11,19}

The amount of blood drawn from the athlete depends on the testing required, according to the WADA. If the blood sample needs further immediate processing (eg, centrifugation), the athlete remains present until the final sealing occurs in a tamper-evident kit. The athlete secures this seal prior to its transportation to the testing site.¹⁹

Implications of a Failed Test

An athlete can fail a drug test for a number of reasons, most notably for the presence of a banned substance. The following is a list of violations causing a failed drug test:

1. prohibited substance or its metabolites or makers,
2. prohibited method,
3. reusing or failing to submit to the sample collection without justification,

4. violating requirements of availability for out-of-competition testing,
5. tampering or attempting to tamper with the doping control process,
6. possessing prohibited substances or utilizing prohibited methods,
7. trafficking or attempting to traffic prohibited substances or prohibited methods, and
8. administration or attempted administration of a prohibited substance to any athlete in competition.¹⁸

Athletes that violate the WADA's antidoping regulations can be sanctioned with lifetime bans, based on the extent of the violation.¹⁸

The indications for NCAA sanctions include

1. failing to sign the consent form for testing prior to the first practice, competition, or fourth Monday of class, whichever date occurs first;
2. a positive drug test;
3. refusing to sign the notification form or custody-and-control form;
4. failure to arrive at the collection station at the designated time without justification;
5. failure to provide a urine sample according to protocol;
6. departing the collection station without authorization before providing a specimen according to protocol; and
7. attempting to alter the integrity or validity of the urine sample or collection process.¹¹

Athletes who violate the NCAA antidoping rules lose their eligibility to compete for 1 year and are subject to further drug testing at the NCAA's discretion. An athlete found guilty of an antidoping regulation can appeal the decision and sanction. This appeal must be filed within 2 days. The appeals committee may choose to decrease, maintain, or even strike the sanction. Additionally, any athlete who has been sanctioned by a WADA-regulated body will be sanctioned from NCAA sports throughout the duration of WADA ineligibility.^{11,19}

Therapeutic Use Exemptions

A therapeutic use exemption can be requested for an athlete, requiring a banned medication for a legitimate medical purpose. This can be requested when (1) an alternative nonbanned medication is not available, (2) withholding the medication would significantly impair the athlete, (3) the substance would not provide additional performance enhancement aside from returning the athlete to a more normal state of health, and (4) there is appropriate physician documentation.^{9,20,21}

For the WADA and USADA, exemptions should be requested by the athlete's sports organization at least 21 to 30 days in advance of a competition.^{20,21} The NCAA requires that student

athletes obtain a therapeutic use exemption prior to using any peptide hormones or anabolic agents.¹³ However, athletes can use banned medications when there is a physician order and appropriate documentation that supports the medical use of the banned substance. This is especially important if an athlete tests positive for the banned substance; the documentation should be presented immediately to the chair of the drug-testing and drug education subcommittee.^{11,13} A retroactive therapeutic use exemption can be obtained in emergency care of the sick or injured athlete.²⁰

Each organization has a contact person identified on its website for therapeutic use exemptions.^{8,9,13} The WADA does not grant therapeutic use exemptions but does monitor them and assists in the appeals processes. Athletes can appeal denials upon determination of a failed drug test to their respective international athletic federation and the WADA.²⁰

CONCLUSION

The WADA, USADA, and NCAA have similar banned substance classes and drug-testing requirements to uphold fair play and maintain the safety of sports competitions. The number of banned substances grows annually. The antidoping agencies work year-round to ensure athlete safety and the purity of sports. Antidoping agencies update their banned substances and methods annually on their websites and offer resources to athletes, coaches, and regulatory bodies. The WADA, USADA, and NCAA provide the foundation of true and fair competition.

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