




## GENETICS & BIOETHICS

### If Gene Therapy Is the Cure, What Is the Disease?

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#### I. Can Philosophical Analysis Really Help?

It may strain credulity to believe that the analysis of concepts such as 'health', 'disease' or 'normality' can shed any light on the ethical and policy issues associated with the vast amounts of new knowledge being generated by the human genome project and related inquiries in biomedicine. However, credulity must be strained.

The focus of attention qua philosophy tends to be on who owns the genome or whether an insurance company can boot you off the rolls if you are at risk of succumbing to a costly disease. But this is not really where the ethical and philosophical action is with respect to the ongoing revolution in genetics.

Politics, economics, psychology, social work, education and philosophy all presuppose certain facts about human nature. In one sense the old nature/nurture battle is written on every page of the classic texts of Western thought. But the genome project, the attempt to map and sequence, to crack the code of our heredity, promises to make nature/nurture an issue in a way that we have rarely seen in the history of science. Conceptual revolution on a par with Darwin, Freud, Copernicus worldviews changing our understanding of who we are and what makes us tick—or sick.

The understanding that our society or others have of the concepts of health, disease and normality will play a key role in shaping the application of emerging knowledge about human genetics. If this is so, why is it so difficult to direct the attention of those interested in the ethical, legal and social consequences of new knowledge created by the human genome project toward the analysis of these concepts?

One reason is that many of those who deliver health care are not beset by doubts or ambiguities about the aims, goals, definitions or purposes of their activities. Most people who seek health care do so because they believe that something is wrong with them. The aim of the doctor or nurse is clear—fix the problem by correcting anomalies, reversing pathological processes or, if cure is not possible, providing some means of accommodation and palliation. In most interactions between health care provider and patient both parties reach agreement that something is wrong and on what the goal of consequent medical intervention should be.

Even when the goal of medical intervention is the subject of disagreement between provider and patient, for example in making decisions about undertaking continued resuscitation efforts or kidney dialysis for imminently dying terminally ill patients, or, the prolonged, intense utilization of life-sustaining treatments for extremely elderly patients who have been in permanent comas for many, many years, health care providers, families or guardians are almost always able to reach an agreement about what should be done (Miles, 1991).

Unless financing is an obstacle it is almost always the case that when patients want treatment that has some chance of being effective doctors will agree to provide it. In American medicine, respecting autonomy is the core principle used to settle disputes about the ultimate goals that ought guide the provision of care. In situations where doubt as to the goal of care exists adherence to the principle of autonomy requires clinicians to defer to the wishes and preferences of those receiving care or their surrogates even when patient choice results in forgoing likely benefits (Childress, 1982; Engelhardt, 1986). The rule, 'yield in the face of autonomy', minimizes the need to carefully examine more general questions about the aims and goals of health care. (But, see Pellegrino and Thomasma, 1988; Faber-Langendoen, 1991, Miles, 1991).

Still another reason for the relative absence of discussions of the definition of health and disease is that when there is a lack of consensus about the appropriate classification of particular traits, states or behaviors as constituting instances of either disease or health the disagreements sometimes become so heated that there is little incentive to join what may appear to more closely resemble a fray rather than a discussion. There is still disagreement about the scope or application of the concepts of health, disease or normality to gambling, sexual promiscuity, pre-menstrual syndrome, hyperactivity or homosexuality). The battles over the classification of these behaviors and traits have been heated and fierce (Caplan and Engelhardt, 1981; Bayer, 1981; Engelhardt and Caplan, 1987). Uncertainty about whether or not to attempt to treat short stature in children, low blood sugar and hypertension have also produced heated controversies as to their disease or health classification and, consequently, the appropriateness or inappropriateness of therapeutic intervention. Controversy about the scope and domain of the concepts of health and disease sometimes is so divisive that it may seem prudent to some to simply avoid asking questions about the application of concepts such as health and disease to new knowledge in the area of human heredity.

There is another reason why the implications of new knowledge in genetics for understanding health, disease and normality are not always center-stage. Those who are actually engaged in mapping and sequencing the human genome, or the genomes of other organisms, often do not have any particular practical goal or application motivating their work. Despite all the hand-wringing which has accompanied the evolution of the genome project, and the promises of therapeutic benefits that it will produce, many of those involved are simply interested in understanding the composition of the genome, its infrastructure or anatomy (see Lander, this volume). Basic researchers have fewer reasons than clinical researchers to struggle to clarify the conceptual foundations of health, disease and normality and they will, of necessity, control the direction of the human genome project for many years to come.

Not only do basic researchers have less reason to explore the conceptual foundations of health and disease, in the case of the genome project they have a positive disincentive to participate or encourage such an inquiry. If uncertainty about what to do with new knowledge in the realm of genetics is a cause for concern in some quarters, then those who want to proceed quickly with mapping the genome might

find it prudent to simply deny any application of new knowledge in genetics is imminent (see Lander, this volume; testimony MN House of Representatives on genetic testing, 1991) or to promise to forebear from any controversial applications of this knowledge

Promising to try and avoid doing anything that will grossly offend societal mores is the simplest strategy if one's aim is not applying new knowledge but merely to be allowed to proceed to acquire it. Some involved in the genome project have tried to defuse worries about the thorny issues of what constitutes health, what are the boundaries of normality and what justifies referring to a particular genetic state as a disease by self-imposed restrictions upon the application of new knowledge concerning the genome. The clearest example of this prophylactic strategy is the promise that germline gene therapy will not be done (Walters, 1986; Anderson, 1989; Hall, 1990). The messy problem of how to fit new knowledge about heredity into existing categories of disease, normality and health can, perhaps, be forestalled by arguing that the sole therapeutic goal of the human genome project is somatic genetic therapy for obvious, clearcut instances of human disease (Anderson, 1989; Elias and Annas, this volume).

## II. What Is Disease?

An especially interesting and important place to start an examination of how new knowledge of the human genome will influence how we ought understand the goals of health care is by asking what is it today that doctors, nurses, psychologists, physical therapists and the myriad other professionals who work in health care are supposed to do? The most obvious and commonsensical answer is that they are to combat disease. While there are many other goals that might and have been added, ranging from screening for eligibility for government benefits to certifying persons as fit to play sports or serve in the military, the fight against disease occupies center-stage in what people expect health care providers to do. So if it is possible to become clearer about what disease is then it may be possible to have a better understanding of the boundaries of what is and is not licit with respect to the application of new knowledge arising from the human genome project.

There are two major points of contention evident in the literature which discusses the meaning of the concept of disease (Caplan and Engelhardt, 1981; Caplan, 1989). One major source of disagreement concerns the role played by the determination of normality in the identification of disease. The other concerns the role played by values in the definition of disease.

Many physicians and nurses equate difference with disease or, at least with a reason for suspicion that disease may exist. To put the point another way, abnormality is often viewed with suspicion either because it is seen as disease or, because it is seen as symptomatic of an underlying state of disease. As E. A. Murphy cogently observed in his book, *THE LOGIC OF MEDICINE*

"...the clinician has tended to regard the disease as that state in which the limits of the normal have been transgressed." (Murphy, 1975, p. 122).

For example, many physicians and public health experts believe that blood pressure readings which vary from what is considered typical or normal for specific age groups within the population are, in themselves, indicative of disease. For American physicians variations skewed toward high numbers are disturbing. For German physicians both high and low numbers are equally likely to be diagnosed as disease and, therefore, as sufficient to merit medical intervention. Similarly, variations, even of a modest sort, with respect to height, weight, attention-span, sperm production or blood cholesterol levels may trigger disease labels and consequent efforts at therapy.

Critics of what can be called the 'disease as abnormality' approach point out that there is nothing inherent about difference that makes a particular biological, chemical or mental state a disease. Moreover, since variation is an omnipresent feature of human beings, it is especially odd to argue that extremes of variation are somehow indicative of disease. If there is nothing at all unnatural about variation, then abnormality cannot in itself be equated with disease. Indeed, critics of the view that equates difference with disease note that this equation has throughout the history of medicine led to the classification of differences with respect to race, gender and ethnicity as diseases which in turn has been the basis for unfair and even harmful interventions against persons suffering from nothing more than a darker skin color or the presence of ovaries (Gamble, 1991).

Those who are skeptical of the equation of disease with abnormality make two points worth pondering in the context of new knowledge about human heredity. Simply labelling abnormality or difference as disease is, of necessity, to impose a value judgment on a physical or mental state that does not wear its disease-status on its sleeve. Second, abnormality is not in itself bad. Afterall, those who are unusually smart, strong, fast, or prolific are not classified as diseased. If abnormality is to be equated with disease then at a minimum it must be abnormality that is associated with something that is disvalued and, further, there must be some connection between the difference or abnormality and the dysfunction that is disvalued (Clouser, Culver and Gert, 1981).

These criticisms of the equation of abnormality and disease raise another major point of contention in defining the concepts of health and disease --whether or not it is possible to do so without reference to values. For if values must be used to decide whether or not a particular abnormality or difference is indicative of disease then many worry that the entire process of defining health and disease must be subjective and especially vulnerable to political or social influences (Caplan, 1989). If disease refers to abnormal states, either mental or physical, that are disvalued then the appearance of values seems to some to make the prospects grim for objectivity or consensus about what states are or are not healthy or diseased. Subjectivity and a lack of consensus could bode especially ill for the uses to which new knowledge of human heredity might be put since applications might be controlled by the powerful or the economically privileged to advance their own values.

Some believe that values need not be invoked in defining health or disease. Those who espouse non-normativism, the view that the definition of disease need not involve any invocation of values (Boorse, 1975, 1976, 1987; Kendell, 1975; King, 1984; Scadding, 1967) usually invoke some notion of natural function or design to ground the definition of disease.

Non-normativists doubt that values must enter into the assessments of organ function and behavior. For example, if a cardiologist says that the function of the heart is to pump blood or a renal physiologist claims that the function of the kidney is to cleanse the blood of impurities, it is not because they hold certain values about hearts or kidneys. Rather, based upon both functional and evolutionary analysis it is possible to arrive at an understanding of what it is that the organs are supposed to do. By removing both kidneys or seeing what happens if the heart is damaged it is possible to ascertain the functions of these organs. Therefore, non-normativists argue, it is possible to utilize concepts such as cardiac or renal disease without invoking any sort of value judgments as to whether or not it is good that hearts beat or commendable that kidneys filter the blood

Normativists argue that the concept of disease is inherently and inextricably value-laden. They believe

that functional analysis by itself cannot reveal whether or not a particular state of the body or mind is indicative of disease (Clouser, Culver and Gert, 1981; Engelhardt, 1986; Fabrega, 1972; Goosens, 1980; Margolis, 1976; Pellegrino and Thomasma, 1988; Reznick, 1987; Sedgwick, 1973).

For example, the fact that someone is nearsighted or farsighted may or may not be indicative of disease or disability. It depends whether one is going to spend one's day in the library, in the operating room or hunting on the savannah.

Even the failure of a major organ may not be an obvious instance of a disease if other options exist for performing the same function. The fact that a kidney can no longer cleanse the blood of impurities may or may not be indicative of disease depending upon such value-laden judgments as whether its owner wants it to do so. Artificial kidneys can supplant the function of natural ones so there is nothing inherent about the desirability of having a natural kidney cleanse the blood. It is possible that some people might prefer to have their blood cleansed by a machine (maybe a more efficient and safe futuristic one then is now currently available) to having their own kidneys do the job. Consequently, normativists say, the view that a kidney incapable of cleansing the blood of impurities is diseased is as much a claim about values and options as it is about renal physiology.

Normativists almost always subscribe to the view that assessments of health and disease are value-laden and that as a result they are inherently subjective not objective (Fabrega, 1972; Sedgwick, 1973; Engelhardt, 1986). However, the link between the presence of values and the threat of subjectivity is open to question. The presence of values may make the definition of disease or health suspect in terms of its objectivity. But the existence of values in the assessment of health and disease does not mean that it is impossible to reach consensus about the definition of disease in spite of the fact that values play a role in the definition (Clouser, Culver and Gert, 1981; Flew, 1983; Caplan, 1989; Reznick, 1987).

### **III. Non-normativism vs. normativism: finding a middle ground.**

Equating normality with health and abnormality with disease as ways of defining these key concepts seems open to devastating conceptual and empirical problems. The view that what is different is, in and of itself, disease simply does not square with ordinary experience. Many differences are viewed as desirable or beneficial. Difference may be a cause for inquiry into whether or not a particular state is indicative of health or disease but, it is not in itself sufficient as a basis for deciding whether abnormality or variation represents health or disease in an individual or group. This is especially true for genetic differences where it is already known that wide variations exist in terms of the genetic makeup of individuals that are not in any way manifest in their overt features, traits or behaviors. Difference in and of itself does not always make a difference.

However, it does seem that the definition of disease and health is closely tied to those differences or abnormalities that are disvalued by the individual or group. If a particular trait or behavior or physical structure is seen as causing impairment, dysfunction, pain, or other disvalued states then it is a prime candidate for categorization as a disease.

The problem with linking values and abnormalities is that not all states commonly recognized as diseases are necessarily indicative of difference or abnormality. Nor are all dysfunctions or impairments always disvalued. For example, every human being may suffer from the common cold, acne, anxiety or dental caries. The universality of these conditions does not make them any more palatable or any the less disvalued. It is possible for a state to be typical, normal, common or universal and nonetheless for it to be sufficiently disvalued that it is classified by both lay persons and health care professionals as disease.

Not every dysfunctional or impaired state is disvalued. Those who do not wish to have children may rejoice to discover that they have ovaries that are incapable of ovulation, lack a uterus or possess testes that cannot create sperm. Someone born with only one functioning kidney may remain entirely indifferent to and even unaware of this dysfunction. Not all dysfunctional states are necessarily disvalued meaning that not every abnormal state can be viewed as a disease.

Nevertheless, there does appear to be a conceptual link between abnormality, dysfunction and disvaluation. If we restrict the definition of disease to cover only those mental or physical states of human beings that are abnormal, dysfunctional and disvalued, then we will be able to identify many of the diseases recognized within a group or in a society.

Two questions confront those who admit the tie between disvaluation and dysfunction. Is it possible to determine the existence of dysfunction without invoking value judgments? If not, does the presence of disvaluation as a key criteria of the definition of health and disease makes these concepts so subjective as to be either useless or extremely vulnerable to abuse by those powerful enough or privileged enough to impose their personal values on others (Caplan and Engelhardt, 1981; Engelhardt, 1986).

### **IV. XYY, Oculocutaneous Albinism and deafness and being short: Are These Diseases?**

There is no need to try and resolve the disputes about normality or the role of values in the definition of disease in order to see what the consequences of these disputes are for new knowledge that is arising and will, it is to be hoped, continue to arise in the domain of human genetics. The stance that those in clinical genetics adopt toward assessing the significance of difference and abnormality at the level of the genome, the role of values in defining genetic disease and the need to link genetic disease to dysfunction will play pivotal roles in what is done with the knowledge generated by ongoing work to map and sequence the genome.

The question of how disease is currently assessed in the realm of clinical genetics is not entirely a hypothetical one. Afterall, counselors and clinicians have been treating patients for genetic diseases for decades. It is instructive to look and see how they currently define disease and health in order to try and forecast how new knowledge about human heredity will be absorbed into clinical and counseling practices. Two forms of genetic abnormality illustrate how much uncertainty and confusion exists about both the criteria that ought to be used to define disease and the proper application of the concepts of health and disease at the level of genetic difference and abnormality.

Not so long ago a woman at a large medical center was informed by a genetics counselor that the fetus she was carrying possessed an abnormal chromosome. The child had XYY syndrome -- an extra Y chromosome. The mother and father had sought genetic testing since she was in an age group at somewhat higher risk for a different genetic condition, Down's Syndrome. The information that the baby had a different chromosomal abnormality from the one that had concerned the parents came as a bit of a surprise. Subsequently, in counseling sessions, the mother and father were told that a few researchers had posited a connection between criminality and this chromosome abnormality. They were also told that some researchers believed there was also a link between this condition and tall physical stature and even severe acne. After talking about the situation with their family doctor and various friends the couple decided to abort the pregnancy. Is XYY syndrome a disease? If not, why were the parents told that it had been detected? And if it is, is it a disease which merits aborting a fetus with this condition?

OCA albinism is a disorder in which melanin is absent or decreased in the skin, hair and eyes. Albinism actually refers to a group of autosomal recessive traits in which the enzyme necessary for melanin production, tyrosinase, is present or absent in varying degrees causing a fair degree of heterogeneity. Most forms of OCA albinism are associated with a very distinctive set of complications (Abadi and Pascal, 1989). Tyrosine-negative albinism, which occurs at a rate of about 1 in every 34,000 births (Wyngaarden, 1989), is associated with extreme sensitivity to light (photophobia), nystagmus, severe impairment in visual acuity, and a greatly increased risk of squamous cell skin cancer.

The genes involved in OCA albinism are rapidly being mapped (Spritz, et. al., 1990). Prenatal diagnosis is already a possibility using fetoscopy to obtain samples of fetal skin or scalp hair around the 16th week of development in order to see if the follicles contain melanin, but, the relatively low incidence of the condition and the costs involved mean that such testing is rarely done. It will not be long, however, before a routine test will be available to detect this genetic abnormality from any sample of fetal DNA. But, unless albinism is a disease, why should anyone try to detect it much less provide information about it to parents?

Looked at in light of the issues raised in the earlier discussion of the definition of disease it is evident that decisions about what makes a condition a disease have direct implications for what will be done with information about XYY syndrome or OCA albinism. If one subscribes to the disease as abnormality definition then both conditions will constitute disease-states and both ought to be reported as such to parents. If one believes that it is necessary to draw a connection between disease and dysfunction then OCA albinism will certainly qualify as a disease whereas, in lieu of more evidence, XYY syndrome may not. And if one takes the position that to be a disease a state must be both dysfunctional and disvalued then it is possible that neither XYY syndrome or OCA albinism qualify as diseases.

My own view is that it is difficult to defend the decision to label either XYY syndrome or OCA albinism as diseases. The former is an abnormality for which there is no reliable evidence that it causes or is associated with dysfunction. The latter is an abnormality that produces dysfunction but, the problems associated with the condition are readily amenable to various interventions and coping strategies. It seems accurate to say that a person with OCA albinism is not diseased, but they do have an abnormality which causes some impairment.

Deafness and the decision to screen and abort

It should be obvious that the decisions which are made regarding the application of the concepts of health and disease in the realm of genetics require explanation and justification. It should also be obvious that not everyone will arrive at the same conclusion about the classification of human genetic differences since they may hold different views about what it is that justifies classifying a trait or characteristic as a disease, an abnormality or a healthy state. Serious consequences follow the determination of disease states. Those in clinical genetics who diagnose and treat genetic diseases must not invoke the oft-espoused desire to remain value-neutral as a rationale or an excuse for avoiding the obligation to carefully think through the criteria that are now used, or others that might be used in the future, to classify genetic diversity and differences as indicative of health or disease.

#### **V. Implications of Defining Disease for the Study of the Human Genome.**

The realization that there is a broad spectrum of opinion about what makes something a disease is troubling in speculating about the ways in which new knowledge about the human genome is likely to be analyzed and classified. It is important to remember that much of the information that is likely to be acquired will reveal far more about the structure and composition of the genome than it does its function. If we forget this, there is a grave danger that the disease as abnormality approach will find fertile ground in the realm of genetics in the future.

Some agreement must be reached about whether it is necessary to establish a link between genetic information and dysfunction, or between dysfunction and disvaluation in order to establish the disease status of particular bits of the genome. Otherwise, increased screening and testing will reveal more and more differences and variations among our genomes which will lead an incoherent set of responses in terms of counseling, reproductive choices and therapy. While consistency need not always be desirable, it seems morally incumbent on those who will be faced with the challenge of applying new knowledge about the genome to strive for some sort of professional and societal consensus as to how these questions ought to be answered.

For the present it seems clear that the first wave of new information about the human genome is likely to bear a fair amount of news about human differences that may have uncertain or unknown phenotypic consequences. Clinical genetics is still in its infancy. As such it ought to proceed with great caution in labeling states or variations as abnormal much less diseases. For now, clinical genetics ought to restrict itself to the identification and assessment of only those genetic states which are known to be dysfunctional as well as different. It should discourage efforts to allow 'fishing expeditions' to become part of prenatal, carrier or workplace screening. And, it should assert clearly that the central goal of human clinical genetics is the prevention or amelioration of disease not the improvement of the genome. It is important to note that abjuring eugenics as a proper goal of clinical genetics is not the same thing as foregoing any effort to meddle or intervene with the genetics of reproductive cells.

#### **VI. Please Leave Us Alone, We Promise to Be Good!**

Those who believe in the value of the human genome project, a group to which I belong, often try to calm fears about the misapplication of the knowledge the project intends to create by assuring all within earshot that their intentions are pure. This promise meets the concern of some of the harshest critics of the project (Rifkin, 1985a, 1985b). A few of those who doubt that humankind knows what to do with more information about its own hereditary makeup or who simply believe that it is unnatural to mess around with genes sometimes try to arouse legislative or public concern by spinning scenarios in which man-animal chimeras slink out of the corridors of MIT, Cal Tech, Genentech or Fort Dietrich to commit maniacal man-animal misdeeds against hapless humans. If such grim scenarios aren't scary enough, the occasional critic resorts to even more horrifying futuristic timeworms in which hordes of clones derived from the embryos of businessmen, sports stars, and politicians (no attempt is made to mitigate the horror) descend on an unsuspecting and defenseless world. In the most hyperventilating form of such criticism warnings are issued that if the genome project is not stopped now the result will inevitably be a planet teeming with millions of knockoff copies of Adolph Hitler, Genghis Khan, Saddam Hussein, Idi Amin and Joseph Stalin.

Those who want the genome project to proceed apace are quite willing to promise never to xenograft a gene or clone Adolph Hitler. If, by promising not to clone or even to perform germline interventions the defenders of the genome project can allay the fears of their most strident and publicly visible critics, they are more than happy to do so (Anderson, 1989; Hall, 1990). This is especially true when the science fiction scenarios being spun are either scientifically impossible (cloning Hitler) or well beyond the reach of contemporary science (gene xenografting).

The greatest challenge to securing continuing funding for the genome project does not originate from concerns about privacy, confidentiality or coercive genetic testing. It is eugenics, manipulating the human

genome in order to improve or enhance the human species, that is the real source of worry. This is reflected in the content of the futuristic horror scenarios spun by the project's critics (Swazey, this volume). It is also rooted in the historical reality of social policies based upon eugenics that led to the deaths of millions in this century (Proctor, 1988, and Proctor, this volume).

Promising not to do anything that remotely hints of germline engineering, where eugenics is the goal, is relatively easy for those connected with the genome project since none of them believe that anyone is even remotely close to knowing how to alter the germlines of a human being, much less whether germline engineering will actually work. If the situation were different with respect to the practicality of germline interventions, then statements to the effect that germline intervention ought never be attempted might be far more muted. Even without the prospect of imminent application, they should be.

The promise never to do germline engineering, invoked merely as an expedient way to silence critics, is implausible because it rests on a flimsy moral foundation. Why shouldn't a couple concerned about passing along hemophilia or sickle cell disease hope that medicine can help alter their genomes so as to minimize their risks of doing so? Why shouldn't clinicians fervently want to undertake some forms of germline interventions so as to eliminate diseases such as Tay-Sachs, thalassemia, or Hurler's syndrome?

If it were possible to eliminate a lethal gene from the human population by germline alterations is there any convincing moral reason why this should not be done? If those carrying a lethal gene request treatment so that they are able to reproduce without guilt or fear, ought not health care providers feel not reluctance but a duty to help them? If the prevention and treatment of disease are the goals of human clinical genetics then not only should germline therapy not be forgone it may be morally obligatory in cases where no somatic therapy is possible.

#### **VII. Should Germline Interventions Be Forgone?**

Some believe that any attempt at germline therapy is wrong since it requires imposing the risk of harm on future generations either by causing unanticipated side-effects in unborn infants or by introducing dangerous genes into the gene pool. Future persons have no say in whether or not they consent to having risks imposed upon them. They, not their parents or ancestors, will suffer should attempts to manipulate the germline produce untoward results. Many bioethicists (Ramsey, 1970; Kass, 1975; Levine, 1986) believe, and existing government policy in the United States, Germany and other nations maintains, that it is wrong to impose the risk of serious harm on those who cannot themselves consent. Newborns, very young children, the severely mentally ill and the severely mentally retarded should simply not be recruited as the subjects of research.

The other major reason for not undertaking germline interventions is that hereditary information which is of value, not for the individual but for the species, may be lost. If lethal or disabling genes are removed from a certain individual's gametes it may be that benefits conferred on the population when these genes recombine with other, non-lethal genes will be lost.

The other argument against germline therapy is that no one would really want to use it for the purposes of eugenics. But this is patently false.

Even putting aside Germany's three decades long embrace of race hygiene and eugenics (Proctor, this volume) there are examples in our own time of governments and private organizations avidly and unashamedly pursuing eugenic goals. The government of Singapore instituted numerous eugenic policies during the 1980s including a policy of providing financial incentives to 'smart' people to have more babies (Chan, 1987). The California-based Repository for Germinal Choice, known more colloquially as the Nobel Prize sperm bank, has assigned itself the mission of seeking out and storing gametes from men selected for their scientific, athletic or entrepreneurial acumen. Their sperm is made available for use by women of high intelligence for the express purpose of creating genetically superior children who can improve the long-term happiness and stability of human society. Few protests have greeted these activities whereas the hypothetical suggestion of someday directly modifying the genetic blueprint of a sperm or an egg has elicited great concern in many quarters.

Granted, eugenics has been horribly abused in the past and may still result in terrible abuses today. But, it is simply a confusion to equate eugenics with any discussion of germline therapy.

Should scientists or clinicians really promise never to try to eliminate or modify the genetic messages contained in a sperm or an egg if that message contains instructions which may cause sickle cell disease, Lesch-Nyhan Syndrome or retinoblastoma. The grim history of eugenically inspired social policy tells why it is important to protest and even prohibit the activity of the Nobel sperm bank or to vehemently criticize the birth incentive policies of Singapore (Duster, 1990). It does not provide an argument against allowing voluntary, therapeutic efforts using germline manipulations to prevent certain and grievous harm from befalling future persons.

There is no slope that leads inexorably from therapeutic germline interventions intended to benefit future persons to the creation of eugenically-driven, genocidal social policies. Nazi eugenic policies were not aimed at benefitting individuals. The state or the Volk, not the individual, was the object of Nazi eugenic policy. Public health not individual therapy was the driving force behind the Nazi medicalization of eugenics.

Worries about imposing harms on future persons without their consent or robbing the gene pool of the value of diversity are even less persuasive reasons for foreswearing germline intervention. If the harms that will befall as yet unborn person are serious, even fatal, then it is far from self-evident that it would be wrong to try and prevent the harm even if it means the imposition of possible risk on the child who will be born. The risk must be such that the child who is the involuntary subject of germline experimentation is at grave danger of being made worse off by the intervention than would have been true had the child been born with no effort to alter his or her genetic defect. Some genetic diseases are so miserable and awful that at least some genetic interventions with the germline seem justifiable.

It is at best cruel to argue that some people must bear the burden of genetic disease in order to allow benefits to accrue to the group or species. At best, genetic diversity is an argument for creating a gamete bank to preserve diversity. It is hard to see why an unborn child has any obligation to preserve the genetic diversity of the species at the price of grave harm or certain death.

Forgoing efforts at germline engineering make some political sense in the current climate of concern about the genome project. But, they make no sense conceptually or ethically. The danger inherent in such stances is that they will result in important benefits being delayed or lost for persons who have impairments or diseases that might be amenable to germline engineering. The way to handle legitimate concerns about the dangers and potential for abuse of new knowledge generated by the genome is to forthrightly examine what are and are not appropriate goals for those who provide services and interventions in health care. There is nothing sacrosanct about the human genome. It is only our inability to openly and clearly define what constitutes disease in the domain of genetics that makes us feel that

intervention with the germline is playing with moral fire. If it is eugenics we abhor then it is eugenic goals which should be forgone.

(A version of this paper appears in "*If Gene Therapy is the Cure, What is the Disease?*" G. Annas and S. Elias, eds., Gene Mapping, Oxford University Press, 1992, pp. 128-141.)

Posted: 2002-11-08