Clinical Chemistry

Breaking Boundaries: Exploring Performance Enhancement and Anti-Doping Testing in Sports

Article:
Imir G Metushi, Allison Wagner, Brian Ahrens, Magnus Ericsson, Olivier Rabin, Tim Sobolevsky, and Travis T Tygart.
Breaking Boundaries: Exploring Performance Enhancement and Anti-Doping Testing in Sports.
Clin Chem 2024; 70(7): 897–904. https://doi.org/10.1093/clinchem/hvae074

Guest: Dr. Imir Metushi is an Assistant Professor at the University of California, Los Angeles.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Elite athletes feel tremendous pressure to perform at the highest level, which for certain individuals leads to the use of performance enhancing drugs. Despite regulations banning these substances in athletic competition and the known health risks associated with their use, the allure of obtaining a competitive advantage occasionally proves difficult to pass up.

To identify athletes who use banned substances, many professional leagues and international federations have implemented anti-doping programs that involve laboratory testing of patient specimens. How do these testing programs work and how do they differ from a typical clinical laboratory? What laboratory tools are at the forefront of anti-doping efforts and can they keep pace with a very determined athlete looking for new ways to avoid detection? Lastly, is it possible to determine whether the presence of a banned substance represents intentional use or simply a contaminant introduced during the process of manufacturing a legitimate product? A new Q&A article appearing in the July 2024 issue of *Clinical Chemistry* describes efforts by anti-doping laboratories to detect banned substances and ensure fairness and athletic competition.

In this podcast, we welcome the article's moderator. Dr. Imir Metushi is an Assistant Professor at the University of California, Los Angeles. His interests are in biomarker discovery, as well as immunoassay and mass spectrometry applications utilized in the clinical chemistry laboratory. Dr. Metushi, let's start with this. Why do athletes continue to dope despite the dangers it can present to the user and the ongoing international efforts to detect doping and promote fair play?

Imir Metushi: Right. So, there are several reasons here that are driven by complex motivations and societal pressures. First and foremost, the competitive nature of the sport creates an immense pressure to perform at the highest level. Winning not only brings prestige to these athletes, but also financial

rewards, you know, sponsorship deals and also career longevity. So, this immense pressure can push athletes to seek any advantage, including the use of performance enhancement drugs. Secondly, there are cultural factors that also play a role.

In some sporting communities, there is a pervasive culture of winning at all costs. This mindset can be perpetuated by teammates, coaches, and even national sport organizations that prioritize success over ethics. When athletes see their peers are using these drugs and achieving success, especially when they evade being caught, it can create a sense of necessity to follow suit to remain competitive. On the other hand, however, misinformation and lack of education about these drugs can also be a reason. Many athletes may not fully understand the health risks associated with these substances or may be misled by their legality and ethical implications. Some might be influenced by misleading information from their peers, trainers, and certainly online sources, believing that certain drugs are safe or even undetectable.

Also, there are instances where doping occurs from contaminated supplements and misguide from medical staff. Therefore, there is need to focus more on comprehensive education of not only athletes, but also of all the people that surround and support the athlete, such as the training staff, team leads, and medical personnel.

Bob Barrett: Well, given that doping still does occur, how does its prevalence impact the morale and mindset of the clean athletes?

Imir Metushi: So, witnessing the success of athletes who dope can instill a sense of doubt and skepticism about the legitimacy and the fairness of the playing field. For many clean athletes, this reality is demotivating and disillusioning and can lead to loss of motivation. This emotional toll can result in feelings of depression due to the inability to control these systemic issues. Eventually, the widespread nature of doping can erode trust within the sports community, which can have long-term consequences for the credibility of sports as a whole.

Moreover, the perception that doping is prevalent because everyone is doing it, it exacerbates the pressure on clean athletes. This belief, which is often cited by athletes who dope, suggests that to remain competitive, doping becomes a necessity. This perception further demoralizes clean athletes who strive to maintain their integrity. Now, in response to this, the World Anti-Doping Organization, also known as WADA, are actively working to understand and address these issues.

Through initiatives such as prevalent surveys and empirical investigations, WADA aims to reinforce clean sport behaviors and provide better understanding of how doping affects athletes' morales and mindset. Now, with all that being said, it's worth noting that despite these challenges, many clean athletes remain resolute in their commitment to competing with integrity and upholding the principles of fair play, and they serve as role models for future generations.

Bob Barrett: Dr. Metushi, do we have the right tests and are they good enough to catch dopers while minimizing the chances of a wrongful conviction?

Imir Metushi: Yes, we do. However, it is important to note that the effectiveness of anti-doping testing is an ever-evolving effort. Thanks to advances in detection technology, such as mass spectrometry and chromatography that have greatly improved the sensitivity and specificity of anti-doping tests, we can now detect even trace amounts of banned substances in athlete samples. This has been crucial in enhancing the accuracy of tests while minimizing the chances of wrongful convictions.

Another robust tool for detecting doping has been the introduction of athletes biological passport programs. These programs monitor an athlete's biological markers over times, looking for irregularities that may indicate doping practices such as blood doping or steroid use. This longitudinal approach is an additional tool that helps to identify doping patterns that single tests may miss. Therefore, as the testing has gotten better, we have gotten very good at detecting the majority of performance-enhancing substances at very low levels. However, the process doesn't stop at detection, it relies on thorough follow-up investigation by results management partners, ensuring that potential rule violations are properly examined and adjudicated, sometimes including arbitrations.

And certainly, athletes have the right to request reanalysis of their samples. So, there is this comprehensive approach that helps to ensure that any sanctions are based on solid evidence, thus protecting clean athletes from wrongful convictions. Now, as I have mentioned before, with all that being said, there's always room for improvement. Making testing more economical and increasing the use of alternative matrices could enhance detection. For example, collecting dry blood spots in addition to urine samples may help determine whether a substance was taken in or out of competition, particularly when urine levels alone may not be definitive.

Also, WADA and its partners are continuously refining anti-doping testing and application rules to integrate optimal specificity and sensitivity and so far, through its research program, has invested over 90 million U.S. Dollars since 2001. And WADA is dedicated to improving existing methods and developing new ones to address the expanding list of banned substances. So, as we can see, there is high degree of certainty in anti-doping testing that goes beyond standard scientific rigor to prevent wrongful accusations.

Bob Barrett: Anti-doping testing has been in place for quite some time now. Has it been effective?

Imir Metushi: Yes, it has. However, the effectiveness of anti-doping testing has been a topic of continuous improvement and debate. The anti-doping system, while robust in its methodology, it's only as strong as its weakest element. There are some disparities in the analytical capabilities and quality of different laboratories globally, which can lead to inconsistent results. While some countries and sport federations invest heavily in these programs, others barely meet the minimum requirements. This inconsistency underscores the need for more frequent testing and also harmonized global effort, with WADA playing a crucial role in standardizing and enhancing these anti-doping measures worldwide.

Despite these challenges, the anti-doping system has seen considerable success. High profile cases and those resulting sanctions serve as powerful deterrents, reinforcing the message that doping is not tolerated. This success fosters trust among clean athletes who feel they are competing on an even playing field. In addition, the effectiveness of anti-doping testing is further supported by the integration of Intelligence and Investigation Standards, which allows for the collection of non-analytical evidence to strengthen cases against doping violations.

Bob Barrett: Well, finally, Doctor, let's look ahead. How can collaborations between sports organizations, scientific communities, and regulatory bodies pave the way for more effective and comprehensive anti-doping measures?

Imir Metushi: So, these type of collaborations are essential. An example of this is the Partnership for Clean Competition, which facilitates research and development to enhance doping detection methods by identifying emerging trends and developing new technologies for anti-doping testing. As we move forward, the increase in sophistication of doping methods, an example is gene therapy, underscores this need for partnership between medical researchers and anti-doping communities. As the benefits of such treatment become more apparent and the associated health risks diminish, the temptation to misuse

them will grow and this type of collaborations will become increasingly important in order to catch dopers.

It is also worth noting that broader engagement beyond traditional anti-doping laboratories can foster innovative ideas and solutions. This includes closer collaboration between laboratories, regulators, and sample owners for intelligence operations aimed at catching cheaters. Concrete examples of successful collaborations include the Anti-Doping Intelligence and Investigation Project in Europe, where since June 2022, WADA has received a grant from the European Commission to enhance anti-doping intelligence and investigation capacity in Europe.

This project aims to reduce the prevalence of doping in sports and maximize health benefits for European youth practicing clean sports. By promoting collaboration between anti-doping organization and law enforcement agencies, the project has already achieved excellent results and is set to expand to Asia next. Lastly, WADA recognizes that not all countries have the same resources to address anti-doping. Therefore, WADA focuses on establishing and maintaining effective relationships with anti-doping organizations, implementing development and capacity building programs, and supporting operational independence. Furthermore, WADA also collaborates with pharmaceutical companies to stay on top of the latest trends in new substances and methods used to dope.

Bob Barrett: That was Dr. Imir Metushi from the University of California, Los Angeles. He is the moderator of a Q&A article discussing anti-doping testing in sports in the July 2024 issue of *Clinical Chemistry,* and he's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.