

*OPINION ARTICLE*

DOPING DROOPS

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**Abstract :** Drug abuse is a major concern in the athletic world. The misconception among athletes and their coaches is that when an athlete breaks a record it is due to some “magic ingredient” and not because of training, hard work, mental attitude and championship performance. The personal motivation to win in competitive sports has been intensified by national, political, professional and economic incentives. Under this increased pressure athletes have turned to finding this “magic ingredient”. Athlete turns to mechanical (exercise, massage), nutritional (vitamins, minerals), pharmacological (medicines) or gene therapies to have an edge over other players. The World Anti-Doping Agency (WADA) has already asked scientists to help find ways to prevent gene therapy from becoming the newest form of doping. The safety of the life of athletes is compromised with all forms of doping techniques, be it a side effect of a drug or a new technique of gene doping.

**Key words :** doping world anti-doping agency gene therapy athlete

Whenever you cheer for an athlete are you sure that you are cheering for him and not for his or her chemist. The earliest reported doping dates back to the 3rd century B.C., when great athletes used stimulants to improve their athletic performance (1). In the 1870's officials noted that bicyclists in the European 6-day races, dipped caffeine based sugar cubes in ether alcohol and nitroglycerine to increase stamina and staying power (2).

With the discovery of androgenic steroids, such as testosterone in 1935, came the

gradual appearance of steroid use among athletes. The first known was a soviet weightlifting team in 1950's (3).

The term doping came from the Dutch “doop” which means viscous opium juice and today signifies any stupefying drug or in the athletic parlance, any ergogenic drug (4). Pierre de Coubertin, founder of the modern Olympic games, was one of the first to point out the necessity of protecting sport from the dangers of doping (5). Despite repeated scandals many athletes have an irresistible desire to doping, if only to keep pace with

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athletes who are doing it. Where winning is paramount, athletes leave no stone unturned to gain an extra few split seconds of speed or a small boost in endurance.

Following the amphetamine-related deaths of several cyclists in the late 1960's the international Olympics committee (IOC) set up a medical commission charged with eradicating drug abuse in Olympic sports (6). Testing was first introduced comprehensively in the Mexico games. The first Olympic in which testing for steroids took place was Montreal in 1976 after the development of a reliable radioimmunoassay technique by Professor Raymond Broke, of Saint Thomas Hospital, London (6).

With the development of sports as a business, the interaction between two different rationales, that of athletic performance and that of profit, has become increasingly complex. There is a complex interaction of the athletes who compete mainly for glory; of show business companies which try to reconcile the interest of public with those of their clients; of federations who aim to ensure that rules and traditions are strictly followed; of journalists hunting for pictures and news which could be of public interest.

In 1963, the council of Europe formally defined doping in sports as "the administration or use of substance in any form alien to the body or of physiological substances in abnormal amounts and with abnormal methods by healthy persons with the exclusive aim of attaining an artificial and unfair increase of performance in competition (7)." While most physicians do not violate laws, regulations and medical standards of anti-doping rules, significant minorities of doctors justify doping athletes.

Physicians have played a significant role in the doping of many athletes over past 50 years (8).

Today, doping is defined as the occurrence of one or more of the anti-doping rule violations set forth in Article 2.1 through article 2.9 of these anti-doping rules (9). Anti-doping rules, like competition rules, are sport rules governing the conditions under which sport is played. Anti doping rules seek to preserve the intrinsic value of sport referred to as "the spirit of sport", it is the essence of olympism, it is how true we play. The spirit of sport is the celebration of the human spirit, body and mind.

#### *Anti-doping rules violation*

- 2.1 The presence of the prohibited substance or its metabolites or markers in an athlete's bodily specimen.
- 2.2 Use or attempted use of a prohibited substance or a prohibited method (success or failure of the use of prohibited substance or prohibited method is not material).
- 2.3 Refusing or failing without compelling justification, to submit to sample collection after notification as authorized in these anti-doping rules or otherwise evading sample collection.
- 2.4 Violation of the applicable requirements regarding athlete's availability for out-of-competition testing including failure to provide required whereabouts information.
- 2.5 Tampering or attempting to tamper, with any part of doping control.
- 2.6 Possession of prohibited substances and methods (unless the athlete establishes that the possession is pursuant to a therapeutic use)

- 2.7 Trafficking in any prohibited substance or prohibited method.
- 2.8 Administration or attempted administration of prohibited substance or prohibited method to any athlete,
- 2.9 Assisting, encouraging, aiding, abetting, covering up, or any other complicity involving an anti doping rules violation or any attempted violation (9).

#### *The World Anti-Doping Program*

The World Anti-Doping Program (WADP) consists of three levels (Fig. 1) needed in order to ensure optimal harmonization and best practices in international and national anti-doping programs. The salient features of various levels have been mentioned in Table I.

#### *2007 List of prohibited substances and methods*

The use of any drug should be limited to medically justified indications.

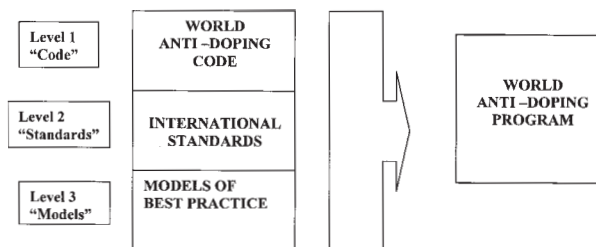


Fig. 1: The main elements of WADP.

Substances and methods prohibited at all times (in-and out-of-competition).

Prohibited Substances are :

#### *S1. Anabolic Agents*

1. Anabolic Androgenic Steroids (AAS).
  - a. Exogenous AAS e.g. 1- androstendione, desoxymethyltestosterone, nandrolone.
  - b. Endogenous AAS e.g. androstenedione, testosterone, dihydrotestosterone.
2. Other Anabolic Agents, including but not limited to: Clenbuterol, tibolone, zeranol.

TABLE I: Salient features of the three major levels of WADP.

	<i>World anti-doping code :</i>	<i>Explanation</i>
<i>Level 1 : "Code"</i>	Definition of doping <ul style="list-style-type: none"> <li>• Scope and organization</li> <li>• Roles and Responsibilities</li> <li>• Education and Information</li> <li>• Research</li> <li>• Doping Control</li> </ul>	<ul style="list-style-type: none"> <li>• Fundamental and Short document</li> <li>• Universal-applicable and acceptance for all</li> </ul>
	<i>International standards</i>	<i>Explanation</i>
<i>Level 2 : "Standards"</i>	<ul style="list-style-type: none"> <li>• List of prohibited substances and methods</li> <li>• Standards for sample collection</li> <li>• Standards for analysis of doping control samples</li> </ul>	<ul style="list-style-type: none"> <li>• Reference standards addressing particular aspects within anti-doping</li> <li>• Updated and improved regularly by experts</li> <li>• Ensure best practice and harmonization</li> </ul>
	<i>Models of best practice</i>	<i>Explanation</i>
<i>Level 3 : "Models"</i>	<ul style="list-style-type: none"> <li>• Detailed model rules and regulations based on the code</li> <li>• Other model documents on best practices e.g. national legislation, national anti-doping programme, result management etc.</li> </ul>	<ul style="list-style-type: none"> <li>• Customized for each of the major groups of stakeholders</li> <li>• Present alternative option stakeholders may select :               <ul style="list-style-type: none"> <li>◦ Adopt fully or with modifications</li> <li>◦ Develop own rules and regulation etc consistent with the code</li> </ul> </li> </ul>

*S2. Hormones and related substances*

The following substances, including other substances with a similar chemical structure or similar biological effect (s), and their releasing factors, are prohibited:

1. Erythropoietin (EPO)
2. Growth Hormone (hGH), Insulin-like Growth Factors, Mechano-Growth Factors (MGFs)
3. Gonadotrophins (LH, hCG), prohibited in males only
4. Insulin
5. Corticotrophins

*S3. Beta-2 agonists*

All beta-2 agonists including their D- and L-isomers are prohibited.

As an exception, formoterol, salbutamol, salmeterol and terbutaline when administered by inhalation, require an abbreviated Therapeutic Use Exemption.

*S4. Agents with Anti-Estrogenic activity*

1. Aromatase inhibitors
2. Selective Estrogen Receptor Modulators
3. Other anti-estrogenic substances

*S5. Diuretics and Other Masking Agents*

E.g. Diuretics, epitestosterone, probenecid, alpha-reductase inhibitors (e.g. finasteride, dutasteride), plasma expanders (e.g. albumin, dextran, hydroxyethyl starch) and other substances with similar biological effect(s).

Prohibited methods are:

*M1. Enhancement of oxygen transfer*

1. Blood doping, including the use of

autologous, homologous or heterologous blood or red blood cell products of any origin.

2. Artificially enhancing the uptake, transport or delivery of oxygen, including but not limited to perfluorochemicals, efaproxiral (RSR13) and modified haemoglobin products (e.g. haemoglobin based blood substitutes microencapsulated haemoglobin products).

*M2. Chemical and physical manipulation*

1. Tampering, or attempting to tamper, in order to alter the integrity and validity of samples collected during Doping Controls is prohibited. These include but are not limited to catheterization, urine substitution and or alternation.
2. Intravenous infusions are prohibited, except as a legitimate medical treatment.

*M3. Gene doping*

The non-therapeutic use of cells, genes, genetic elements, or of the modulation of gene expression, having the capacity to enhance athletic performance, is prohibited.

*Substances and methods prohibited in competition**Prohibited substances*

In addition to the categories S1 to S5 and M1 to M3 defined above, the following categories are prohibited in competition:

*S6. Stimulants*

E.g. Adrenaline, amphetamine, ephedrine, methylephedrine.

Adrenaline associated with local anaesthetic agents or by local administration (e.g. nasal, ophthalmologic) is not prohibited.

Each of ephedrine and methylephedrine is prohibited when its concentration in urine is greater than 10 micrograms per milliliter :

*S7. Narcotics*

*S8. Cannabinoids*

*S9. Glucocorticosteroids*

All glucocorticosteroids are prohibited when administered orally, rectally intravenously or intramuscularly. Their use requires a Therapeutic Use Exemption approval.

Other routes of administration (intraarticular/periarticular/peritendinous/epidural/intradermal injections and inhalation) require an Abbreviated Therapeutic Use Exemption except as noted below :

Topical preparations when used for dermatological, auricular, nasal, ophthalmic, buccal, gingival and perianal disorders are not prohibited and do not require any form of Therapeutic Use Exemption.

*Substance prohibited in particular sports are :*

*P1. Alcohol* is prohibited *in-competition* only, in the following sports.

Aeronautic, Archery, Automobile, Boules, Karate, Modern pentathlon, Motorcycling, Power boating.

*P2. Beta Blockers*

Unless, otherwise specified, beta-blockers are prohibited *in-competition* only, in the following sports.

Aeronautic, Archery, Automobile, Boules, Modern pentathlon, Motorcycling, Billiards, Bobsleigh, Bridge, Curling, Gymnastics, Nine-pin bowling, Sailing for match race helms only, Shooting (also prohibited out-of-competition) Skiing, Wrestling

*"Specified Substances"* are listed below :

All inhaled Beta-2 Agonists, except salbutamol (free plus glucuronide) greater than 1000 ng/ml and clenbuterol;

- Probenecid;
- Ephedrine, methylephedrine, Sibutramine and any other stimulant not expressly listed under section S6 for which the athlete establishes that it fulfils the conditions described in section S6;
- Cannabinoids;
- All Glucocorticosteroids;
- Alcohol;
- All Beta Blockers.

A doping violation involving such substances may result in a reduced sanction provided that the athlete can establish that the use of such a specified substance was not intended to enhance sport performance (11). Which type of drug or method an athlete requires depends on the type of sport he plays and the ultimate performance aim he requires (Table II).

**Drug testing**

Today sophisticated techniques are applied for drug testing. Most commonly used is a combination of a gas chromatography and a mass spectrophotometry (14). Till 1992 there were no approved definitive tests for detection of peptide hormones like human growth hormone, human chorionic gonodotrophic hormone and adrenocorticotrophic hormone (15). How long a drug can be detected depends on the particular drug; the dosage; whether taken orally or injected; whether it has an oil base; the clearance rate; and the individual's

TABLE II: Commonly misused drugs in sports (7, 12, 13).

<i>Performance Aim</i>	<i>Agents or methods used</i>	<i>Effect</i>	<i>Misused by</i>	<i>Adverse effect</i>
Strength and body weight	Anabolic steroids, growth hormone, insulin like growth factor-1, beta adrenergic drugs	10%–30%	Weightlifters, Body Builders, football players	Hair loss, gastric distress, sexual impotency, liver diseases, allergic reaction, glucose intolerance, hypothyroidism, raised intracranial tension, tremors tachycardia
Endurance	Erythropoietin, blood doping, caffeine, amphetamine, ephedrine, cocaine	5%–15%	Swimmers, baseball, football, basketball players	Sudden increase in hematocrit, blood viscosity, peripheral vascular resistance, clot formation, flu like symptoms, addiction
Relieve pre competition anxiety and to come down from “highs” caused by stimulant drugs	Barbiturates, phenothiazines, benzodiazepines, alcohol	? (Insufficient data)	Golfers, rifle shooters	Respiratory failure, dependence and death
Control fatigue and pain	Amphetamines, ephedrine, local anesthetics, alcohol, analgesics	3%–5%	Misused by a variety of athletes	Additional injury and damage to the athlete
Anti-test	Diuretics, saline infusion	? (Insufficient data)	Misused by a variety of athletes	Insomnia, hallucination, electrolyte imbalance, hearing loss, hyperglycemia.

metabolic rate, size and percent body fat. If the pH of urine is too alkaline or too dilute, the athlete is detained until urine of normal acidity and concentration is passed. The procedure for testing is as follows :

1. When an athlete provides urine, he/she will select the container and two bottles as well as select a code number from a list.
2. The athlete pours the urine from the container into the two bottles and observes the code number application.
3. Both bottles are secured (cap and wax seal) and sent to the laboratory in a secured shipping case for analysis as specimen A and specimen B.
4. Specimen A is analyzed; if “positive”, it is reanalyzed and confirmed.
5. If the occasion for drug testing stipulated

punitive action for users, the athlete is given the opportunity to be present when specimen B is analyzed for reconfirmation (14).

#### *Penalties or sanctions*

- (a) Athlete whose “B” sample proves positive in IOC-based testing has the right to appeal the findings to their sports and governing or administrative bodies.
- (b) If athletes with positive tests choose not to appeal or if their appeal is rejected sanctions can be and usually are levied.
- (c) Recommended sanctions :
  - Class I offense: Include anabolic steroids, amphetamine type and other stimulants, narcotic analgesics, diuretics, hormones, blood doping and manipulation of test sample and beta blocker.

- 1) Suspension for 2 years for the 1st offense, depending on the organization involved.
- 2) Lifetime ban for any subsequent offense (15).
  - Class II offense: Involves sympathomimetic amines.
1. Suspension for a maximum of three months for the 1st offense.
2. Suspension for 2 years for a second offense.
3. Lifetime ban for any subsequent offense (15).

**Essential components of any testing process are the following:**

- The athlete must be formally notified in writing of selection for testing.
  - The drug testing room must be clearly identified, private and secure.
  - All personnel must be clearly identified.
  - A choice of sealed drinks must be offered to help with rehydration.
  - A choice of clean containers for urine must be provided.
  - The chaperone (of the same sex as the athletes) must observe the passage of urine, ensuring that the athlete is naked between the chest and knee so that no manipulation of the sample can occur.
  - Only the athlete should handle the sample until it has been sealed in the official containers.
  - A choice of clean sample containers for both the A and B samples, each individually numbered and recorded, must be provided.
- The athlete must ensure that the container is sealed and tamper proof, and all numbering correctly recorded.
  - The urine should be tested for pH and specific gravity to ensure it is suitable for analysis. If it is not, additional urine will be required, until a suitable sample is obtained.
  - All paperwork should be fully completed and countersigned by the officials of the drug testing authority, and the athlete's representative.
  - Paperwork accompanying the sample itself should not identify the athlete by name. Identification should be by code, with details held by the testing authority.
  - The athlete should be given a copy of all the paperwork.
  - Secure passage of the samples to the laboratory must be ensured.

In case of a positive test, the athlete is notified and is given the opportunity to attend the opening and testing of the "B" sample to confirm the result. If the result is confirmed it is the responsibility of the relevant sporting federation to hear the case, and impose an appropriate sanction (16).

**Recent trends in doping**

*Gene doping*

Sports authorities fear that a new form of doping that will be undetectable and therefore less preventable is gene doping. Gene doping is defined as "The non-therapeutic use of cells, genes, genetic elements or of the modulation of gene expression, having the capacity to enhance athletic performance (11)." The world anti



doping agency has already asked scientists to help find ways to prevent gene therapy from being used as the latest means of doping.

Advantages of gene doping to athletes

1. Chemicals are indistinguishable from their natural counterparts (17).
2. They are generated locally in the muscle tissue. Nothing enters the blood stream or urine (17).

*Mechanism of Gene doping* — H. Lee Sweeny a professor and chairman of physiology at the University of Pennsylvania school of Medicine is working on treatments that introduce a synthetic gene that regenerates muscle, increases its strength and protects it from degradation. They selected adeno-associated virus (AAV) as a vector, because it infects human muscles readily but does not cause any disease. It was modified with a synthetic gene that would produce IGF-1 only in skeletal muscle and began by trying it out in normal mice. On injecting his AAV-IGF-1 combination into young sedentary mice, they saw that the muscles overall size and the rate at which they grew were 15 to 30 percent greater than normal (17).

Another recent approach to cause muscle hypertrophy may come from drugs designed to block myostatin. Myostatin seems to inhibit muscle growth throughout embryonic development and adult life. Experiments on genetically engineered mice indicate that the absence of this growth factor results in muscle fiber hypertrophy and hyperplasia. Nature has already provided examples of the effects of Myostatin blockade in the Belgian blue and fiedmontese cattle breeds, both of which have an inherited genetic mutation

that produce an ineffective version of myostatin. The first myostatin blocking drugs have been developed are antibodies against myostatin (17).

Repoxygen, developed by UK firm Oxford Biomedica, delivers the gene for erythropoiten to muscle cells in a vector configuration that brings the gene under the control of an oxygen-sensitive gene switch. Repoxygen is still in preclinical development, according to the oxford Biomedica web site (18).

In one email, the coach Thomas Springstein, wrote that “New repoxygen is hard to get. Please give me new instruction soon so that I can order the product before Christmas.” (According to German news service Dentschewelle) (19, 20). Geoffrey Goldspink from University College London who is working on gene therapy for muscle mass says “Its not rocket science to make genes”, he said “many graduates in biochemistry can make them if they are experienced enough (21).” In 1997 Leiden et al., used an adenovirus to deliver the EPO gene in mice and monkeys. This raised the hematocrit from 49% to 81% in the mice and from 40% to 70% in the monkeys. The effects lasted for over a year in the mice and for 12 weeks in the monkeys (22). Similar findings have been seen with other primate models (23).

Like EPO gene can improve aerobic performance, muscle strength can be improved by mechano-growth factor (MGF) one of the isoforms of insulin like growth factor-1. MGF does not circulate in blood. One research group from London reported a 20% increase in muscle bulk over a two-week period in mice when using MGF gene transfer. This similar effect was seen with



IGF-1 and that too in the absence of any special exercise programme (24).

Currently there are over 100 chromosomal loci, including nuclear and mitochondrial DNA, involved in human performance. Similarly the potential targets for gene doping also expands opening up further awareness for athletes (25, 26).

The genetic and physiological modification that led to those "Schwizenegger mice" (by knocking out myostatin gene) as they became known in news, could prove tempting to weight lifters, wrestlers and other athletes whose sports hinge primarily on strength (27).

Another set of experiments, were carried out at the Salk Institute in San Diego, by Ronald Evans and his colleagues producing mouse muscles that would be of help to long distance swimmers and runners. The change produced the "marathon mouse" (insertion of a fat burning protein called PPAR-delta) and runners. The researchers inserted genes that code for a fat-burning protein called PPAR-delta. Such mice stayed trim and also developed a large number of slow-twitch muscle fibers required during extended exertion (28).

#### *How safe is gene doping?*

The more we become masters of our genetic make up, the greater is the burden of responsibility we bear for the talent we have and the way we perform. Jim Wilson, a professor of medicine at the university of Pennsylvania in Philadelphia presided over a clinical trial in which 18 year old Jesse Gelsinger died in 1999 after suffering a massive immune reaction to the virus used to deliver a target gene (27). Wilson said that we need to pay attention to these kind

of immune responses. Athletes who try gene doping could find themselves dead before they win any gold medal. Gene therapy has substantial potential to treat diseases but we cannot overlook the risk involved with this therapy.

WADA president Richard W. Pound notes, "We need to start fighting this threat now, before it becomes a reality." In fact the agency's fight against gene doping began in March 2002 when they held a meeting to discuss the issue at the Banbury conference centre Long island, NY, USA (29). In 2003, WADA decided to include a prohibition of gene doping, which was formalized in 2004 World Anti Doping Code.

The first product to be associated with genetic doping emerged on the approach to the Torino 2006 Olympic Winter Games, where reoxygen was discussed as a potential threat in use at the Games (30).

It could take anywhere from 100,000 to a million dollars to set up a black market gene therapy lab. Sweeney told USA in March that athletes would be willing to spend US\$100,000 for a new set of muscles and that much money is very attractive, especially to scientists in the Soviet Union who have lost most of their research funding (31). WADA and International Olympic committee (IOC) have conservatively guessed that some athletes may use gene therapy at the 2008 Olympics Beijing.

One of the several researches being funded by WADA to develop a test for gene doping is Geoffrey Goldspink from University College London in the UK. Goldspink has shown that mice injected with the gene for normal growth factor have of 30% increase in muscle mass within 3 weeks (29). Goldspink's group is working to develop a

test that can distinguish between introduced and endogenous growth hormone and IGF-1.

Potential approaches to detect gene doping

1. Tomographic detection of mRNA being formed in unusual tissues after gene transfer.
2. Microarray searches for alterations in the expression profile of gene coding for white blood cells after application of growth hormone.
3. WADA is working towards developing a new testing approach that might be applicable for looking for the effects of an introduced substance on the body, rather than looking for the substances itself.
4. WADA plans to start taking a more longitudinal approach to testing of individual athletes and looking for changes in their normal concentrations of protein or RNA. Each athlete will be, in the future, his or her own reference (29).

#### ***Bicarbonate/Phosphate loading***

The latest developments in doping have centered on the ingestion of significant amounts of either bicarbonate or phosphate in an effort to favorably alter physiologic parameters that influence maximum performance.

*Bicarbonate loading* : Almost all of the lactic acid generated during anaerobic metabolism is buffered by bicarbonate. Since extra cellular bicarbonate enhances diffusion of hydrogen and lactate ions from intracellular to extra cellular space it would seem logical that increasing the

concentration of the bicarbonate available would forestall fatigue and improve performance (32, 33). Pate and co-workers have studied this effect in athletes (34).

*Phosphate loading* : It is well known that increasing serum phosphate results in increase in RBC cell 2, 3 DPG levels (Diphosphoglycerate). Increasing 2, 3 DPG shifts O<sub>2</sub>-Hb dissociation curve to the right and thereby enhance O<sub>2</sub> delivery to tissues, it might seem logical that increasing serum phosphate would improve maximum O<sub>2</sub> consumption (31). Cade and colleagues at the University of Florida studied effect of 1 g of sodium phosphate for three consecutive days compared with placebo in athletes (36).

#### ***Cobalt chloride: a new perspective in blood doping***

Cobalt chloride is a well-established chemical inducer of EPO gene in response to hypoxia like adaptive responses (37). Cobalt supplementation to athletes has not been banned and has not been included in the list of prohibited list. Its use is hazardous and potentially dangerous because it accumulates in liver and kidney promoting organ damage even at low doses of 33.3 mg/kg (38). Excessive cobalt administration also promotes hypothyroidism (38). Accordingly the WADA is currently working on the introduction of cobalt salts testing within revised anti-doping panels.

#### ***Why doping should be banned?***

1. It is harmful to the athletes' health
2. It violates the "spirit of sport" which is to win by exhibiting natural physical skills
3. It is unfair to have a competition between doped and un-doped athletes.

*There are viewpoints that favor legalization of doping*

1. Anti-doping policies exist, in therapy, to encourage fair play. However, they are unfounded, dangerous and excessively costly. The anti-doping rules often lead to complicated and costly administrative and medical follow-up to ascertain whether drugs taken by athletes are legitimate therapeutic agents or illicit.
2. Anti-doping control is judged necessary to prevent damage from doping. However, sports are dangerous, even if no drugs are taken. Playing soccer comes with high-risk injuries for knee and ankle and boxing can lead to brain damage. It is believed that use of drugs should be permitted under medical supervision.
3. If doping were allowed, would there be increase in the rate of deaths and chronic illness among athletes? Legalization of doping, we believe, would encourage more sensible, informed use of drugs in amateur sports, leading to an overall decline in health problems associated with doping. Finally, by allowing medically supervised doping, the drugs used would be assessed for a clearer view of what is dangerous and what are not (39).
4. The cost of anti-doping control rises year on year. In the competition between increasingly sophisticated doping (e.g. genetic transfer) and anti-doping technology, there will never be a clear winner. Consequently such a futile but expensive strategy is difficult to defend

(39). We have known for decades that genetic differences between athletes can result in markedly improved performance (40). The plain fact that athletes are already more genetically gifted than most of us e.g. Finnish cross country skier Eero maentyranta won two gold medals at 1964 winter Olympics .He was born with variant of EPO gene that caused him to produce 25–50% more red blood cells than an average person (41, 42). The athletes by gene doping can insert a gene that results in an effect similar to that, which occurred in Mantyranta (43).

A five year old German boy with unusually strong and large muscles was found to have a mutation that deactivated a gene that would normally slow his growth. Should he be forbidden to compete? If we exclude gene doping, perhaps we should also disqualify athletes who tend to perform greater than two standard deviation above the mean. If the doping ban is for fairness in sports, it requires more fine tuned doping regulations (44, 45).

*In lieu of conclusion*

Various doping techniques have become so complex but so early available and so numerous, that doping has become more and more dangerous for top athletes. Since their positive effects manifest well before their negative effects, it is difficult to convince athletes and coaches not to use them. Objective education and information should be provided not only to the athletes but also to the parents, educators, officials, and the general public for better handling of this problem.

Sufficient funds should be available for improvement of actual detection techniques and for promotion of research on future techniques e.g. gene doping. Sports schedules must be changed to avoid overworking

the athletes. So make sure today that whenever you cheer for the winner he or she may not be the “best player”, he could be the one, who best managed to escape doping abuse.

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