

Anti-Doping Awareness in Sports

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Athlete Biological Passport

Good morning friends, and welcome to this edition of the anti-doping program brought to you by NPTEL in association with IIT Madras. I am Professor Dobson Dominic, and this is a continuation of Week 7 lectures; Lecture 2, and today we are going to look into the Athlete Biological Passport in detail. So, in Week Seven, the previous lecture was about the several ways adopted by the World Anti-Doping Agency and the National Doping Organization in doping control. Today, we are going to look into one of the important strategies adopted by WADA, that is, the Athlete Biological Passport. We are going to look into this in detail. So, in this lecture, we look into what is the Athlete Biological Passport and how athletes abuse this passport, what are the different methods in detection in anti-doping, the prevention strategies in doping control, and we will conclude with the future of doping control.

To start with, the fundamental principle of the Athlete Biological Passport is to monitor selected biological variables over time that indirectly reveal the effects of doping, rather than attempting to detect the doping substance or method itself. That means an athlete need not be caught using the banned substance, and neither sample might test positive, but there are several variables in the biological sample, in either urine or blood, that may indirectly reveal the effects of doping. This is the fundamental principle of the Athlete Biological Passport. This was employed by WADA and first approved by WADA's Executive Committee and took effect on December 1st, 2009.

So, the timeline for the Athlete Biological Passport: the concept was developed in early 2009, and there was a formal introduction in 2009 by WADA, where they initially launched the hematological module, and then expanded in 2014 with the steroid module, and latest, in 2023, they also added the endocrine module. So, what are the objectives of the Athlete Biological Passport? The first objective is flagging athletes and samples for

further testing. The Athlete Biological Passport uses longitudinal data to highlight suspicious patterns that may indicate doping. When unusual profiles are detected, they can trigger targeted testing. That means additional testing is focused on the flagged or the suspicious athlete.

ABP helps optimize resources for the doping organization by focusing testing efforts on athletes with abnormal biomarker profiles. The second objective of ABP, the Athlete Biological Passport, is that it is not a standalone test but it complements the analytical testing. It detects physiological changes over a course of time rather than identifying a specific banned substance, thus strengthening the overall anti-doping strategy. Retrospective analysis and investigations: by monitoring biomarker data over time, the Athlete Biological Passport allows for long-term storage of samples for future testing as newer methods develop. It assists in investigations by providing evidence that can be re-examined if new suspicions arise or newer testing technologies become available. The Athlete Biological Passport also supports anti-doping rule violations based on use of substances rather than just the presence, thereby enhancing the reach of anti-doping efforts.

So, the fundamental structure on which the Athlete Biological Passport is based are three modules: one, the hematological module; two, the steroid module; and three, the endocrine module. Together, they monitor various biomarkers to identify abnormalities that suggest doping. Each module targets a specific type of doping using longitudinal data analysis to uncover patterns indicative of substance use. What do you mean by that? It need not test positive when the athlete is tested, but if there is a pattern with the longitudinal data analysis, these modules help in preventing substance use or prohibited methods.

The hematological module is the first module in the Athlete Biological Passport. Its purpose is focused on detecting blood doping, which artificially enhances the athlete's oxygen-carrying capacity to improve endurance performance. This can involve the use of substances like erythropoietin or methods like blood transfusions.

The key markers in the hematological module: the first one is hemoglobin. As a primary oxygen transporter, elevated levels of hemoglobin can indicate the use of either erythropoietin or blood transfusions. This increase is due to artificially raised RBC count. The second key marker in the hematological module is hematocrit. This is the proportion of red blood corpuscles in the blood. Abnormally high values may signal an increase in red blood cell mass, which is associated with manipulation of the blood sample.

Continuation of the key markers; reticulocyte percentage or RET percentage. Reticulocytes are immature red blood corpuscles, with the percentage reflecting the rate of new RBC production. Unusual levels may suggest either the use of ESAs or blood

transfusion. The next marker is a composite score called OFF score, which is a combination of hemoglobin and reticulocyte values. The OFF score helps flag blood doping by identifying inconsistencies between two markers that may suggest abnormal red blood cell dynamics.

What is the mechanism of detection? By monitoring these markers regularly, it reduces the chances of athletes avoiding detection through timing or microdosing. With a longitudinal approach, small but consistent changes in blood values can reveal blood manipulation, even if traditional doping substances are no longer present in the system. This mechanism can even capture small fluctuations that may go undetected with single time-point testing. It also adds depth to anti-doping strategies by identifying prolonged patterns rather than transient spikes in the biomarkers. The hematological module is especially relevant in endurance sports like cycling, cross-country skiing, and long-distance running, where enhanced oxygen delivery can significantly boost performance.

The second Athlete Biological Passport module is the steroid module. Anabolic steroids are often used synthetically to increase muscle mass, strength, and enhance recovery. The steroid module detects anabolic steroid use by tracking fluctuations in an athlete's steroid profile. It is highly sensitive to both synthetic and endogenous steroid use, with a focus on detecting even small deviations from an athlete's typical steroid profile. It is very effective at identifying both direct steroid use and indirect signs like sample tampering.

So, what are the key markers in the steroid module? The first one is the T/E ratio, or testosterone to epitestosterone ratio. The T ratio is central to detecting synthetic testosterone use. The normal level of T is 1:1. An elevated ratio above 4:1 may suggest exogenous testosterone administration. The second marker in the steroid module is androsterone to etiocholanolone (Etio).

As elevated levels of testosterone metabolites can indicate steroid use, abnormal ratios between these two metabolites, androsterone and etiocholanolone, can trigger further testing. The other ratios in the steroid module are the A/T ratio or A/Etio ratio, that is, the androsterone to testosterone ratio or the androsterone to etiocholanolone ratio. By examining the ratio between various metabolites, subtle changes in the steroid profile can reveal doping that would normally not be shown in absolute levels alone. The last key marker in the steroid module is GC/C/IRMS testing.

If suspicious markers or ratios are detected, gas chromatography combustion isotope ratio mass spectrometry, or GC/C/IRMS, can confirm synthetic testosterone use by identifying distinct carbon isotope patterns. So, to detect synthetic testosterone, gas chromatography and combustion or isotope ratio mass spectrometry are used. The detection mechanism in the steroid module establishes an individualized steroid profile, making it challenging for

athletes to mask steroid use. By monitoring markers over time, it captures the physiological changes that accompany steroid administration. It can also detect attempts to evade detection through sample tampering or urine substitution, as baseline steroid profiles are typically stable and deviations are easily red-flagged and caught.

The application of steroid modules is very widely applicable in sports where increased strength and muscle recovery are advantages, such as in weightlifting, athletics, track and field, and also combat sports.

The third and last module was recently added in 2023 by WADA. The endocrine module focuses on detecting growth hormone abuse by tracking biomarkers that reflect the use of growth hormone. Growth hormone is typically used or misused by athletes to enhance muscle growth, recovery, and overall physical ability. The advantage of the endocrine module is that it offers a focused approach to detecting hard-to-trace, hard-to-track forms of doping, which is the use of growth hormone through indirect biomarkers.

By tracking long-term effects rather than transient peaks, it enhances detection reliability. The key markers in the hormone module are insulin-like growth factor 1, a key indicator of growth hormone activity. This IGF-1 level may be increased when growth hormone is administered, and a high level can also indicate growth hormone or growth hormone secretagogues, which are substances that promote growth hormone release. The next key marker in the hormone module is N-terminal propeptide of type 3 collagen. Growth hormone stimulates collagen synthesis, and P-III-NP levels may suggest doping with growth hormone.

The third key marker in the growth hormone module is the growth hormone 2000 score. It is a composite score that incorporates several biomarkers and also considers factors such as age and gender, which are used to improve accuracy. It sets a threshold to flag potential growth hormone abuse. The detection mechanism of the endocrine module tracks hormonal markers longitudinally, similar to the other two modules, the hematological and steroid modules. It provides a robust mechanism for detecting growth hormone use by identifying sustained deviations in IGF-1 and P-III-NP.

It captures the prolonged physiological effects of growth hormone that can remain even after growth hormone itself is no longer detectable. This offers a long detection window. So if an athlete has abused growth hormone during the training period, they can still be caught during a competition period or even later. The application of the hormone module is very relevant in sports that benefit from rapid recovery, muscle growth, and enhanced physical capacity, such as swimming, track and field athletics, and rugby. So we have seen the three important modules: the hematological module, the steroid module, and the hormonal module.

Now, what is the role of WADA in the Athlete Biological Passport? WADA plays a central role in the development, implementation, and ongoing management of the ABP program.

By setting standards, overseeing compliance, and coordinating with national organizations, WADA ensures that the Athlete Biological Passport remains a reliable and effective tool in the fight against doping. So, the key responsibilities of WADA are the development and standardization of the ABP, oversight and compliance, data management and data security, supporting investigations, and ensuring strict sanctions. They also help in the research, development, and education of athletes and athlete support staff. WADA also helps in global coordination in anti-doping.

Next comes the Passport Management Unit, PMU. They are responsible for the effective implementation and management of the Athlete Biological Passport. They work closely with anti-doping organizations, laboratories, and WADA to oversee data collection, analysis, and review, ensuring the program's integrity and reliability. The key responsibilities are centralized coordination, data collection and profiling, expert review of findings, data security and privacy, support for investigations and sanctions, and continuous improvement. Collection and transport of samples are essential. The sample protocols enable detailed requirements for blood and urine collection, including timing post-exercise.

Transportation guidelines: the athlete's sample must be kept at a controlled temperature because the specific gravity of the sample is very important, along with proper data logging. Analytical requirements for laboratories are needed. So the lab standards have to follow strict guidelines for blood and urine analysis, including proper equipment and procedures.

Quality assurance: the lab must be WADA-accredited, like the National Anti-Doping Agency lab in New Delhi. And this lab has to participate in external quality assessment. Only then does WADA make it an accredited lab. The athlete profile and data analysis are very important, commonly termed the ADAMS database. What is the ADAMS database? It is a centralized system for managing Athlete Biological Passport data, ensuring privacy and integrity.

They also build a profile using an adaptive model to track individual biomarkers, such as urine and blood, over time. Next comes the expert review process: the role of expert panels in evaluating abnormal profiles and recommending further investigations or sanctions. The stages of review range from initial screening to potential confirmation of doping. Finally, the result management procedures handle abnormal findings. Established steps are in place for managing an atypical result, including a potential anti-doping rule violation.

And there is a flow in the process that involves testing, analysis, and expert review to ensure due process is followed. And lastly, the athlete passport sharing and custody are discussed. The coordination of information is important, thereby ensuring only one passport per athlete, which is managed in the central database of ADAMS. The role of the anti-doping organization is very important in coordinating the Athlete Biological Passport.

So these are the references: primarily, the World Anti-Doping Code and the National Anti-Doping Rules.

Happy reading, and Jai Hind.