PERSPECTIVE

A genetically augmented future

Gene therapy could one day be used for bodily enhancement, creating an ethical minefield for physicians, says **Ellen Wright Clayton**.

The year is 2030. Gene therapy to insert the DNA sequence for dystrophin has been approved by regulators and is commonly used in children with Duchenne muscular dystrophy (DMD), a disorder linked to the X chromosome. Evidence shows that the intervention increases muscle mass in anyone who receives it. The treatment is widely available, but very expensive.

Alex, a slender adolescent, walks into a physician's office, accompanied by well-to-do parents. Alex does not have DMD, but wants to be stronger. Exercise is not providing enough benefits, and anabolic steroids have too many side effects. Alex is adamant about wanting dystrophin gene therapy and accurately cites its risks and benefits. Alex's parents are willing to pay for the treatment.

The cure for DMD described previously represents a cherished goal for gene therapy, and there is a lot of public support for fixing such heritable disorders in this way[1]. Yet Alex's request raises a host of questions.

We do not know why Alex wants to be stronger. Alex could have a milder form of muscular dystrophy or, if female, could be a carrier who experiences milder symptoms of DMD[2]. Alex might have some other cause of muscle weakness — or might want to be stronger for the sake of appearance, or to be more competitive in athletics. As is the case for many medical interventions, the potential uses of this therapy go beyond the specific disease for which it was developed. Possible applications range from treating milder disease to improving human characteristics — a continuum that could lack clear boundaries.

CONCERNS ABOUT EQUITY SHOULD LEAD SOCIETY TO DEVELOP GUIDELINES FOR GENE THERAPY TO AVOID A NIGHTMARE FUTURE.

Let's assume that Alex does not have a diagnosed physical problem and wants the therapy simply to become stronger. The main debate about using medical interventions for such bodily enhancements focuses on the extent to which they give individuals an advantage over other people. A 2017 report by the US National Academies on gene editing in humans captures the debate well[1]. The authors summarize surveys that show that most people disapprove of using gene therapy to improve a person's physical and intellectual characteristics. The public tends to honour narratives of success based on personal diligence, or even accident of birth, over traits that can be purchased. This preference touches on a larger issue: the extent to which uses of gene therapy would exacerbate social inequality. If there is a widespread perception that this would be the result, society might try to limit its use to the few people who genuinely need it to treat their disease. Or there might be an effort to make such therapies available to all who want them.

Back to Alex in the world of 2030. Assuming that the US Food and Drug Administration's regulations are still the same, physicians would be free to use the approved DMD intervention for any purpose. After all, many medicines are legally prescribed for reasons that have nothing to do with their original indication. So what should happen? How hard should a physician try to understand the source of Alex's desire to be stronger?

Alex's wish might be a product of the social and cultural environment. The request might reflect issues with self-image. The desire to be stronger could reveal a psychological problem that needs to be resolved. Or a physician could conclude that Alex is suffering, thereby making the case for gene therapy more compelling. For example, medical and surgical interventions are sometimes prescribed to prevent or relieve psychological distress in children or young people who are abnormally short[3] or who have potentially stigmatizing physical features[4]. It is important to ensure that Alex understands and agrees to the therapy, but in the end, it can be hard to ascertain the source of a person's desire for a given treatment — especially if the person is an adolescent.

Are Alex's parents wrong to support their child's desire? Perhaps they are putting undue pressure on Alex. Perhaps they want to alleviate Alex's distress. Perhaps they are just indulgent. Society's default position is that parents should have the last say in such matters because they are assumed to care more for their children than does anyone else. Parents have a responsibility for shaping their children's future, creating opportunities and drilling into them all sorts of values. Parents are largely free to pursue their vision for their children's lives, unless those actions are illegal or constitute abuse or neglect.

So what is the physician to do? Assuming that gene therapy for enhancement has not been outlawed, he or she can and should turn to medical ethics and the goals of medicine[5] for guidance. Respect for persons — a fundamental principle of medical ethics — would direct the physician to attempt to discover more about what is driving the patient and their parents' wishes, and to ensure that they understand what is at stake and that their expectations are realistic[6]. If the decision to proceed was made to relieve suffering, and with the adolescent's informed assent and the parents' permission, pursuing the goals of medicine would lead the physician to use the therapy to confer only traits within the normal range of human characteristics.

Ultimately, the ethics of enhancement are intertwined with views of fairness. Concerns about equity should lead society to develop guidelines for gene therapy to avoid a nightmare future in which a group of privileged people becomes stronger, smarter and more beautiful than the rest. But because drawing lines between treatment and enhancement is difficult, the more likely and more unsettling scenario is that physicians will be left to rely on their own ethical commitments to decide when to use gene therapy. ■

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