

DOPING: THE SEAMY SIDE OF SPORT

Steve Elliott

Nothing damages and breaks the spirit of sport more than doping. "Doping to enhance performance is not only unfair, it is also unsafe," writes a scientific executive director of Amgen, a biotech company. He adds: "We must protest against those who would demean the sports they participate in, and educate the athletes, coaches and fans about the dangers of doping." He concludes that we must also encourage policy-makers to support initiatives that make doping illegal and create ramifications serious enough to discourage it.

Rien n'est plus nuisible au sport que le dopage, rien ne ternit autant l'esprit sportif. « L'usage de substances améliorant la performance est non seulement injuste mais dangereux », écrit le conseiller scientifique en chef d'Amgen Canada. « Nous devons nous prémunir contre ceux qui dégradent les sports auxquels ils participent, ajoute-t-il, tout en sensibilisant athlètes, entraîneurs et partisans aux dangers du dopage. » Mais il nous faut aussi exhorter les décideurs à appuyer les mesures qui rendent le dopage illégal et imposer des sanctions suffisamment sévères pour dissuader les tricheurs.



In February, an epic event will consume Canadians and, for that matter, the world, as the 2010 Winter Olympic Games begin in Vancouver. We will revel in the competition, and emotionally commit ourselves to the stories of sacrifice and the drama of the competition. There will be excitement as those dedicated athletes surprise us with the performances of a lifetime. We will root for our favourites and sympathize with those who worked hard but did not win. Many of us will go to the Winter Games in Vancouver to watch our favourite event live, watch on TV or follow the events on the Internet. We will share stories with our friends, families and everyone else who will listen.

However, we must also be prepared for a more sinister side of sport. There will be a few who will choose to cheat by doping in order to increase their likelihood of winning. Unfortunately this is not a new problem; there are too many tragic examples from recent history that highlight the disappointment and pain felt by proud nations and fans dealing with the ugly reality of doping in sport.

I recall all too well three stories.

Remember the 1988 battle between Carl Lewis and Ben Johnson: Johnson had established himself as Canada's top sprinter, set a world record in the 100 metre final (9.79 seconds) and received an Olympic gold medal in Seoul? There was rejoicing and newspapers recounted the event in detail. Then the world found out that Johnson had tested positive for stanozolol, a steroid. His medal and world record were rescinded and he was banned from the sport for two years.

Initially he protested, denied doping and was allowed to compete again, but during a Canadian government investigation into drug abuse, Johnson admitted that he had lied. We found out that Johnson had been using steroids since 1981.

We also remember Geneviève Jeanson, a top female cyclist from Quebec. In 2005 she won first place in the Montreal world cup but, also in 2005, she tested positive for recombinant erythropoietin in an out-of-competition anti-doping test. She initially denied using banned substances, but in 2006 she announced she was retiring from cycling, and in 2007 admitted to having doped since the age of 15. Particularly troubling in this case was her insistence that her use was encouraged by her coach.

And then there was US athlete Marion Jones, an elite Olympic athlete who grew up in Thousand Oaks, California, a few kilometres away from where EPOGEN (epoetin alfa) was discovered and manufactured by my company, Amgen. Jones had made the American public proud by winning gold at the Olympics. She was subjected to extensive testing, but claimed to be clean. Then, in 2007, in a tearful press conference, she admitted to doping with recombinant erythropoietin. She announced to the American people: "I stand before you and tell you that I have betrayed your trust...and you have the right to be angry with me."

We can also draw some lessons from the unfortunate doping events that took place in East Germany between the 1960s and the 1980s, before the reunification with West

Germany. It is now acknowledged that young men and women were given anabolic steroids and other banned substances to enhance their performances, sometimes without their knowledge. We can debate about which and how many athletes and coaches were involved and which sporting events were impacted. What are not subject to debate are the major mood distur-

ances; the masculinity of some female athletes; the risk of kidney and liver damage, the effects on tendons, ligaments and muscles resulting in crippling injuries, sometimes lifelong; and the deaths. It is of relevance that even though the allegations are now acknowledged to be true, no East German swimmer was ever caught or penalized for drug use. The achievements of those East Germans who participated and won, particularly in Montreal in 1976, are now looked at suspiciously, undermining the achievements of those who in fact competed cleanly. We also cannot forget the achievements of those who competed against the East Germans who should have won but did not.

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The doping problem is not limited to the Olympic Games. The ski federation, the cycling union and professional sports (baseball, football, hockey and soccer) have all been tainted by doping allegations. In professional cycling, in particular, businesses have withdrawn their sponsorships because of the possible association of certain teams with doping.

Doping is the presence of a prohibited substance in any amount in the athlete's urine or blood, substances that are used to improve athletic performance. The primary reason for having a list of prohibited substances and methods is to protect athletes' health. For

this reason their use is banned in most organized events, particularly those regulated by the various sporting bodies. Agents used for doping include a wide and growing list of substances. There are steroids to increase muscle mass, of particular relevance in events requiring strength such as weight lifting; stimulants used in speed events; and beta blockers in shooting events,

which may improve aim. Banned substances also include agents whose sole purpose is to evade detection of other banned substances. These include diuretics (to increase elimination from the body) and plasma expanders (to reduce the concentration of the banned substance in blood).

One medicine that has been abused, banned and is of particular interest to this writer is recombinant erythropoietin, commonly referred to as erythropoietin (EPO). It is a hormone that is naturally produced by the kidney and its primary function in the body is to stimulate formation of hemoglobin (Hb) containing red blood cells. Hb in red blood cells carries oxygen to oxygen-dependant tissues such as working muscles. The reason for doping with EPO was evident. There was a direct relationship between Hb levels and increased performance due to the increased capacity to transport and utilize oxygen. This enhancement can translate into a change in time trial performance and endurance in long distance events, even though unfortunately many athletes fail to realize the risk that accompanies the boost.

Recombinant human EPO (rHuEpo) was developed by Amgen in the 1980s to treat anemia (low Hb concentrations). Anemia occurs in patients with kidney disease, and in cancer

patients due to the chemotherapy used to slow or halt growth of their tumors. For some anemic patients, the benefit of the medicine can be life-changing. These patients, who have difficulty getting out of bed, going up or down stairs and even travelling to the doctor for treatment, due to shortness of breath, often can return to work and have normalized lifestyles.

Some have argued that doping is little different from the use of new equipment or training methods. Others suggest that rather than consume ourselves with catching dopers, we should change the rules and let the athletes with the best doctors and drugs win. After all, if everyone could use drugs legally, we would level the playing field, and the best or most committed athletes would win. However, the problems with doping are manifold, and we should not give in to those who wish to excuse the cheating.

Medicines and the scientists who discover them are offended by doping, because doping is not the intended and appropriate use of the medicines. Fu Kuen Lin was an Amgen scientist who typified the dedicated and motivated individuals who worked late nights and weekends in order to make a difference for patients. He was the first to isolate the gene for erythropoietin in the 1980s and, subsequently, to produce human erythropoietin in a form and quantity that made its therapeutic use possible. The discovery led to the development of epoetin alfa, which in 1989 would reach anemic kidney dialysis patients whose treatment options for anemia were limited. Epoetin alfa, sold under the brand name EPOGEN, was Amgen's first marketed product — and one of the biotechnology industry's first blockbuster medicines. Amgen employees are proud and excited about the profound changes that this medicine has had and continues to have on millions of patients.

I was particularly saddened when it became apparent that doping with dar-

beпоetin alfa, whose discovery I was involved in, was occurring. Darbeпоetin alfa is Amgen's second marketed ESA (erythropoietic stimulating agent), marketed under the brand name Aranesp; it has a longer serum half-life (meaning it takes longer for the body to eliminate it) and thus can be administered less frequently. This is an important feature for many patients, as it is an injectable drug. It was first approved for use in 2002 in treating anemia but was rumored to be the drug of choice for doping in endurance sports prior to the 2002 Olympic Winter games in Salt Lake City.

When I first heard that healthy athletes were using this medicine inappropriately (to dope with), my first reaction was, "How dare someone abuse a medicine whose purpose is to treat people with serious illness!" Years of work and hundreds of millions of dollars were involved in its discovery and development, including clinical trials and the construction of manufacturing facilities. This involved close coordination between dedicated scientists, physicians and regulatory agencies to develop and optimize a description of how best to treat patients and maximize the risk-benefit profile. Such inappropriate use by doping ignores the findings and recommendations of the above groups, solely to improve athletic performance. In addition, doping with ESAs is illegal in many countries, and it is absolutely not an approved indication by any regulatory agency.

My next reaction to the abuse of the ESA product I had helped bring to market was that something must be done to prevent the inappropriate use of this medicine — for the sake of the spirit of sport and for the safety of the athletes. Five months before the 2002 Winter Olympics opened in Salt Lake City, darbepoetin became available on the market. I attended a meeting with the World Anti-Doping Agency (WADA) and the testing labs in

November 2001 in Lausanne, Switzerland, to discuss epoetin and darbepoetin testing procedures and strategies. Endurance athletes knew they would be tested at the 2002 Olympics, but because darbepoetin was so new, most figured that the lab scientists would not know how to detect it. However, due to close consultation with the lab, a test was put in place before the Salt Lake City Games. When darbepoetin test results were positive in three cross-country skiers, Amgen supported WADA with expert testimony. The athletes were stripped of gold medals and suspended from competing for two years. The inevitable courtroom appeals were heard and all three appeals were denied. More importantly, allegations of doping with darbepoetin alfa declined dramatically. The story made headlines around the globe, and is recounted in a children's book, *The Night Olympic Team*, written by Caroline Hatton, an Olympic Lab scientist.

Amgen has long approached the doping issue with efforts to speak out against abuse of the therapies it makes, and in doing so wishes to deliver a potentially lifesaving message to athletes and to the public at large. One recent strategy was to use its sponsorship of a professional cycling race as a platform to launch an antidoping educational campaign that targeted the athletes that participated in and the

should be used appropriately — certainly not for doping.

The problems with doping go beyond the inappropriate use of medicines issue. The athletes caught with banned substances in their bodies may be punished by having their medals taken away and being banned from the sport they trained a lifetime for. Additionally, the athlete caught doping loses the trust of the fans. Furthermore, we all lose when doping allegations occur. We begin to wonder if our favourite athlete who does well in a sport that had cheaters is really exceptional, or did he/she cheat too? Was the new Olympic record due to the exceptional performance of the athlete or to the drugs taken? Athletes who through exceptional effort achieved an earlier milestone are also cheated, along with their supporters, when their records are beaten.

Some athletes may believe that the only way to compete is to dope also, creating a vicious cycle. The cross-country skier who is struggling to keep up with the cheater 200 metres ahead may sacrifice him/herself to try to keep up and end up tenth, instead of with a second- or third-place medal. Will they later risk their health by doping because they believe it is the only way to succeed? Unfortunately, they may be encouraged to do so by coaches who believe it to be true.

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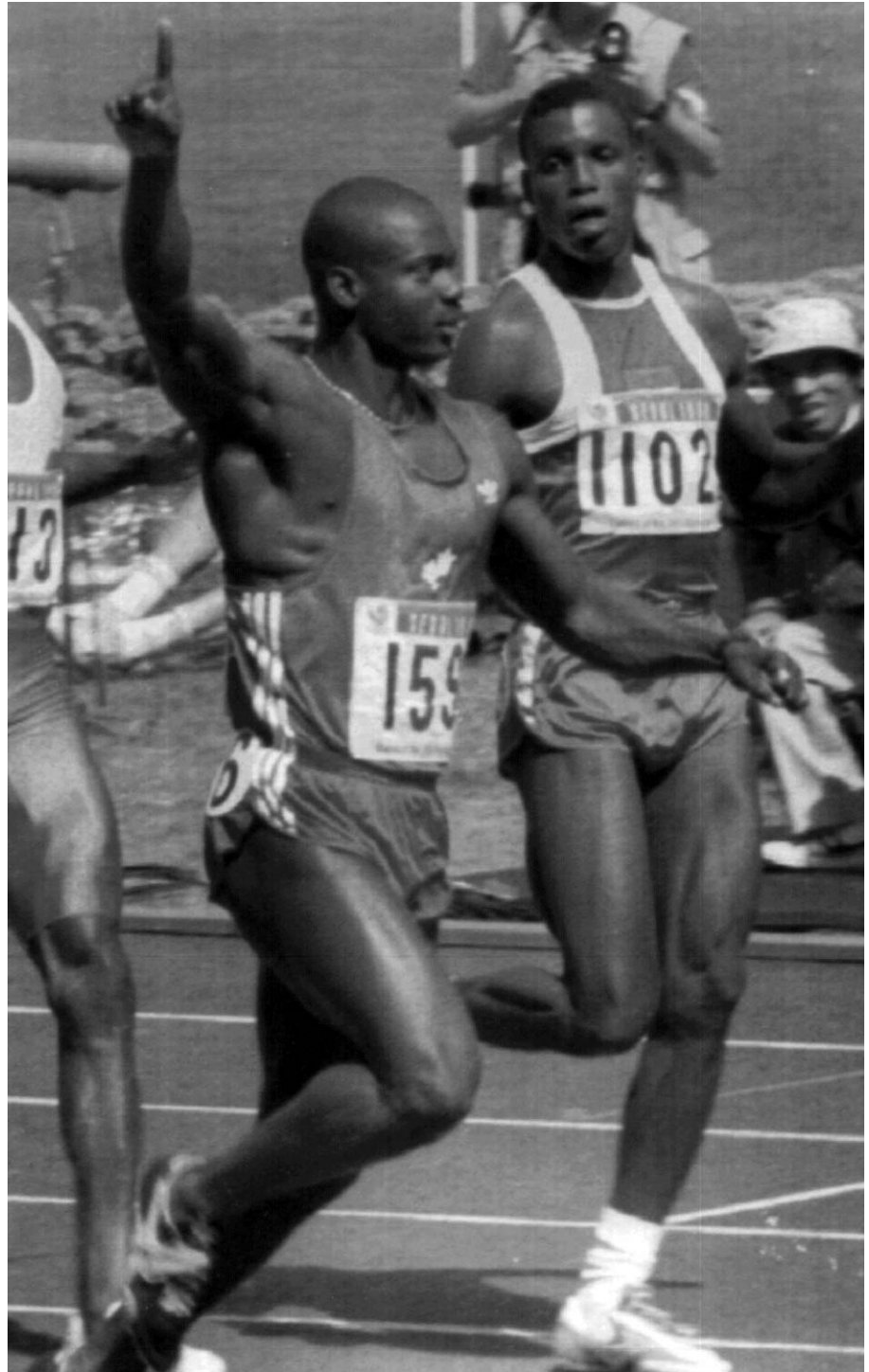
fans that enjoyed cycling. The campaign included public service announcements, speaking engagements, and brochures containing antidoping messages that were distributed to athletes and spectators. Doping was contrasted with the intended medical use, so that participants and fans would understand the importance of breakthrough medicines and how they

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The use of banned substances such as ESAs by athletes trying to enhance their performances, or "EPO doping," is not only unethical and unsportsmanlike, it is potentially very

unsafe. Patients who are anemic use ESAs to raise their Hb levels, to a higher, but still subnormal level and the dose and dosing regimen and final Hb level is based on results from extensive clinical testing. The risk-benefit ratio of ESA treatment is carefully considered, in consultation with regulatory agencies and health care practitioners. In contrast, the athlete who abuses medicines considers primarily the benefit to performance and ignores or discounts the potential short- and long-term liabilities. They are also using the drug in a dangerous and unapproved manner. Such athletes, who initially have normal Hb levels, attempt to increase them to abnormally high amounts with ESAs. The objective is to increase their performance through an increase in their capacity to transport and utilize oxygen. However, the resulting higher-than-normal red blood cell concentration, combined with the dehydration associated with intense exercise, can increase blood viscosity, which may reveal undetected cardiovascular risks, including high blood pressure, seizures and sudden heart failure. It can even be fatal. The risks increase when the treatment is not administered under the care of a qualified health care practitioner. Specific examples of adverse events in athletes who chose to administer ESAs are mostly anecdotal but disturbing nevertheless, such as the rumors of fatal strokes suffered by Dutch cyclists who reportedly used Epoetin alfa following its approval for patients in 1989.

Some sporting organizations are already fighting back. Many athletes are subjected to continuous and unannounced out-of-competition testing. Sudden or unusual changes in the parameters associated with drug use are grounds for dismissal from teams or sporting events. Certain professional cycling teams, for example, have a zero-tolerance attitude toward doping and have implemented their own testing programs. Those team members who show suspicious test results are dis-



CP Photo

Canada's Ben Johnson nips America's Carl Lewis at the wire for the gold medal in the 100-metre dash, in a world record time of 9.79 seconds, at the 1988 Olympics. Except that Johnson later tested positive for performance-enhancing drugs, was famously disqualified, forfeited his medal and was banned from competition.

charged. The teams who have implemented these policies are competitive, and it is satisfying to watch them. These efforts should be applauded.

What else is being done and what more do we need to do? I believe that, fortunately, most athletes are clean. In addition, drug testing has increased

significantly in recent years and some athletes have been caught and sanctioned. However, this is not enough. The athletes who are caught show remorse — sometimes. It is not uncommon to hear of vigorous denials, and a mounted defence, both in the press and in the courtroom. “I have been falsely accused” and “I have never tested positive in an anti-doping test” are common refrains. Unfortunately the fans still watch the performance of athletes who have been accused of on caught doping, not being

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sure of the truth or perhaps accepting it as something we must live with.

Perhaps the approach we have taken at Amgen can be considered by others. Amgen has a strong position and has made it clear that it absolutely opposes the illicit use of erythropoiesis stimulating agents (ESAs) and other medicines in doping, and it has supported antidoping efforts and education campaigns. Our company has supplied funds to pay for additional out-of-competition testing and to research labs to develop new and better tests; it has also supplied medicines free of charge to testing labs wishing to develop new and improved testing procedures. Plus, Amgen works behind the scenes with the authorities who oversee testing and sanctioning of athletes who dope with its medicines.

To be successful, we all need to work together — anti-doping authorities, policy-makers, athletes, coaches, sports organizations, sports fans and industry scientists — to stop the dangerous and unethical use of medicines by athletes. Governments and the governing bodies of the various sports need to take the lead in resolving the very serious issue of athletes and doping, and we hope the owners, promoters and other sponsors of teams and events will join in this effort.

I believe that if we do the following we can win the battle:

- Biotech and pharmaceutical companies must collaborate with authorities — as Amgen and other companies have done — to help ensure our important medicines are not used inappropriately.
- Athletes, coaches and sports organizations need to be educated so that they realize the dangers of doping and the damage it does to the spirit of sport. This is especial-

ly true for our young and future Olympic champions, who need to know the dangers to their health and to be taught early that they can compete cleanly.

- Anti-doping authorities should intensify development of tests and testing procedures, including out-of-competition testing strategies, and there must be funds to pay for it.
- Sports fans must protest vigorously against doping. It is not enough to sit quietly in the living room and protest by throwing shoes at the TV, or stop watching.
- Policy-makers need to make doping illegal, or otherwise discourage it with tough anti-doping laws.

The battle is already being fought by many, but with the upcoming Olympic Games in Vancouver it is naïve to expect that all the events will be squeaky clean. Some 2010 Olympians will be tempted to dope with banned substances, including ESAs. However, anti-doping authorities are determined to win the fight with ever-improving tests, in combination with freezing and storing samples for future testing.

Those who decide to ignore the rules and cheat are at increasing risk of being stripped of their medals in the days, weeks or years ahead. Athletes

need to be aware that the anti-doping authorities, supported by the bio-chem and pharma industries, work full time, year round to develop new tests and means of catching doping athletes, and they will be working around the clock in Vancouver with the intent of catching athletes who make the mistake of doping during the 2010 Winter Games. But until we clean up sports, I will still continue to wonder if the sporting events I enjoy are clean. And until I stop wondering, I for one will continue to try to do something about it.

We must continue to support our favourite sports, teams and athletes, even if there are allegations of doping. We should not discourage young athletes from abandoning their dreams because we worry that the only way they can win is to cheat. Let's cheer them on, let them enjoy their youth, find out how good they can be and be proud of their athletic achievements — without cheating. I hope that others with a dream of becoming the best they can be are one day able to do so without the threat of having to compete with those who cheat. Personally, I long ago gave up my dream of being a professional basketball, cyclist or baseball player — I am not big enough or fast enough and I have bad knees. I now consider myself a sports fan. However, I continue to cycle, golf when I can, and I still try to stay fit and be the best I can be. I will take medicines to treat my pains or illnesses but never to dope. I will watch and cheer for my favourite athletes and teams and I will watch the Olympic events. I thank Canadians for hosting the Vancouver 2010 Winter Olympic Games and look forward to an event that celebrates the spirit of sport for Olympic fans around the world. Let the Games begin!

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