

## **Anti-Doping Awareness in Sports**

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**Lecture -10**

### **Side Effects of Prohibited Methods**

Good morning friends, and welcome to the Anti-Doping course programmed by NPTEL in association with IIT Madras. This is our Lecture 5 in Week 2. Today, we are going to look into the side effects of WADA's prohibited methods. I am Professor Dobson Dominic, and let us go into the lecture.

In week two, we have seen what is on the WADA World Anti-Doping Prohibited List, we learned what are the substances prohibited in competition only, what are the prohibited methods. Then, in the previous lecture, we also looked into what are the side effects of the prohibited substances or prohibited drugs. In this lecture, we are going to look into what are the side effects of the prohibited methods.

So, in the overview of this lecture, we are going to look into the side effects of the three main methods which are banned by WADA: the side effects of blood doping, side effects due to sample manipulation, and side effects due to the recent, newly developing gene doping. So, what are the prohibited methods according to WADA? M1 stands for manipulation of blood and blood components, commonly known as blood doping. Method 2 is chemical and physical manipulation of the substances, and M3 stands for genetic or cellular doping.

Let us look into the side effects of each. Method 1, which is banned by the World Anti-Doping Agency, is blood doping and EPO or erythropoietin. What is blood doping? WADA defines blood doping as misuse of certain techniques or substances, commonly synthetic oxygen carriers, transfusion of red blood corpuscles, infusion of hemoglobin. Why do athletes use this? The athletes who are involved in endurance sports use this form of method to increase one's hemoglobin mass. This allows the endurance athlete to transport more oxygen to the working muscles.

In simple words, it increases stamina and performance, especially in endurance sports like cycling and marathon. Very difficult to detect blood doping, and that is why WADA does both in-competition testing and out-of-competition testing. So, strict implementation of the Athlete Biological Passport and newer investigations like RNA marker technology has enabled WADA to scientifically detect blood doping and EPO.

Now, what are the side effects of blood doping? So, the endurance athletes misuse blood doping to enhance performance without knowing the harmful side effects of blood doping. The main side effects are increased blood viscosity. As a result, blood becomes thicker and this can lead to clotting tendencies, clotting susceptibility. There is an increased likelihood of hypertension in athletes who misuse blood doping over a period of time, and in the long term, it can also lead to kidney damage or kidney dysfunction. There is definite risk of cardiac arrest, brain stroke, and pulmonary embolism.

So, all three: central nervous system, cardiovascular system, and respiratory system can get affected if athletes misuse blood doping. One of the main side effects of blood doping is that there is increased risk of infectious diseases, especially hepatitis and AIDS. So, these are all the common side effects of blood doping.

The second method which is banned by WADA is the ban on chemical and physical manipulation. So, Method 2 stands for intravenous infusion or injection of more than a total of 100 ml of blood per 12-hour period, except for those legitimately received in the course of treatment or surgical procedures. So, if an athlete actually requires blood transfusion, he can go ahead, and that should be in less than a 12-hour period. What are the common side effects of manipulation of these blood transfusions? Repeated blood transfusion or improper blood transfusion can lead to cystitis, bladder infection, and can also lead to other blood disorders depending upon the type of manipulation.

The last method which is banned by WADA is the very recent evolving technique of gene doping. So, doping currently has evolved from performance-enhancing substances or performance-enhancing drugs to performance-enhancing genes. So, what is gene doping? It is the usage of nucleic acids or nucleic acid analogs that may alter genome sequences or alter genetic expression by any mechanism.

This includes, but is not limited to gene editing, gene silencing, and gene transfer technology. So, it can also be the use of normal or genetically modified cells: all this constitutes genetic doping. A little bit of history of gene doping, as it is a newer evolving method of doping by athletes. The basis of genetic doping is gene therapy. Gene therapy was originally started by scientists to treat genetic disorders like Hemophilia A and B, and cystic fibrosis, which are all congenital genetic disorders.

So, in the 2000s, the famous scientist Ronald Evans in the USA created “marathon mice” by administering a virus carrying gene expression IGF-1 or insulin-like growth factor 1, which had the tendency to keep on running over a long period of time without getting fatigued. So, that is why it was termed as marathon mice. So, gene doping is done under the misconception or under the premise that it can enhance endurance and strength performance, and this has been found to be true. These parameters can be dramatically enhanced through genetic manipulation. The concept of gene doping emerged alongside the development of gene therapy in the 1970s. So, the World Anti-Doping Agency, only in 2008, gave a definition for gene doping as non-therapeutic use of cells, genes, genetic elements, or modulation of gene expression having the capacity to enhance athletic performance.

Some of the important milestones in gene doping include: in June 2001, Theodore Friedman, one of the pioneers of gene therapy, and Johann Olav Koss, an Olympic gold medalist in speed skating, published a paper that was the first public warning about gene doping.

More recently, in 2003, the BALCO scandal where Marion Jones, the famous U.S. sprinter, was caught handling several banned substances like EPO became public. In this scandal, there was widespread coherence between chemists, athletic trainers, and athletes; they all conspired together to evade the doping control with newer undetectable doping substances, widely alleged or thought to be of gene doping. So, in 2003, WADA proactively added genetic doping to the list of banned doping practices.

Why do athletes try gene doping? The reason is very important. Genetics have a large influence on athletic excellence, such as important parameters like muscle strength, muscle size, muscle fiber composition which is very important, whether it's slow twitch fibers or fast twitch fibers, anaerobic threshold (very important for time-trial cyclists), lung capacity (again useful for cyclists), and flexibility (useful for sports like gymnastics).

All these genes play some important roles. Like, see the effect of genes on the characteristic anthropometry of athletes; say, for example, the height and length of limbs, the effect of genes is large. Muscle fiber composition: whether the athletes have a lot of fast twitch fibers or slow twitch fibers; again, the role of genes is very important. That is why if you see the Africans, Kenyans, Ethiopians; they have a lot of slow twitch fibers and they dominate events like marathon and endurance running. While the other parts of Africa like Jamaica, made famous by the legendary Usain Bolt, they all have more fast twitch muscle fibers in the calf muscle.

So, genes definitely have a role in athletic performance; even in lung size and volume. All this genetics has a very important role in the anthropometry and body composition of athletes, and as a result, athletes tend to misuse gene doping.

Some of the famous genes which have been isolated and are known to be favorable performance-enhancing genes are the ACE gene and ACTN3 gene, which are commonly seen in skeletal muscles involved in fast twitch fibers. The other genes like PPAR-delta, which are commonly seen in skeletal muscle and adipose tissue, promote fat metabolism and also increase the number of slow twitch fibers in the calf muscle.

What are the potential methods of gene doping? There are two main methods: direct gene transfer: where scientists introduce the desired genes into athletes' cells using a vector such as virus, or through cell therapy, modifying athletes' cells in a laboratory and then reintroducing them into the body. So, these are the two potential methods of gene doping.

Now coming to the main part: the important side effects of gene doping. The most significant one is the propensity to develop tumor formation. So, athletes or people who undergo gene doping have a very high likelihood of developing carcinoma or cancer in later stages. The other very dangerous side effect is organ failure; either liver or kidney organ failure is common. Unpredictable genetic consequences, immune system reactions; athletes can become immunocompromised, and in certain conditions, even risk of passing genetic changes to their offspring/children becomes very eminently possible. So, these are all the side effects of gene doping.

These are my references. At the end of this Week 2 lecture, you will have some 20 MCQs which will be shared with you.

Happy reading. Thank you and Jai Hind.