Gene Doping: A Review of Performance-Enhancing Genetics

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The World Anti-Doping Agency (WADA)\textsuperscript{[1]} defines gene doping as “the non-therapeutic use of genes, genetic elements and/or cells that have the capacity to enhance athletic performance.” The WADA Code is the ethical document developed by the quasi-governmental organization, in partnership with the International Olympic Committee, to pioneer and coordinate sports antidoping efforts around the world. Without a single known human incident of gene doping, WADA bestowed the technique of gene doping a dishonored place on the list of prohibited substances.

For an entire biomedical technique to be banned, before even acquiring regulatory approval by any government or before acceptance by any branch of organized medicine, seems to be unprecedented\textsuperscript{[2]}. Why would a sports regulatory administration express such preemptive concern about a putative medical technique of the future? This article answers that question and predicts the future of gene doping.

Drug doping uses therapeutic advances in exercise physiology and clinical pharmacology to provide unfair advantages to athletes who covertly use anabolic drugs, thus dramatically enhancing competitive performance. Similar to drug doping, gene doping manipulates scientific advances originally developed for the treatment of disease. Rather than drug interventions, the gene-doping athletes appropriate advances in gene therapies. Gene doping, in concept, uses scientific developments that manipulate DNA in the most basic regulation of biologic processes, to dramatically improve aspects of athletic performance, such as speed, power, or endurance\textsuperscript{[2–10]}. Molecular biology, particularly the “discovery” of DNA by Watson and Crick in 1953, revolutionized biology and medicine. The rate of genetic
discovery in molecular biology rapidly accelerated throughout the last half of the twentieth century and into the twenty-first century. The new millennium was to be the dawning of practical, effective treatments for genetic diseases, such as muscular dystrophy, X-linked hemophilia, and other single-gene disorders [5]. Further, with molecular biology advances that included insertions of new genes into organisms, cloning of organisms, and use of human stem cells, more than single-gene diseases could be treated. Any number of serious or fatal medical conditions might be altered with the introduction of genes that would produce “in vivo pharmacies” delivering biochemicals, including proteins and hormones, to injured or impaired tissue.

Gene therapy also could improve a general disadvantageous condition, such as aging-related muscle atrophy, by introducing a transgene to produce the depleted factors involved in muscle repair and regeneration [5]. Therapeutic genes could be targeted directly into cells, tissues, and organs limiting effects to a localized site, thus reducing the systemic side effects produced by a typical drug administration.

Implications of novel genetic interventions fascinated not only researchers, physicians, and gene therapists, but also coaches, athletes, and trainers looking for athletic performance enhancement of biologic parameters, such as strength, power, and oxygen delivery, to create a critical edge in sporting competition [5]. The creation of a superman or superwoman athlete could be planned by well-placed genetic physiologic tweaks.

Background: from performance-enhancing drugs to performance-enhancing genes

Drug cheats in sports long used steroid hormones, amphetamines, and blood manipulations to achieve advantages in competition (performance-enhancing drugs or PEDs [9]. Steroid hormones produced rapid gains in muscle size, strength, and recovery. Amphetamines improved alertness and concentration. Blood doping improved oxygen delivery to tissues allowing more endurance in competition; however, each of these drugs/manipulations showed significant side effects. Steroids produced atrophy of sex organs, gynecomastia, emotional rages, and other serious side effects. Amphetamines reduced appetite and—in large doses—produced paranoid or psychotic symptoms. Blood doping resulted in a hematocrit so high that the erythrocytosis caused thrombosis and embolism. These blood dyscrasias, combined with erythropoietin (EPO)-related serious cardiac effects, seemed to be particularly lethal [9].

As laboratory detection become more sophisticated in catching drug cheats, the athletes turned to novel peptides, such as human growth hormone (HGH), to gain an edge or to avoid detection by antidoping authorities. Substances like HGH were expensive and dangerous, however; HGH was
harvested from cadavers, some of whom died from contagious spongiform neurologic conditions. Other peptide hormones, including EPO, which regulates red blood cell (RBC) production, remained unavailable as drugs.

The emerging biotechnology industry changed these limitations with the implementation of recombination DNA production of peptide drugs and hormones. Manipulating genes inserted into mammalian cells, the new industry produced recombinant (r) drugs, such as rHGH, rEPO, insulin-like growth factor (r-IGF)-1, and r-insulin in great quantities. Essentially identical to human hormones, these advanced drugs produced a significant impact on the medical treatment of anemia, growth deficiency, and diabetes, for example; however, biotechnology advances did not go unnoticed by the coaches and athletes who look for every advantage in competition [5].

Soon after introduction of a new recombinant peptide or hormone, the sports doping community appropriated the drug if it offered an advantage in competition. Unscrupulous physicians and trainers used rHGH and rIGF-1 to increase strength and power among a wide variety of athletes, including Major League Baseball and National Football League players. rEPO proliferated among cycling competitors to increase oxygen delivery to muscles during lengthy and demanding races like the Tour de France.

The detection of these new recombinant DNA–produced peptide hormones in rogue athletes presented formidable challenges that continue to be problematic for antidoping laboratories [9,10]. Although the use of rHGH, rEPO, and insulin in sports like football, cycling, track, and baseball is widespread, antidoping laboratories continuously must play catch-up in developing detection procedures. Thus, the introduction of recombinant drugs into the sports doping field might be considered the first step in genetic-related doping.

With the advent of gene therapy, a more direct way to deliver proteins and hormones to an athlete’s tissues and organs became reality. The sophistication and the power of these biologic alterations piqued the ingenuity of the drug-cheating coaches and athletes. A substance that can alter the basic genetic expression of DNA—such that muscles grow larger, contract more forcefully, and recover more quickly than non-doped muscles—and cannot be detected by antidoping laboratories would be ideal to gain a competitive advantage while not running afoul of the regulatory officials.

**Genetic therapies**

In the broad sense, genetic therapies include several categories of biotechniques [7,9,10]:

1. Use of recombinant DNA techniques to produce new peptides or drugs (rEPO)
2. Pharmacogenetics, or the use of knowledge of the specific genome of an athlete to tailor pharmacologic interventions
3. Somatic cell modification, which produces genetically modified cells (e.g., modified RBCs to increase blood-carrying capacity)
4. Germ-line modification, where the gametes or early embryos undergo gene modification to express more athletically expedient traits
5. Genetic preselection, where a gene scan would inform parents about the distribution of desired genes in a potential offspring
6. Genetic selection, where individuals are selected for particular traits (widely practiced in animal husbandry)

This article’s main focus is on the modification of cells to express proteins or other biochemicals to enhance athletic performance.

Defined as “the transfer of genetic material to human cells for the treatment or prevention of a disease or disorder,” gene therapy uses genetic materials, such as DNA, RNA, or genetically altered cells [3]. In the simplest form, gene therapy introduces a “therapeutic gene” (transgene) into an organism by way of a vector, often an inactive virus. Within the organism itself, the new “transgene” synthesizes the defective/missing protein or biologic substance to correct dysfunctional tissues and organs. Other gene therapy strategies involve manipulation of genes, turning them on or off as the desired physiologic response dictates.

Initial gene therapy trials included protocols to treat an X-linked immune deficiency disease and hemophilia variant [5]. A trial of human vascular endothelial growth factor produced positive results in patients who had angina [10]. More than 1000 gene therapy trials are ongoing in various states of clinical study [2,6,7]. No gene therapy protocols have been approved for medical practice by the US Food and Drug Administration, the regulatory agency charged with overseeing the development and clinical use of the medical procedure.

Genetic enhancement

Gene doping also could use the technique of genetic enhancement/engineering. In practice in agricultural settings, genetic enhancement places advantageous genes into organisms, not to cure disease, but to confer advantages to the organism that would improve the organism’s survival or the organism’s “product”: hardiness, better insect resistance, or greater yield. Genetic enhancement exploits the same techniques as gene therapy; however, it can be applied outside of medicine [3].

Genetic performance enhancement: gene doping

Using basic principles of gene therapy (and genetic enhancement), gene doping injects genes directly into the athlete’s body by one of two methods: in vitro delivery and ex vitro delivery [5,10]. In gene therapy, the clinician introduces a gene that covers for a deficient gene or modulates the activity
of an existent gene to correct a disease state. The goals of gene doping include the injection of novel genes or the modulation of existing genes too; however, the gene doper introduces the gene products for the enhancement of physiologic parameters expedient to the athlete’s competitive tasks, rather than the treatment of a medical illness.

**In vivo gene doping**

The delivery of the new gene into the athlete can be through biologic, physical, or chemical methods. Viruses can be modified to biologically insert the artificial gene into cells in a specific organ or target tissue or into cells throughout the competitor’s body. Virus lines modified to transfer genes to mammalian cells include retroviruses, adenoviruses, and lentiviruses [10,11]. Physical methods to deliver genes into cells use microsyringes, or gene guns. Biochemical injection vehicles use plasmids or liposomes [10,11].

**Ex vivo gene doping**

The technique of exogenous gene doping involves gene transfer to cells in culture first, then implantation of the tissue into the recipient. Once implanted into the athlete’s cells, the new genes express hormones or biochemicals that again enhance tasks of the athlete in competition [11].

**Candidate genes for athletic gene doping**

Any physiologic process involved in producing a motor action or assisting in the implementation of a motor movement could be a candidate for gene doping (Table 1; Fig. 1). The physiologic processes of pulmonary respiration, cardiovascular circulation, oxygen delivery, striated muscle growth/efficiency/repair, and even neuromuscular coordination could be altered to give an athlete an edge over his or her competition. Although more esoteric, neurophysiologic processes, such as mental alertness, motivation, and central nervous system recovery, also might be amenable to gene doping. The list of physiologic processes related to athletic competition is long and likely only limited by current understanding of exercise physiology and exercise psychology [10].

Even now, in the exploratory phase of gene therapy/gene doping, there are obvious candidates for the aspiring gene cheat. These primary gene candidates exist as targets of biomedical researchers looking for legitimate disease treatments [10].

**Hematopoietic/vascular systems**

The classic example of a genetic alteration to enhance athletic performance occurred naturally in 1964. A Finnish skier, Eero Mantyranta, dominated Olympic Nordic skiing. Studies later demonstrated that Mantyranta benefited
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<td>VEGF</td>
<td>Vascular endothelium</td>
<td>Glycosylated disulfide-bonded homodimers</td>
<td>Promotes fat metabolism and increases number of slow twitch fibers</td>
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Abbreviations: ACE, angiotensin-converting enzyme; ACTN3, actinin binding protein 3; EPO, erythropoetin; HGH, human growth factor; HIF, hypoxia inducible factor; IGF-I, insulin-like growth factor; PPAR-delta, peroxisome proliferators-activated receptor (delta); VEGF, vascular endothelial growth factor.
from a natural mutation in the EPO gene that produced a greater number of RBCs, with a concomitant increased oxygen-carrying capacity [3,5]. This skier possessed what every blood doper in history tried to achieve—a physiologic advantage in delivering more oxygen to various tissues, including muscles.

rEPO (epoetin and darbopoetin) is a much-abused injected recombinant protein that increases RBC production, leading to increased oxygen-carrying capacity and oxygen delivery to tissues. The abuse of rEPO is epidemic in cycling, leading to frequent controversy, tedious forensic investigations, and serious side effects, including death [9].

Using gene doping, an additional EPO gene could be delivered to the athlete by way of a viral vector. Once in the athlete, the gene would express much more EPO than normally produced, even with training. The desired result would be an increase in the oxygen-carrying capacity of the blood, thus bestowing a clear competitive advantage in endurance sports.
Laboratory experiments have been successful in injecting the gene into monkeys and mice. Although the procedures successfully raised hematocrit, severe side effects, including a paradoxical anemia, resulted [12–15].

**Hypoxia inducible factors**

The hypoxia inducible factor (HIF) family of proteins modulates the activity of genes in low-oxygen environments. Various HIFs increase production of RBC, as well as increase cellular energy use. Enhancement of these proteins clearly would benefit the aerobic athlete [16–18].

**Vascular endothelial growth factor**

Clinical studies are currently ongoing for vascular endothelial growth factor (VEGF), a gene product that encourages development of new blood vessels [3]. This genetic manipulation would be advantageous to patients suffering from coronary artery disease. The gene-doping athlete would benefit from a putative increase in vasculature and more delivery of oxygen and nutrients to the peripheral tissues.

**Skeletal muscle system**

**Actin-binding peptides**

The proteins actin and myosin form the machinery of muscle contraction. The family of actin-binding proteins in humans includes α-actinin alleles ACTN2 and ACTN3. Alpha-actinins maintain the structure of the myofibrillar array and regulate myofiber contraction. A defect of ACTN3 regulation occurs when the ACTN3 gene codes for a premature stop codon; ACTN2 seems to compensate in these persons. Correlation studies found evidence that the ACTN2 endows muscular endurance traits upon athletes. Conversely, elite sprinters benefit from more copies of ACTN3. Depending on the event of the competitor, gene doping with the appropriate ACTN allele could enhance endurance capacity or sprint effectiveness [18].

**Angiotensin-converting enzyme**

Physicians are well aware of angiotensin-converting enzyme (ACE) inhibitors used for the treatment of hypertension; however, the ACE gene, like the ACTN gene, codes for proteins that seem to endow different exercise capacities. Research suggests that the ACE-I allele endows advantages in endurance, which would be useful for distance runners. The ACE-D allele seems to be associated with elite sprinting performance [18–20]. Again, a gene-doping athlete could inject the appropriate gene to influence better performance in his or her event, be it a sport featuring short bursts of speed and power or a sport in which endurance is the key to success.
Insulin-like growth factor

Several sophisticated studies, most notably at the University of Pennsylvania [5,21], targeted IGF-1, a peptide, in conjunction with HGH, intimately involved with muscle growth, repair, and power. These studies demonstrated eloquent ways in which IGF-1 controlled mammalian muscle development and demonstrated that targeted gene therapy could successfully produce hypertrophied and powerful muscles in laboratory mice. The primary investigator, Lee Sweeney, designed the procedure carefully so that the virus and the gene were not expressed systemically; by avoiding systemic distribution of the peptide, the researchers hoped to avoid the serious side effects of IGF-1, including myocardial hypertrophy and carcinogenesis. Thus, for therapeutic reasons, the researchers designed the gene therapy to be effective locally, in injected muscles. That particular feature also would benefit a doping athlete, because the transgene IGF-1 would not enter the systemic circulation where it might be detected by laboratory testing. In this University of Pennsylvania protocol, “fingerprints” of the gene therapy did occur; however, the theoretic aim of the study itself would present problems for antidoping agencies.

Myostatin

Myostatin, known to be a negative regulator of muscle development, presents another candidate gene. This regulator protein seems to turn-off muscle growth. Substances that block myostatin or genes that produce ineffective myostatin proteins would allow superphysiologic muscle growth in terms of number and thickness of cells (as seen in certain breeds of cattle through a natural mutation) [22,23]. Not only do striated muscles hypertrophy without myostatin regulation, but less fat is gained on the body of the animal. The manipulation of this regulatory protein has obvious advantages for the athlete.

Peroxisome proliferator-activated receptor delta

The peroxisome proliferator-activated receptor delta (PPAR-delta) gene seems to be a prime candidate for gene doping [24–26]. This gene codes for an increase in mitochondrial biogenesis and promotes an adapted muscle fiber transformation. The gene promotes an increase in type 1 muscle fibers (slow twitch). Elite athletes show an increase in PPAR-delta gene levels. A PPAR-delta gene was inserted into mice; it dramatically improved the animal’s endurance capacity. It was concluded that “…these genetically generated fibers confer resistance to obesity with improved metabolic profiles, even in the absence of exercise. These results demonstrate that complex physiologic properties such as fatigue, endurance, and running capacity can be molecularly analyzed and manipulated.”
Central and peripheral nervous system

**Endorphins**

In injuries, as well as in competition, pain limits athletic achievement. Athletes sustain countless painful injuries for which they consume an abundance of anti-inflammatory drugs and pain-relieving medicines. Likewise, the buildup of lactic acid during competition induces pain. Clearly, increasing the pain threshold—and alleviating the discomfort of nagging injuries—would improve performance.

The introduction of genes producing analgesic endorphins and enkephalins would increase the pain threshold in an athlete, for pain experienced in competition as a result of lactic acid buildup and pain due to acute and chronic injury. Clinical trials are testing the efficacy of genes encoding these natural narcotic peptides for pain relief in humans [3].

**Other potential candidate genes**

Interleukin-15 may prove to be an anabolic protein amenable to gene doping [27]. Interleukin-1RA gene injection trials reported good results; this gene could be used therapeutically for osteoarthritis and to promote joint superlubrication [28]. Mechano-growth factor may aid in the repair of damaged skeletal muscle tissue [9].

**Risks and complications of gene doping**

Examining the history of clinical pharmacology reveals that side effects of novel treatments can be unexpected and occasionally fatal. From thalidomide to valdecoxib, newly introduced medications, even with exhaustive preclinical trials, produce unanticipated untoward side effects. Consider the potential side effects of introducing a foreign gene, by way of a viral vector, into an organism’s chromosomes. Gene therapy trials made headlines several times with unexpected and fatal side effects. Then 18, Jesse Gelsinger died in 1999 as the victim of an immune response to the virus used in a well-publicized gene therapy trial [4]. That death shocked the biomedical world and resulted in regulation as well as multiple legal actions. Several patients who were treated for an X-linked hemophilia with a gene therapy protocol developed leukemia, an obviously unexpected side effect [4].

A gene therapy trial of EPO in macaque monkeys produced such stimulation of RBC production that the monkeys’ blood thrombosed [13]. Moreover, many of the monkeys suffered anemia, the result of an immune response to the gene therapy. The overactive immune response attacked endogenous EPO as well as gene-stimulated EPO [14]. A similar experiment using gene-therapy EPO revealed that the gene-induced EPO was slightly different from natural monkey EPO [15]. Likewise, the use of transgene
EPO in human gene doping might induce erythrocytosis to a dangerous level, with potentially lethal consequences.

Although not generally considered a risk from gene therapy, the virus vector could infect other humans. Clinical trials monitor subjects for viral shedding [3]. It would be unlikely that gene cheats would monitor their secretions for viral contamination. Furthermore, rogue gene-doping laboratories (like their steroid-synthesizing counterparts) would not implement proper preclinical trials. Thus, there may be a possibility of a modified infectious virus passing from a gene cheat to other persons.

If the experience with anabolic steroids is any indicator, athletes generally ignore common dosing recommendations. When a Maryland physician introduced the anabolic steroid methandrostenolone (D-bol) to power lifters in the 1960s, it was not long before the athletes increased the dose and the duration of drug beyond medical recommendations. Contemporary anabolic drug users stack multiple anabolic steroids mixed with other anabolic drugs in megadoses that lead to serious side effects and even death. A prominent and successful athlete like Barry Bonds, in a quest to become a more powerful hitter, allegedly used multiple anabolic substances including anabolic steroids, HGH, modafinil, insulin, clomiphene, and EPO [29]. Given this phenomenon with drug doping, expect the use of multiple gene-doping protocols by the athlete looking for every edge in competition. Genes for strength, power, recovery, analgesia, oxygen delivery, concentration, injury, and repair could be transferred to the same athlete. As with anabolic steroids and other PEDs, there will be unpredictable side effects and fatal interactions.

Laboratory detection of gene doping

Frequent battles occur between drug cheats, antidoping agencies, and the lawyers representing all sides. The drug cheats eternally search for an undetectable PED; thus, the antidoping laboratories play “catch-up” forensic detective in developing sensitive tests for any new PEDs. Elite sport has entered the world of forensics, where winners and losers of competitive events can be declared in the courtroom, not the playing field. Further, legal proceedings take months. Because of forensic procedures, the 2006 Tour de France will not declare a winner until months after the finish of the race. Are regulatory agency antidoping laboratories developing methods to detect possible gene-doping use, and will these methods stand up in court?

The WADA initiated research to prepare for the world of gene doping [2,4]. Research scientists suggest several biologic/laboratory tests that could operate to expose gene-doping cheats [2–4,9,10]. The usual parameters of laboratory tests—sensitivity, specificity, validity, and reliability—would need documentation to allow such innovative tests to withstand the certain legal scrutiny when elite athletes test positive for gene cheating.
Muscle biopsy

A biopsy of suspected muscle tissue could reveal viral vehicles or evidence of altered genes; however, that possibility presents a invasive and low-yield antidoping measure [2,4].

Blood monitoring

Proteins and hormones produced by doped genes could be exactly like endogenous proteins. Thus, it may be extremely difficult to detect the difference between the endogenous gene product and the doped-gene product; however, serial monitoring of blood parameters may reveal suspicious elevations of key biologic substances that indicate gene doping [2]. For instance, the dramatic increase in hematocrit, in conjunction with several other hematological parameters, could tip off a regulatory agency that an athlete used a gene-doping technique to improve oxygen delivery to muscles.

Genetic activity tests

Interesting developments could use patterns of gene activity or gene products to detect abnormal gene activity [2]. Detection of these patterns uses cutting-edge microchip gene array technology or nanotechnology breakthroughs. The monitoring or visualization of gene activity or gene products through the expression of DNA and RNA by a sophisticated microchip array could monitor thousands of genes, enabling the laboratory to use a sophisticated detective tool for gene doping [9].

Protein fingerprints

In this process, similar to gene microarray testing, hundreds of biologic proteins could produce a “protein fingerprint” or a “genetic map” of the biochemistry of individual athletes [10]. Suspicious alterations of such an individualized fingerprint or map would alert sporting authorities to possible gene doping.

Genetic barcodes

It may be possible to label the transgene products with a genetic “bar code”; however, this tactic would require the cooperation of a broad array of professionals from the research scientists to the pharmaceutical houses to the administering physicians [4].

Regulation of gene doping

WADA is the preeminent doping regulatory agency in the world, concerning itself with the ethical application of medical techniques, therapies,
and treatments in the realm of competitive sport. WADA develops the “code” and the “prohibited list” of banned substances for Olympic sport athletes [1–3,6,8].

The ethical criteria for a drug or medical technique to be included on the WADA prohibited list are “scientific evidence, proven pharmacological effect or experience that substances or methods included have the potential to enhance or enhances sport performance” [1–3,6,8]. Two arguments are used for inclusion on the list: the substance or method may be harmful or cause a health risk to the athlete and the use of doping violates the spirit of sport, as defined by WADA criteria. Essentially, the substance or technique is outside “fair play,” which could be construed as “cheating.”

The WADA tenets have been criticized as ambiguous [3]. Clearly, any medical intervention can be a health risk; athletic competition itself is a health risk. The key factor in determining the ethical use of a drug in athletic competitions rests on the point of fair play. When is a drug not given or taken for a therapeutic purpose, but for a purpose of obtaining an unfair competitive advantage? That ethical battle continues every day in many sporting venues. With the advent of gene therapy, the focus of the debate will turn from drugs to transgene products; however, the key element of therapeutic versus manipulative will remain unchanged.

Relevance of gene doping to the practicing pediatrician

Adolescent athletes use anabolic drugs. Studies estimate that approximately 2% to 4% of adolescents have used some sort of anabolic drug [30] by the time they graduate from high school. The entire story is not told, however, because most survey studies focus on anabolic steroids. Many teenage athletes possess sophisticated knowledge about anabolic drugs, such that use of HGH, insulin, and even EPO could appear in this age group. Sources of information about anabolic substances include the daily reports of the athletes suspected or caught using PEDs, peers at the local gym, and, occasionally, unethical coaches or trainers. Physicians must be alert for the use of PEDs in the at-risk age group and alert for side effects, including endocrine, behavioral, hematologic, and cardiovascular complications, of PED use [31].

If gene doping becomes reality among elite athletes, it is almost certain that adolescent athletes will be exposed to the technique. Either through their own volition or through peers, unscrupulous coaches, and overzealous parents, adolescents will try to gain a competitive advantage for the glory of athletic achievement and the scholarships that follow. Although the use of anabolic drugs and techniques increases once the athlete engages in college or professional sports, teenagers will use performance enhancing genetics (PEGs) when such techniques arrive in the gym. Thus, if the technique proves successful in elite athletes, gene doping will appear in the teenage population; pediatricians should prepare themselves for new syndromes.
and unusual side effects. A physician should understand the possible target organs and putative doping genes.

Although most clinical research and clinical reports concern athletes looking for a competitive advantage, nonathletes use anabolic substances for an enhancement of physical appearance. Exhibiting muscle dysmorphia or the Adonis Complex [32,33], these youth mimic the good looks and enhanced bodies of actors and models. A thriving black market delivers anabolic drugs to this group of adolescents for narcissistic purposes. If available, and if successful, expect teenagers to use gene-doping techniques for cosmetic purposes.

Perhaps the most sinister example of gene doping, in the broad sense, would be germ cell modification and genetic preselection [34]. In germ cell modification, a gamete or embryo would have DNA modified to enhance the expression of athletic advantageous genes. This technique, as futuristic as it sounds, would alter the entire genomic makeup of the developing human to produce a superior athlete.

In genetic preselection, the genome would be scanned, allowing parents to choose the most genetically athletically gifted offspring to survive. This process is a sophisticated twenty-first century variant of the ancient Spartan child-selection process. Although no reports exist of parents scanning the genome of their prospective children, there are reports of a sporting organization using a limited genome scan to select prospective athletes or to genetically tailor training [35].

Summary

Examination of the history of sports competition reveals unethical athletes who use medical advances, mostly pharmaceutics, to gain an edge in competition. The elucidation of the genetic basis of biology leaves medical science on the precipice of clinically useful gene therapy; however, it is expected that unscrupulous athletes and their mentors will divert the new techniques to gain an edge over competitors. Much remains to be determined in this area; however, a multitude of candidate genes exists [36]. The biologic techniques to introduce these genes into athletes are developing rapidly; it seems to be only a matter of time before the genetically enhanced performance athlete takes the field of competition. Sporting regulatory agencies initiate and maintain programs to monitor and test for gene doping. Physicians will be part of the professional net involved with these futuristic gene-enhanced athletes.

Although gene doping sounds like a science fiction plot, the physician should not underestimate the capacity of humans to find an edge in competition—legal or illegal. As athletes, professionals, parents, and coaches, the authors have experienced numerous examples of cheating in sports. From the simple falsification of player records to the importation of foreign athletes to the use of anabolic steroids and PEDs, athletes, coaches, boosters, parents,
and physicians will bend the rules of fair play. The greater the stakes, the higher the rewards; the temptation to cheat becomes more alluring. If gene therapy becomes reality in humans—and the technique is poised to become clinically useful—those participants who hold no moral compunctions against cheating fellow competitors will use the technique. Indeed, officials expressed great concern that an unscrupulous coach was experimenting with gene doping at the 2004 Turin Olympics [37]. At some point in time, performance-enhancing genetics will be a reality; as professionals, be forewarned and be prepared.

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