Reflections on the ethics of genetic enhancement

Thomas H. Murray, PhD

The technologies made available by new research in genetics and genomics have been and will be used not only to diagnose and treat disease, but also to attempt to enhance human traits and capacities. A broad definition of genetic-enhancement technologies, not merely gene manipulation, but also indirect genetic technologies, such as biosynthetic drugs, is needed to capture the full range of possible applications. It is difficult, but often possible, to anticipate the enhancement temptations of new therapies. Such anticipation may help us in shaping the marketing, availability, or other aspects of those technologies. Appropriate public and professional policies are needed, and work on them should begin immediately. Most important, we must stimulate public education and dialogue to encourage personal ethical reflection on the appropriate uses and limits of genetic-enhancement technologies. ***Genet Med*** **2002:4(6, Supplement):27S–32S.**

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The ethics of genetic enhancement is largely, but not entirely, a hypothetical issue. So let me begin with two true stories and one hypothetical case. The first true story: Several years ago, I was lecturing at a major American medical university about human growth hormone (hGH) and the issues involving its use for enhancement, rather than for therapeutic, purposes. hGH, of course, is normally produced in the human body. It results in, among other things, growth of the long bones and therefore is a major determinant of the height that a child reaches as an adult. Some children do not make normal growth hormone; others have other failures in the metabolic cycle. In either event, children can end up being very short. During the lecture, as I spoke about the ethics of using growth hormone for normal children—that is, children who make physiologically active growth hormone within the normal range— one of the members of the seminar spoke up. A pediatric endocrinologist, he ran the growth hormone clinic for that institution. He told me about two recent cases. One involved a young woman, 5 feet 9 inches tall—already tall for a young female adolescent. She played volleyball. Her coach told her parents that if she could grow 4 more inches, she could get a scholarship to any university in the United States that had a women's volleyball program. So her parents came to this clinic and asked the physician if he could give her 4 more inches. The second case involved a young man, also 5 feet 9 inches tall. In the United States, typically at about age 2, the pediatrician measures the child's height, doubles it, and predicts that as the adult height. These parents came in and said, "When our son was 2, his doctor said that he would be 6 feet 1 inch. He is only 5 feet 9 inches. We owe him 4 inches. Would you please give him growth hormone?" I asked the physician what he did. In both cases, he refused because there was no medical indication for administration of growth hormone to either of these children.

The second story has to do with human reproductive cloning. After the birth of Dolly the cloned sheep was publicly announced, there was much discussion in the United States about the prospect of human cloning. The National Bioethics Advisory Commission, a Presidential Commission of which I was then a member, was asked by the president at the time, Bill Clinton, to provide advice about the nation's response to the possibility of human reproductive cloning.[1] Meanwhile, I was asked to appear on our National Public Radio network, on a show called "Talk of the Nation," where the host first interviews the guests and then takes telephone calls from listeners. The very first telephone call came from a man who said that the idea of human cloning is terrific and that he wanted to have himself cloned and then raise his clone without making the mistakes that his parents made. I expressed my reservations. This child would live in the shadow of expectations that he would be perfect, would do everything the parent wished that he had been able to do, and would be the sort of person the parent wished he could be, but was not. This could be a horrible way to grow up.

These are two examples of human enhancement. The first, using hGH to increase height, would employ physiological manipulations to obtain social and economic advantages. The second, cloning oneself to have another opportunity to "get it right" in terms of child-rearing, would attempt to use biological replication in concert with what its proponent must believe are predictable and readily controllable child-rearing practices that would yield an improved or enhanced final "product."

Now, the hypothetical situation: In this situation, six things happen. First, an embryo is created with in vitro fertilization. Second, the embryo is allowed to divide a few times. A single cell is plucked from the embryo and subjected to what is called

From The Hastings Center, Garrison, New York.

Thomas H. Murray, PhD, The Hastings Center, 31 Malcolm Gordon Road, Garrison, NY 10524.

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preimplantation genetic diagnosis. The rest of the embryo is chilled to temporarily arrest its further development while the detached cell is used for the particular genetic analysis desired by the family. The third stage involves performing gene transfer on the embryo in an effort to improve certain traits. The fourth step, after the embryo has been implanted, is fetal cell sorting. It is now well documented that in the peripheral blood of a pregnant woman, not only are her own cells found but also some cells from the fetus. If those fetal cells can be separated from the maternal cells in a regular blood sample, a genetic analysis can be performed on them without the intrusiveness or the risks associated with chorionic villus analysis or amniocentesis. Fifth, hormonal manipulation is done to steer the development of the fetus. Finally, the resulting infant is cloned.

Of the six steps I've listed, four can be performed with current technologies. In vitro fertilization is performed regularly. Preimplantation genetic diagnosis is still regarded as an experimental method, but it is in use in the United States and elsewhere. Despite recent advances in gene transfer, this cannot be counted as a current technology because, with very few exceptions, it cannot be performed effectively and safely. Furthermore, performing such genetic manipulations on an early embryo would also entail germ-line genetic manipulation, which is not permitted. Fetal cell sorting, although in a relatively early stage of development, is here and in use. Hormonal manipulation can be done. Cloning, specifically mammalian cloning, has been accomplished, but does not work reliably. Several mammalian species have been cloned, but no primates. Besides, by and large, the results of cloning have been fairly dismal in that there have been many failures of development, many deaths in the perinatal period, and many abnormalities varying from gross to subtle in those animals that have been born. In this hypothetical case, we cannot count cloning as a successful technology. Nonetheless, four of the six described technologies are here and are working.

Scenarios such as these can frighten—or excite—people. I use them to give a sense of the likely architecture of the foreseeable future and the choices that we will have to face.

Drugs as performance enhancers in sport

I first came to think about the ethics of enhancement not in the context of genetic enhancement but rather in the context of sport. Many years ago, The Hastings Center received a grant from the National Science Foundation to study ethical issues in nontherapeutic drug use.[2] One of those uses was to enhance performance. As we looked around for where drugs were used for enhancement, not for therapy, sport was an area in which some information had begun to emerge. In that research, we asked a number of questions, such as, Why do athletes use drugs to enhance performance? For one thing, there are many pressures on athletes to succeed. Some are external, such as the pressures exerted by coaches, trainers, and parents. The enticement of fame or money can be enormously powerful.

Sometimes the pressures are internal, particularly when young people invest a great portion of their self-esteem and devote a great deal of their young lives to becoming successful athletes. In many sports, they must begin very young to have any chance of becoming world-class athletes. Having made such great emotional and personal investments in sport, the internal pressures to succeed can be quite enormous.

Add to the pressures on athletes to succeed the fact that the differences among competitors are often very small. Connie Carpenter Phinney won a gold medal in the first Olympic women's cycling road race by the width of a wheel rim. Such a tiny margin after many miles is typical of the differences among competitors in Olympic events. The difference between the first and last sprinter may be no more than a fraction of a second. In throwing events, it may be fractions of inches. Even in long races, it may be only seconds. Therefore, if something can give an athlete even a modest competitive advantage, it can mean all the difference between a gold medal or finishing deep in the back of the pack.

How should we think about the ethics of performance enhancement in an endeavor such as sport? In countries such as the United States, it is reasonable to begin such an ethical analysis with a presumption in favor of individual liberty. That is, if you want to argue that people ought not to be permitted to do something, you have to provide good reasons why they should be prohibited from doing so. Therefore, if we wish to argue that athletes ought not to take performance-enhancing drugs, the burden of proof rests on those making the argument. One common argument is what philosophers call paternalism, which is roughly defined as trying to further the interests or well-being of the person for whom the decision is being made, without regard for the wishes of that person.

Is that always bad? I would guess some readers of this article are parents. Parents of young children act paternalistically. Suppose one of your children, at age 3, told you that he or she wanted to go outside and play on a very busy street. I imagine that you would not say, "I respect your independence. If that is your wish, you may go out and play in traffic." Instead, I suspect, you would tell your child, emphatically, "No! You will stay in the yard where it is safe." In this case you are acting paternalistically. Not only is paternalism justified here, but it would be a terrible neglect of parental duties if you didn't object to your child's doing such dangerous things at that age. Paternalism can be a very sound moral justification for an action that limits the freedom of children and young adolescents. Paternalism, however, is much more difficult to justify with adults. For the most part, we believe that adults must be given the freedom to make their own decisions, including their own mistakes.

Adult athletes, even young adult athletes, could with good reason note that they are encouraged to participate in certain sports, downhill skiing, for example, that have very high injury rates, including possible fatalities. How then can one justify denying those same athletes the right to take a drug to enhance performance when the drug's risks may be much smaller? What justification could we cite for forcibly substituting our judgment for the athlete's judgment? For adult athletes, paternalism is difficult—not impossible, but very difficult—to jus-

tify. For such athletes, we need a more robust ethical justification for prohibiting the use of performance-enhancing drugs.

A more persuasive justification for banning performance-enhancing drugs emerged from research begun in the early 1980s that entailed talking to athletes and others—coaches and officials—in high-level sport. This research made it abundantly clear that athletes do not see the decision whether to use anabolic steroids, stimulants, or other performance-enhancing drugs as an entirely free choice. On the contrary, such choices are often highly constrained. We now know that at times athletes have had drugs literally forced upon them, sometimes without even being told what drugs they were being given. The collapse of the Iron Curtain revealed what many had suspected, namely, that the East German sports establishment had created a massive, sophisticated, successful, secret—and immoral—organization to perfect doping and evade detection. To accomplish this, it used the services of more than 100 physicians and scientists.[3]

In its boldness and organization, the East German doping machine may eclipse all others; but it would be naïve to think that efforts to achieve the same goals have not arisen elsewhere, including in the United States, albeit without government support. Rather, these other doping endeavors may be local, informal, and surreptitious—but no less threatening to the health of athletes or the spirit of sport competition. We are told that in East Germany, young athletes were given powerful drugs and ordered to use them, that athletes were lied to about what they were taking, and that trusted figures, such as coaches and trainers, were involved.

For most athletes, the pressure to use performance-enhancing drugs is less formal and coercive, but it is powerful. Athletes are reluctant to surrender a competitive advantage. If they believe that other athletes are using a performance-enhancing drug that places them at a competitive disadvantage, the desire to "level" the playing field can be enormous.

If we ban performance-enhancing drugs, but they are used anyway, then an athlete faces three terrible choices. One choice is to leave the sport entirely, and some do. These athletes reach the point where they are highly competitive, know they are not going to reach the next level unless they are willing to use drugs as their competitors do, and choose to cease competing at that level. That's their loss, but it is also our loss if honest athletes are leaving the competition. The second choice some athletes make is to continue to compete knowing that they are at a disadvantage and hope that if they are just that much better than their fellow competitors, they will still win. Connie Carpenter Phinney did not use blood doping, despite knowing that some of her teammates did. (Blood doping entails receiving transfusions containing red cells in advance of an event so that you will have normal fluid volume, but an increase in the number of red cells. This procedure is presumed to enhance your blood's ability to carry oxygen to your tissues and waste products away.) In endurance sports, such as cycling road races, long foot races, cross-country skiing, and the like, blood doping may confer a significant competitive advantage. Carpenter Phinney won despite having surrendered a competitive edge. But, more often than not, otherwise evenly matched athletes who refrain from performance-enhancing drugs will end up losing to athletes who have taken them. The third choice that athletes face when we ban drugs but fail to effectively enforce the ban is to give in and use the drugs—to level the playing field by behaving like their competitors. There have been times in some sports when drug use was endemic. It is widely believed that in the sport of weightlifting there were years when many world-class weight lifters may have been using anabolic steroids.

The whole point of drug control is to create a fourth possibility: to ensure fair competition, to assure athletes that, in the metaphor they frequently use, the playing field is level, that the combination of natural abilities, training, hard work, and competitive savvy should determine the difference between winners and users—not whose drugs are more powerful.[4]

A question not yet addressed is, What's wrong with using performance-enhancing drugs in sport? One reason already mentioned is that it creates an uneven playing field. However, a second one requires more explanation: using performance-enhancing drugs violates the meaning of the competition. Imagine someone showing up for the Boston Marathon. He—or she—has properly registered and is wearing a number on his back, as competitors are supposed to. But on his feet, he's wearing roller blades. Suppose further that there is nothing in the rules of the Boston Marathon that prohibits a competitor from wearing roller blades. And suppose, finally, that he is the first to cross the finish line. Now, has he really won the Boston Marathon? Or has he exploited a loophole in the rules in order to be the first to cross the finish line? Most people understand that the Boston Marathon is supposed to be a "foot" race, to be run, not skated. It would be perfectly fine to create a roller-blading marathon, but that would be a different event, with a different meaning and its own set of rules.

The use of performance-enhancing drugs violates the meaning of sport in much the same way that competing in the Boston Marathon wearing rolling blades rather than running shoes violates the meaning of that event. It introduces an element that has no relationship to the meaning we attach to that particular athletic activity. Rather, it corrupts and perverts its meaning. That, I believe, is how most people understand the use of the performance-enhancing drugs in sport.[5]

There are criticisms of the effort to control performance-enhancing drugs in sport, criticisms that have analogies to performance-enhancing technologies in other realms of life. One complaint the critics make is that we cannot distinguish those enhancements that should be permitted from those that should be prohibited. What's the difference between taking an anabolic steroid and a dietary supplement? they ask. What's the difference between using erythropoietin—a biosynthetically produced hormone that stimulates the production of red blood cells—and training at high altitude, which also can increase the concentration of circulating red blood cells? This is an important criticism. The answer is not a simple one. The criticism conflates two things. First, we must acknowledge that it can be difficult sometimes to know, precisely, where to draw

the line between what is permissible and what is not. The criticism errs when it collapses this often difficult task of line-drawing into the much more radical conceptual claim there are *no* differences to be noted, no distinctions worth making at all. Yes, drawing lines can be a difficult and imperfect enterprise at best. Where we draw the line and on what grounds we draw it will be very important choices—ones that must be well defended. But we cannot escape the task of drawing lines as best we can.

A secretary who inadvertently takes home a pencil from the office and a CEO who loots the company of hundreds of millions of dollars could both be said to have "stolen" from the company. We can, I hope, see the difference between the two and the practical need to draw a line somewhere between them. There *is* a difference worth noting.

A second criticism of any effort at drug control in sport is that enforcing a prohibition against performance-enhancing drugs is very difficult, if not impossible, without intruding on the privacy of the athletes. The current schemes of drug control, at least the effective ones, do exact a price. Athletes must provide samples of urine—usually while being observed—or blood, or both. To discourage the use of performance-enhancing drugs that are taken during training rather than just before competing, no-advance-notice testing programs have been established. These programs require knowing where the athlete is at all times—another intrusion on privacy. Perhaps the best defense of such invasions of privacy is that the great majority of athletes welcome them as the most effective methods to ensure that their opponents are not cheating.

Genetic manipulation enhancers

More recently, commentators have emphasized the possibility of genetic manipulation to enhance performance in sport. It is useful to distinguish between what I will call "direct" and "indirect" manipulation. Direct genetic manipulation in this sense is altering a person's genes via gene transfer or the like. Although gene transfer research directed at therapy has experienced some dramatic recent successes, the use of similar techniques to enhance athletic performance remains in the future—perhaps not as far into the future as we might have thought until very recently, but in the future nonetheless. Gene transfer is not a widely available, well-understood, safe technology. Indirect genetic manipulation, on the other hand, has been in use for a good 15 years or more, ever since biosynthetic hGH was first made available. By indirect genetic manipulation, I mean using the fruits of genetic knowledge to manipulate human physiology or anatomy. In the case of hGH, scientists were able to identify the gene that specifies hGH, clone it, and put it into a cellular production system to produce as much growth hormone as was wanted or could be sold. Indirect genetic manipulation will become increasingly available in the future.

Biosynthetic hGH marks one of the first attempts at indirect genetic manipulation. The evidence we now have suggests that injecting hGH in physiologically normal amounts may accelerate the growth rate of a child who makes endogenous hGH with normal activity and within the normal quantitative range, but will not increase the final height such children reach. In other words, it will not enhance height. That fact, however, was not known when biosynthetic hGH first became available. Parents have tried to use growth hormone to make their otherwise normal children taller. There is nothing intrinsically wrong with parents seeking advantages for their children. However, heightism, like ageism, sexism, or racism, involves treating people differently as a function of an attribute that is irrelevant to the judgment in question. Whether a person is taller or shorter should make no difference as to what you would think of the quality of his or her writing, speaking, or teaching; it has nothing whatsoever to do with his or her worth as a human being. Yet there is some evidence indicating that being taller in the United States confers certain advantages. For the record, I am about 5 feet 11 inches tall. I should note when I wrote about this many years ago for a magazine that was owned by the Time-Life Corporation, the editor, who liked the article very much, called me to say he had a problem. His boss, the publisher, was very short. I said, "No problem. Obviously, he is good enough at what he does that he has overcome the heightism that otherwise would have been an obstacle to his success." The editor asked if I would write that in the article. As the magazine was paying me by the word, of course I agreed.[6]

What might have happened if hGH did increase the height of otherwise normal, healthy children? Two scenarios are worth considering. The first one we may call the "market" scenario. In this scheme, hGH would be available to those who wished to purchase it for their children and who could afford it. This last point is not trivial, as a course of hGH can last for years and cost tens of thousands of dollars. What would be the result of leaving hGH-mediated height enhancement to the market? Simply put, instead of a culture roughly divided into the poorer and less well-educated on the one hand, and the wealthy well-educated on the other, we would now have the poorly educated short and the wealthy well-educated tall. We would have added one additional, very visible form of inequality onto other, somewhat less visible forms of inequality. I believe that is a very disturbing scenario to anyone committed to social justice and equal opportunity.

The alternative can be called the "egalitarian" scenario. In that scenario, we make growth hormone available to everyone: Every child in the United States gets all the growth hormone they (or more accurately, their parents) want. Who benefits from the egalitarian scenario? Not the children, certainly. Every child would be taller, but still some people would be taller than others. If anything, differences in height might be treated as even more significant than they now are. After all, we would be spending enormous sums to make children taller, so height must be crucially important, right? In this scenario children don't benefit; parents don't benefit. Instead, the benefits go to people who own stock in the companies that make growth hormone and, perhaps, to those who manufacture fabric, because we'll all need to wear clothing in larger sizes. Society

would not be better off. We would simply have wasted enormous social resources for no good end whatsoever.

Neither the market nor the egalitarian scenarios are at all appealing. The overall impact of one or the other would be to reinforce heightism. These scenarios would also reinforce the idea that we should pursue technological solutions to address the problems of social inequality and prejudice, rather than attacking those problems at their roots. Fortunately, we've been saved from this predicament because of studies that show that growth hormone does not affect the final, adult height of children who make normal growth hormone. But we will not always be so fortunate.

Another possible challenge may come from cognitive-enhancing drugs. The caffeine in a person's morning coffee or tea can enhance alertness and, hence, one's cognitive abilities. The concept, then, of a cognitive-enhancing drug is not new. But more highly tailored pharmaceuticals, designed to improve one or more domains of cognitive function, are coming along. The first one available in the United States, known as Tacrine or Cognex, was marketed as a drug to help ameliorate the symptoms of Alzheimer-type dementia. Its effects are quite modest at best, and it does not work in all persons with Alzheimer's. But for some people with dementia, it may slow the progression of symptoms. Other compounds are in the drug development pipeline. Some of these may be more effective than Cognex; some may target other aspects of cognitive functioning. One or more of these drugs may improve cognitive functioning in persons whose cognitive abilities are not impaired—and would be considered, therefore, an enhancement.[7]

What would be the impact of widely available cognitive-enhancing drugs? Imagine a law firm that hires 10 new young lawyers. They meet the managing partner, who informs them that this distinguished firm would, of course, never require any of its staff to use cognitive-enhancing drugs. However, it will always ensure that an adequate supply of these drugs is available—and the firm will be watching their performance very, very closely. This law firm is, thus far at least, merely imaginary. But, according to some sources, years ago a major league baseball team kept a bowl of amphetamines on the training table, available to its players.

In a related scenario, imagine that cognitive-enhancing drugs could improve a person's ability to function in the crucial examinations that students must take to compete for admission to desirable educational institutions. We have many such exams, from the SAT and ACT for undergraduate schools to the GRE for would-be graduate students and the LSAT and MCAT for applicants to, respectively, law and medical schools. How will we deal with the prospect of some examinees using cognitive-enhancing drugs? One possibility is to implement testing, much like at Olympic events. Another possibility is to create two sets of examinations: one for those who do not use performance-enhancing drugs and another for those who do. The sport of powerlifting did something analogous, in effect dividing itself into two organizations: the United States Powerlifting Federation and USA Powerlifting, also known as the American Drug-Free Powerlifting Association. Sadly, it appears inevitable that someone will try to compete in the drug-free events while looking for a competitive advantage by using drugs.

Policy options for genetic enhancement

In a research project that attempts to anticipate genetic enhancement, it has been proposed that we consider three families of policy options: professional policy, public policy, and personal policy.[8] Professional policy includes the full range of measures used by professions to affect the behavior of their members. These measures include professional self-regulation and professional standards, as well as the setting of more informal professional norms. In the case of hGH in the United States, for example, the Lawson Wilkins Pediatric Endocrine Society, a prestigious body in Pediatric Endocrinology, chose to pronounce a professional standard regarding the administration of hGH, saying, in effect, that it should only be provided for appropriate medical indications, thus excluding enhancement.[9] As a form of professional self-regulation, the statement appears to be widely respected and observed. With respect to efforts to clone in order to attempt to create a human child, The American Society for Reproductive Medicine issued a statement that says "any attempt at human cloning would be scientifically inappropriate and thus unethical."[10] This is another effort at self-regulation and, hence, another example of what we have called professional policy.

Public policy includes efforts by governmental as well as nongovernmental agencies (other than professional associations) to manage genetic enhancement. For example, the International Olympic Committee has a policy on performance-enhancing drugs in sport. In the United States, the Food and Drug Administration classified synthetic anabolic steroids as a restricted class of drugs, making it more difficult to get access to them. Such measures will not always be successful. Epoetin alfa (EPO) is a useful medication for the many people who suffer from chronic anemia, including people who must undergo regular renal dialysis. As a consequence, it is in very wide supply for legitimate therapeutic purposes, unlike the synthetic anabolic steroids. Imposing strict limitations on access to EPO would create an enormous inconvenience for the large number of people who benefit from the drug. The fact that some athletes are able to get their hands on EPO is an unintended consequence of having the drug widely available for legitimate therapeutic uses. The appropriate public policy will not be the same, necessarily, for every drug.

By "personal policy" we mean the moral understandings and social practices of individuals, parents, and families, including those moral convictions that would cause them to refrain from unwise or unfair use of genetic enhancement technologies. *The Worth of a Child,* for example, focuses on ethical issues involving children and parents.[11] How does one engage that sort of personal policy response? The means we have are limited but powerful: education, public dialogue, and the encouragement of ethical reflection.

In conclusion, there are four points worth reiterating. First, as we think about genetic enhancement, we should use a broad definition of genetic-enhancement technologies, not merely gene manipulation, but indirect genetic technologies, such as biosynthetic drugs. Second, we should try to anticipate the enhancement temptations of new therapies. Such anticipation may help us in shaping the marketing, availability, or other aspects of those technologies. Third, we should promote the adoption of appropriate public and professional policies. Finally, we should provide public education and dialogue to encourage personal ethical reflection on the appropriate uses and limits of genetic-enhancement technologies.

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