

WHERE ART THOU? SHOW ME THE WAY:
OPTIMISTIC ASSUMPTIONS MEET FACTUAL MISCONCEPTIONS AT THE
CROSSROADS OF GENETIC MEDICINE AND LAW

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ABSTRACT

Optimistic assumptions abound about the beneficence of genetic research. Many believe that scientific and technological progress will redound to the good, in part because we can make choices about when, where, and how to use knowledge, and the more known the better. Many assume allowing individual choice while protecting basic rights will ameliorate any deleterious consequences, such as those arising from past 'forced' programs of eugenics. To paraphrase: knowledge and technology don't kill, only humans do. These beliefs are examined at the crossroads of two basic medico-legal precepts in the United States: informed consent, and personal care. Assumptions about the paths provided by care, choice, and knowledge are explored. On this odyssey, both God and Devil are in the details.

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The Coen brothers' movie "Oh Brother Where Art Thou?" takes us on an odyssey, following escapes from a chain-gang prison, moving through the backwaters of the Depression Era South, negotiating around numerous obstacles and setbacks, employing baptismal cleansing and optimistic attitudes, leading to a modern age of electrification powered by the damming of its rivers. Similarly, our advances in genetic research seek to take us from relative ignorance and imperfect health, through increased knowledge and technological perfection, negotiating around ethical and religious challenges, to a post-modern age of genetic medicine where we can engineer more perfect unions through informed individual choice.

Throughout current discussions on genetics research run assumptions about our ability to square scientific, technological, and medical developments with our hopes and beliefs surrounding a reverence for life, and the ultimate beneficence of inquiry and innovation. Many share an optimistic belief that evolutionary progress in knowledge will redound to the good, in part because we can contain and guide the process through our laws emphasizing individual autonomy and protection of rights. There is a general (but not universal) belief that increased knowledge in and of itself is a prime goal for us that will benefit all human kind: and the more knowledge, sooner, the better.

At worst, under these assumptions, inquiry and innovation are amoral, neutral processes, posing no intrinsic ethical problems, and allowing informed choices and protecting rights ameliorates any potential pitfalls. To paraphrase from gun regulation discussions: knowledge and technology don't kill or maim, only humans who abuse knowledge and technology do. Because knowledge and technology are simply tools subject to ordinary human use and abuse, modern legal restraints emphasizing individual choice and rights will reduce any deleterious social consequences -- such as those from last century's eugenics: so that on balance genetic research and technology should be supported, albeit with occasional restraints on individual human choices to channel efforts in a positive direction.

These assumptions run into trouble when they confront extended experience with confounding human behavior. There have been decades-long discussions regarding "therapeutic misconceptions" in medical research -- the persistent belief by a large majority of those subjects participating in research that they will be "treated" or "cured" through the research process, notwithstanding extensive 'informed consent' paperwork and protocols to the contrary. Despite many attempts to dispel these misconceptions by clarifying risks in research, this optimistic subject bias persists.

This kind of persistent bias is expressed more generally in positive talk and presumed benefit about the results that may yet obtain for stem cell and other genetic research, notwithstanding some publicized failures and pronounced fraud in prominent announcements of significant research advance.

This article examines these optimistic biases, their persistence in the presence of accumulated wisdom and other rational evidence to the contrary, and attempts to correct these biases. The assumptions upon which these biases are based are subject to significant question and qualification, and it appears both God and the Devil are in the details.

Popular sources for discussions were searched and analyzed. Legal and medical periodicals and other sources were also reviewed. Excerpts, interpretations, and implications for further inquiry are discussed. Various stories are employed to flesh out pitfalls and false trails.

Some medical writers encourage 'negative thinking' to evaluate and improve various medical systems. This article suggests further 'negative thinking' with respect to genetics and the law, to counteract the ungrounded 'positive thinking' that continues to pervade discussions on genetic research. In particular, this article suggests a re-examination of our notions of informed consent and rights to choice in light of persistence therapeutic and other misconceptions.

Method

In addition to participating in the first Pacific Institute session, I have continued to read periodic articles on genetics as they appear in popular news stories. I have reviewed second session materials, and participated in discussions regarding same. I also reviewed legal and medical journals, and the occasional book that came to my attention through various popular book reviews.

Popular sources for discussions, such as articles in newspapers and other periodicals, and sources available through the internet, were then searched and analyzed. Legal and medical periodicals and other sources were also reviewed. For the most part, only articles or abstracts generally available without subscription were used. Excerpts, interpretations, and implications for further inquiry are discussed.

I reflected on previous experiences regarding informed consent -- my father's ultimate decision to authorize a 'DNR' (Do Not Resuscitate) order just before his death, and my sister-in-law's decision not to proceed with autologous bone marrow transplant for her breast cancer, as well as my professional legal work advising a health care insurer on coverage of BMT. And finally, I reviewed those stories and sayings that reflect on the choices we are offered and make on the various paths we take through life.

Results

If current publications accurately reflect the body politic, it seems a majority of both the general public and popular press here in America operate under a belief that stem cell research and other genetic research will result in efficacious medical treatments, that continued public support of such research -- to the tune of billions of tax dollars -- is warranted because of the promise of progress notwithstanding any costs or setbacks encountered along the way, and that opposition to such research ultimately can and should be overcome. Associated with this is an apparent assumption that we can rely upon notions of informed consent and individual choice to

adequately address any ethical concerns. This may be a reflection of a general societal bias for optimism, reflected in a presumption of benefit from science, technology, and medicine.

Two scenarios from the second session materials, and a few newspaper articles about recent developments in genetic medicine and law give rise to significant questions about our assumptions on informed consent, intended consequences, and individual rights to choose. Before discussing those scenarios and developments, research into assumptions is reviewed.

After Decades of Research, Where are Approved Gene Therapies?

According to recent news reports, despite decades of extensive effort, as yet there are no approved safe medical gene treatments:

There have been more than 800 gene therapy studies involving 5,000 U.S. patients since the NIH approved the nation's first human gene transfer study in 1989. Yet there are no approved therapies despite 17 years of research, and the only major success - a cure for the rare inherited immune disorder known as "bubble boy disease" - came with a high cost: leukemia linked in 2003 to the virus that delivered the treatment (Johnson & Tanner, 2007).

Optimism, the Power of Positive Thinking, and Realistic 'Negative' Thinking

Optimism here is akin to general positive thinking: a blended belief that this is a just world in which good things happen, and that we help achieve these good things through self-fulfilling good thoughts -- that believing in positive outcomes will cause positive outcomes. Optimism here is differentiated from realism -- a more objective rational appraisal of risks and rewards. In other words, optimism is hope and belief in positive outcomes in the face of contrary evidence: optimists here significantly underestimate risks. Optimism is opposed to 'negative' thinking -- thinking that is skeptical or critical and focuses on problems, not positive thinking. Optimists here may cite studies associating positive thoughts with positive health and social results, as general support for optimism and against 'negative' thinking.

"One undoubtedly feels more secure if the world seems like an orderly and predictable place." This desire manifests itself in a belief called the "just world theory." *** People differ in their tendency to believe in a just world, but most subscribe to this belief to some degree (Rachlinski, 1998).

As University of Pennsylvania researchers have observed:

Positive psychology is different from positive thinking in three significant ways. First, positive psychology is grounded in empirical and replicable scientific study. Second, positive thinking urges positivity on us for all times and places, but positive psychology does not. Positive psychology recognizes that in spite of the advantages of positive thinking, **there are times when negative or realistic thinking is appropriate**. Studies find that optimism is associated with better health, performance, longevity, and social success (Seligman, 1991; Lyubomirsky, King & Diener, 2005), but there is evidence that

in some situations negative thinking leads to more accuracy and being accurate can have important consequences (Alloy, Abramson, & Chiara, 2000). Optimistic thinking can be associated with an underestimation of risks (Peterson & Vaidya, 2003) (FAQ).

There is some suggestion in the University of Pennsylvania literature listings that lawyers and other professionals tend towards more realistic, or 'negative' thinking (Abstract # 146). In turn, this suggests that this 'negative' thinking is part of the role of professionals in our society -- to help us more accurately appraise risks and rewards. Although our current concepts of informed consent and individual choice formally take into account some 'negative' risks, developments in genetic research challenge assumptions about how 'informed' any choice really is, if optimistic biases obscure actual risks and outcomes.

Dr. Gawande (2007) has promoted this aspect of 'negative thinking' for medicine:

We Americans believe instinctively in the power of positive thinking. Whether one is fighting a cancer, an insurgency or just an unyielding problem at work, the prevailing wisdom is that thinking positive is the key — The Secret, even — to success. But the key, it seems to me, is actually negative thinking: looking for, and sometimes expecting, failure.

Negative thinking is unquestionably painful. It involves finding and exposing your inadequacies, which can be overwhelming. And not every problem discovered can be solved. You live in a state of perpetual dissatisfaction.

That's an unhealthy way to be in large parts of life: you don't want to constantly seek out the inadequacies of your children, your looks, your abilities as you age. But in *** caring for the sick and injured? Negative thinking may be exactly what we need.

Therapeutic Misconceptions: Hope versus Reality

Therapeutic misconception is a term used to describe persistent beliefs by test subjects that the experiment in which they are engaged will actually treat or cure them. Appelbaum notes significant cognitive deficits in test subjects who continue to believe they are receiving personal medical care, and he outlines a number of ethical questions regarding treatment versus research.

The issue of therapeutic misconception has been well documented in genetic research. As Steinbrook (2006) has described last year's South Korean stem cell research problems, a significant part of the problem is that those engaged in stem cell and other genetic research use many different cues that increase the chances of confusion leading to misconception, and that providing more information actually may increase the risk of misconception, not decrease it:

Jung and Hyun (2005) corroborate previous claims by the South Korean team that they clearly explained to each prospective subject that they were donating their eggs for

research purposes rather than therapy. We continue to question the extent to which this is practically possible. The therapeutic misconception presents a major challenge for stem cell research in general. *** The inclusion of language describing exactly whom will receive treatment priority is guaranteed to make it difficult to distinguish donations made for therapeutic versus research purposes. *** If informed consent requires a frank discussion of all of the possible future uses of oocytes or somatic cells, it may be necessary to state that the donated material may be used for basic research, for clinical trials, for therapy, and even for future treatment for the donor. In this case, a full description of all the potential uses increases the likelihood that a prospective donor will fail to understand that there are no embryonic stem cell-based therapies currently available. By combining this with an explanation of the goals of the research and a description of why the research is so promising *** ensures that there will be substantial confusion. ***.

The fact that many somatic cell donors were patients with severe spinal cord injuries further increases the likelihood of therapeutic misconception. ***

The language used to describe scientific experiments also makes a great deal of difference in how accurately we convey the nature of stem cell research. We argued, for example, that referring to the process of deriving stem cells by somatic cell nuclear transfer as “therapeutic cloning” reinforces the mistaken impression that experiments are therapeutic in nature. In fact, there is no therapy currently associated with SCNT.

*** However, there is an important distinction between oocyte donation for research and live organ donation for transplantation. Live organ donation has a clearly established clinical value — stem cell research does not. If that should change, we would agree that allowing women to donate oocytes for stem cell-based treatments would be permissible, if conducted properly. But allowing research donation to take place under these circumstances is an invitation for a new kind of therapeutic misconception, and should be avoided at this early stage of scientific development.

As the Arizona Daily Star noted in a recent report on the risk of death from gene ‘therapy,’ the problems go beyond just ordinary risks of any medical procedure -- those engaged in research and therapy can ‘push the envelope’ in their efforts to profit from involvement on the cutting edge:

It was the the 1999 death of Tucson teenager Jesse Gelsinger — the first in a gene-therapy experiment — that brought human testing in this field to a nationwide halt.

Gelsinger, 18, suffered a fatal immune response to the viral carrier of the gene doctors had hoped would control his disease — an inherited disorder that prevented his body from properly processing nitrogen.

The Food and Drug Administration concluded that the injection of this therapy killed him.

The FDA found that University of Pennsylvania researchers violated safety guidelines in multiple ways, including treating Gelsinger despite having hit the safety stop signs at just one-tenth the dose he received. Financial conflicts of interest and arrogance were aggravating factors, according to FDA and Department of Justice reports, his father, Tucsonan Paul Gelsinger, has pointed out (Gene therapy death, 2007).

Given ongoing concerns about continuing therapeutic misconceptions, one team of investigators has proposed further research:

Patients with serious disease who are potential research subjects are routinely described as vulnerable and as disproportionately anticipating direct benefit from participation in early-phase trials. In our 1999-2003 ELSI project, The Social Construction of Benefit in Gene Transfer Research, we explored how benefit in gene transfer research (GTR) is discussed and understood, and whether and how the therapeutic misconception exists in GTR. Our data identified individual, institutional, social, and structural factors associated with vulnerability and the therapeutic misconception in GTR, but we also found that the relationship between expectation of direct benefit for subjects and these factors is complex and may call into question some generally held assumptions. (Henderson).

While we await the results of yet further study, others examine these assumptions from alternative perspectives.

As noted by a prominent pair of authors who have dedicated significant effort to therapeutic misconception (TM):

“Our concerns about TM's impact on informed consent do not derive from the belief that research subjects have poorer outcomes than persons receiving ordinary clinical care. Rather, we believe that subjects with TM cannot give an adequate informed consent to research participation, which harms their dignitary interests and their abilities to make meaningful decisions. Ironically, Miller and Joffe's approach ends up largely embracing the very position that they inaccurately attribute to us: the belief that, with some exceptions, it is only the prospect of poorer outcomes that should motivate efforts to dispel TM. In the absence of empirical studies on the steps required to dispel TM and the impact of such procedures on subject recruitment, it is premature to surrender to the belief that TM must be widely tolerated in clinical research.” (Appelbaum & Lidz, 2006).

As McCluskey (2002) notes in the context of various drugs used to treat ALS:

“While pharmaceuticals presently in ALS clinical trials may have demonstrated benefit in animal models or other systems, they have not been proven effective in humans. Although the informed consent process should make this clear, it has been repeatedly demonstrated that patients fail to appreciate this or do not fully understand that the drug they are agreeing to take has not been proven to be effective. While this is certainly exacerbated by the fact that many patients do not fully read or understand the informed

consent document, individuals desperate for even the smallest possibility of therapeutic benefit are particularly likely to fall prey to the therapeutic misconception and may be particularly likely to do so when their treating physician also functions as researcher. The difficulty is compounded by the use of such oxymoronic phrases as *experimental therapy* or *therapeutic clinical trial* by some researchers when referring to clinical research. **Given the desperation and hope for treatments and cures, use of phrases that elicit a therapeutic misperception may be therapeutic misrepresentation.**

“Is the unproven nature of these agents emphasized enough? If so, is this appreciated or understood by ALS patients?”

The internet is packed with a veritable cottage industry of alternative therapy options for ALS patients. Some web sites include testimonials from ALS patients who have been helped or even “cured” by such treatment. Others sites remark that they have seen “good results” in ALS patients treated with their particular brand of alternative therapy. Although none of these treatments have been proven with scientific rigor to benefit ALS patients, providers of *** stem-cell infusions *** offer unproven “treatment” for a monthly price that may be equal to, if not greater than, the cost of established therapy. ALS patients and their families, vulnerable because of the devastating physical and psychological toll taken by the disease, are almost certainly unable to truly understand the fundamental difference between alternatives and established therapy or to rationally evaluate the veracity of testimonials and therapeutic claims.

*** It is essential that patients with ALS and their families remain hopeful but grounded in reality. As a clinician, I do everything in my power to keep hope alive, while remaining realistic about future decline and the need for advance planning. For some patients, maintenance of hope does involve the use of unproven, experimental and/or alternative agents. Although this may create a sense that one is “fighting” the disease or “doing everything that I can,” I am concerned that the false hope engendered by the therapeutic misconception and misrepresentation may, at times, be harmful financially, psychologically and even physically to the patients that I am trying to benefit.”

This tension between those trying to provide ‘hope’ to patients, while still trying to ground research subjects in reality, is further described in again discussing the South Korean scandal. We shouldn’t simply assume that researchers and those supporting research are necessarily objective and realistic -- they are humans subject to the same temptations to advance careers and engender hope:

Jonathan Moreno, the cochair of the National Academies committee and a professor of biomedical ethics at the University of Virginia, said in an interview that the recommendations were justified by the sensitivity of egg donation for stem-cell research and by uncertainties about the actual risk of severe complications in donors. The committee's recommendation has been criticized — for example, by John Robertson of the University of Texas School of Law at Austin, who has written extensively on stem-cell research. In a commentary on a bioethics Web site, Robertson said the committee

"made a political choice to get the field moving, not an ethical one grounded in sound analysis."

In the aftermath of the South Korean scandal, there is uncertainty about how many research groups will have the requisite approvals and funding for research on somatic-cell nuclear transfer, the number of donors they will seek, and whether enough women will volunteer if their only monetary compensation is reimbursement for expenses. Some have expressed concern that women who choose to donate will primarily be the friends and relatives of persons with diseases or disabilities, who may have overly optimistic notions of the potential for translating the early basic research into therapies. The debacle in South Korea may discourage egg donation. Conversely, the extensive publicity about the need for egg donors could motivate more women to consider volunteering. Given the passions and pressures associated with stem-cell research, there is a continuing potential for secret payments and other problematic practices.

Other unresolved issues are the standards for informed consent and, more broadly, for the ethical derivation of stem cells. *** Although international consensus is desirable, the inherent complexity of the issues will no doubt make it difficult to achieve (Steinbock, 2006).

The report goes on to note similar problems arose in treating breast cancer in the 1990s, where fraud in reporting positive results led to initial irrational exuberance in promoting therapeutic misconception:

High-dose chemotherapy in breast cancer continues to be a controversial subject. Following an era in which this treatment modality was considered by many to represent a standard of care for patients with high-risk primary breast cancer, many physicians and most of the public now believe that high-dose chemotherapy is both excessively toxic and ineffective. This precipitous shift of opinion has been caused by the publication of a small number of randomized studies that did not show benefit for the high-dose approach. In addition, a scientific misconduct investigation has revealed that the author of the only two randomized studies of high-dose therapy that showed a significant benefit falsified data. This sequence of events is highly unfortunate since both the earlier uncritical belief in the efficacy of high-dose chemotherapy and the more recent rejection of this modality are equally unreasonable and scientifically unsound (Rodenhuis, 2000).

This optimism bias and associated therapeutic misconception is identified as 'presumed benefit' in this study of bone marrow transplantation, and its implications for gene therapy:

Few stories in medicine are as sobering as the American experience with autologous bone marrow transplantation (ABMT) for treating breast cancer. It is a story of young women dying from aggressive disease, well meaning physicians trying to be equally aggressive in treating it, and lawyers arguing that insurers should pay the bill. It is also a story of professional interests, weak research, financial gain, politics, and fraud. Because of its potential relevance to complex cancer therapies currently in development (such as gene therapy) we recount here the story and its lessons.

For over 10 years bone marrow transplantation for breast cancer was seen as an example of the general dilemma about who should pay for costly new life saving therapies

This characterisation obscured the more basic question: Did it work?

Intermediate outcomes and inadequate controls made preliminary evidence misleading

Statements by physicians in the literature and the general press reinforced the presumption of benefit, as did the decision of government bodies to mandate insurance coverage

The findings of major randomised trials did not support the use of the therapy

This experience provides lessons relevant to complex cancer therapies currently in development

For over 10 years desperately ill women had sought bone marrow transplantation as their best chance for survival. Many physicians encouraged this judgment. Fearing bad publicity and lawsuits insurers reluctantly agreed to pay the considerable charges. A strong presumption of benefit and equally strong financial interests impeded progress towards finding an answer.

The obvious lesson from these events was articulated in the *New York Times* by two of the treatment's most visible critics. "As a society we have to accept that rigorous evaluation of a new treatment is essential . . . Skipping this step may seem like a compassionate act, but it can have devastating consequences."

It is important to remember that preliminary evidence can be misleading: intermediate outcomes (such as response rates) may not correlate with survival, and historical controls may not be comparable. And proponents can be persuasive. The lesson is familiar: it is the case for randomisation. Future research may still show the utility of a chemotherapeutic regime for breast cancer which requires autologous bone marrow transplantation, but for now this story serves as a good example of why scepticism is important in medicine. There are also less obvious lessons.

Accepting that new therapies are experimental is difficult in our culture. Given the increasingly commercial nature of medicine, we can expect aggressive promotion of new therapies. Without authoritative statements saying otherwise, benefit will be presumed and enrollment in randomised trials will suffer.

[P]ublic officials should not mandate coverage in the absence of clear data. ***

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Finally, the news media watchdog role should be extended to health care. The media was slow to see that there was more to the story than the question of how to pay for a costly, new, life saving therapy. Proponents were successful in characterising the case against transplantation as simply about money. Yet proponents of "advances" will always be more vociferous than detractors: they usually have stronger interests (both professional and financial) in arguing for a particular technology than detractors have in arguing against it. Given a public primed to believe in medical breakthroughs, the press should focus on evidence of effectiveness before raising arguments about money. All would be well served by a press that displayed the same scepticism about pronouncements from medicine as it does with pronouncements from government (Welch & Mogielnicki, 2002).

Other researchers have emphasized the perils of proceeding with gene research in such circumstances:

As the NRC-IOM report highlights, it is necessary that prospective donors recognize the large gap between research and therapy. This is particularly important in frontier areas of research where therapeutic impact in humans is unproven. Because it is likely that oocyte donors will be recruited from individuals with diseases and disabilities or their close family members, researchers must make every effort to communicate to these volunteers that it is extremely unlikely that their contributions will directly benefit themselves or their loved ones. Also, it is nearly certain that the clinical benefits of the research are years or maybe decades away. This is a message that desperate families and patients will not want to hear. Their vulnerability and the risks of oocyte donation make it imperative that prospective donors are adequately counseled and that risks are weighed carefully against a realistic assessment of benefits before allowing research to proceed. Donors who are family members or friends of patients hoping to benefit from downstream stem cell research are more vulnerable than the so-called altruistic donors who are strangers.

The language used to describe the research can reinforce the therapeutic misconception, misleading donors and subjects into believing that research is therapy. This was recognized as a serious problem in so-called "gene therapy" research and has led to recommendations that this research should more accurately be described as "gene transfer research." Similarly, it is important not to use the term "therapy" when what is meant is "research" and not to refer to hESC research as "therapeutic cloning." There is currently no such thing as "therapeutic cloning" and this is not "therapeutic cloning research," nor can we say with any certainty that "cell therapy" is in the near future. Similarly, referring to research subjects as "patients" contributes to confusion. Introducing such terminology increases the likelihood that individuals have been or will be misled into exposing themselves to risk. It is permissible and perhaps even laudatory for women to contribute voluntarily to moving the field forward. But it would be a mistake to allow our language and the enthusiasm of researchers to allow that research to take place through exploitation of vulnerable patients and their friends and family members (Magnus & Cho, 2005).

Genetic Testing Continues to be Promoted Despite Randomized Trials Showing No Benefit, and Possible Detriment, to Older Women

As noted by other researchers:

A randomised trial in the *New England Journal of Medicine* has rekindled the acrimonious debate about the efficacy and appropriateness of testing for chromosomal imbalance (aneuploidy) before implantation in older infertile women having in vitro fertilisation. These women have such a poor prognosis of having a child by in vitro fertilisation that many will latch on to any promise that might improve their odds. This is the second randomised trial that shows no benefit from preimplantation genetic screening, yet advocates are unwilling to accept the findings (Braude & Flinter, 2007).

Assumptions about Modern Man and Religion

As Lilla (2007) has observed in the context of political theology:

Americans have potentially explosive religious differences over *** biological research and countless other issues, yet they generally settle them within the bounds of the Constitution. It's a miracle.

And miracles can't be willed. For all the good Hobbes did in shifting our political focus from God to man, he left the impression that the challenge of political theology would vanish once the cycle of fear was broken and human beings established authority over their own affairs. We still make this assumption ***. Nothing in our history or contemporary experience confirms this belief, yet somehow we can't let it go. We have learned Hobbes's lesson too well, and failed to heed Rousseau's. And so we find ourselves in an intellectual bind when we encounter genuine political theology today: either we assume that modernization and secularization will eventually extinguish it, or we treat it as an incomprehensible existential threat, using familiar terms like fascism to describe it as best we can. Neither response takes us a step closer to understanding the world we now live in.

DISCUSSION

Accumulated Wisdom

Culturally, we have accumulated many sayings capturing various aspects of 'negative' thinking, reflecting more critical, objective views of human nature and action. For example:

Hell is paved with good intentions. (Proverbial, different versions variously attributed)

Man is a rationalizing animal, not a rational one. (Old saw, different versions variously attributed)

Risk comes from not knowing what you're doing.

Buffett, Warren

Regarding the 'cutting edge' -- "Edged tools are dangerous things to handle, and not infrequently do much hurt."

Replier, Agnes

Freedom's just another word for nothing left to lose. Nothing ain't worth nothing but it's free.

Author: Kris Kristoffersen (popularized by Janis Joplin singing Me & Bobby McGee)

We also have identified various ways to approach and account for those 'negatives':

'The word "ethics" is derived from the Greek word ethos (character), and from the Latin word mores (customs). Together, they combine to define how individuals choose to interact with one another. In philosophy, ethics defines what is good for the individual and for society and establishes the nature of duties that people owe themselves and one another.' (Cochran, 2007)

In genetics, we have a term for multiple consequences of manipulating genes. For example:

PLEIOTROPY refers to the observation that a single gene affects two or more distinct and seemingly unrelated traits. Pleiotropy is one of the most commonly observed attributes of genes, with broad implications in genetics, evolution, development, aging, disease, and drug discovery. ... (He & Zhang, 2006)

Our sense of ethics -- how we choose to interact with one another while mindful of what is good for the individual and for society -- is challenged by our encounters with the unfolding options presented by developments in genetics. Many explanations for decisions along the way appear to be post hoc ad hoc rationalizations, rather than reasoning from a priori principles. Many good intentions appear to lead to troubling results. The following case sketches encourage questioning assumptions about informed consent and choice made in discussions about genetics and ethics.

MO' BETTER INFO

Do we really want more information? With respect to informed consent, there is some suggestion that more information simply confuses the subject -- more knowledge is not necessarily better. More information may also present further challenges to decision-making -- the choices offered may be worse than those presented in relative ignorance.

Two related sets of issues highlight problems with assuming basic agreement on increased freedom of choice. The first is set forth in second session program materials. There are two different scenarios dealing with genetically linked deafness, one of which also mentions genetically linked short stature. In both scenarios, many might assume initially that the couples would seek genetic counseling and make decisions based on a desire to have children that are 'normal' or 'above average' as measured by general mores -- 'better' choices that those in a general population might make for themselves and see as reasonable for others to make.

In the first scenario, we do indeed see a 'normal' couple seeking guidance in getting a 'normal' child a second time around, after giving birth to a deaf child. They are not prepared to choose between deafness, addiction, or short stature. In the second scenario, the couple actually seek to replicate their own 'ab'-normal differently-abled type -- deafness -- and plan to abort a 'normal' 'healthy' child. This is not a far-fetched notion: many deaf and short-stature activists advocate for themselves and others in maintaining their particular 'able'-ness. For example, this was aired in the protests regarding a choice for the new Dean of Gallaudet, a deaf college in Washington, D.C., where deaf advocates argued the new dean wasn't 'deaf' enough, and protested cochlear implants promoted by some as a medical 'cure' for deafness (Page, 2006).

Do we approve of such couples' choices to reproduce -- through genetic testing and selection -- what others might consider 'ab'-normalities or 'defects'? Especially when these 'defects' might be associated with additional costs to the rest of society to accommodate them? How is this different from allowing these couples to procreate without genetic testing?

Compare Scenario 1.3 (Disability & Genetic Counseling) with 4.1 (Genetic Testing & Disabilities) <http://www.faithforum.net/moodle/mod/resource/view.php?id=300> with <http://www.faithforum.net/moodle/mod/resource/view.php?id=324>

Law Professor Dorf (2007) sets forth another scenario, this time regarding Downs syndrome. Genetic testing for Downs results in approximately 90 percent abortion rate, and parents of those children with Downs have reacted by trying to educate those pregnant with a Downs fetus to encourage them not to abort. Dorf sets forth at least 2 somewhat contrary reactions: the first is empathy, the second is a suggestion that as a society we shouldn't be encouraging more 'sick' children. The ensuing comment thread thoughtfully lays forth a number of different perspectives, with one response comparing the deaf community issues, and another obesity issues.

This leads to more questions than answers. For example, should we allow such genetic testing? Should we require full information on the various perspectives, in order to have fully informed consent? Who should be involved in the decision?

The second situation is taken from newspaper headlines earlier this year. An Australian 'bioethicist' argued that it was perfectly 'ethical' for a couple to have their 'severely retarded' daughter administered hormones to stunt the daughter's growth, and sterilize her (by removing her sexual organs, including reproductive organs), because it made it easier for the parents to take care of her -- the daughter would be easier to handle and physically manipulate if she doesn't grow, and can't get pregnant (Singer, 2007).

The Gene Treatment Death Scenario

According to the Associated Press report:

A few hours before she died this summer at the age of 36, Jolee Mohr lay in a Chicago hospital so swollen by internal bleeding and her failing kidneys that her husband decided

against bringing their 5-year-old daughter to say goodbye. The girl wouldn't have recognized her mother.

Robb Mohr couldn't bring himself to watch her die and he spent his wife's last hours talking with her helpless and puzzled doctors. One vowed to get to the bottom of the illness, and there were several clues to go on.

The most unusual was this: Jolee Mohr got sick the day after her right knee was injected with trillions of genetically engineered viruses in a voluntary experiment to find out if gene therapy might be a safe way to ease the pain of rheumatoid arthritis. She was dead three weeks later.

The sponsor of this nationwide experiment, Targeted Genetics Corp. of Seattle, has halted the work and 127 patients are being evaluated, according to a company spokeswoman. No other problems have been reported, and the company believes patients were adequately informed of the treatment's risks.

"To me, it's an avoidable death," [husband] Mohr said during an interview at his home amid the cornfields of central Illinois. "And you're going to have to really show me a lot of stuff to convince me that it wasn't."

Still, the 1999 death of Arizona teenager Jesse Gelsinger is the only reported fatality that has been definitively linked with a U.S. gene therapy study, an NIH spokesman said. And Dr. Theodore Friedmann, who once headed the NIH committee that oversees gene therapy experiments, said developments in medicine often come with problems, even death.

Even if gene therapy is found to be the cause of Jolee Mohr's death, Friedmann said, the method remains promising.

"There's no question that this event is tragic for the family and the woman involved," he said. "It does simply point to the fact that we have a lot more to learn."

*** Jolee Mohr had faith in Trapp, her doctor for seven years, her husband said.

"You trust your physician. He's your doctor. You trust him like you do your minister," Robb Mohr said.

Bioethicists talk of a "therapeutic misconception" - a belief among patients in early-stage research that they will get better. Jolee Mohr thought the experimental treatment might relieve the chronic pain in her right knee, her husband said, though this stage of the study was simply to find out if the treatment was safe.

Jolee Mohr signed a 15-page consent form Feb. 12.

The form mentioned some scary possibilities. It said that the genetically altered viruses in the study - called tgAAC94 - "could spread to other parts of your body. The risks of this are not known at this time."

Altered viruses can "damage the DNA in the cells of your body by inserting itself into your genes," it went on. "If this happens, it could put you at risk for developing cancer."

And on page 9, it said unknown side effects could result in "pain, discomfort, disability or, in rare circumstances, death."

"I think it's great that there's companies out there wanting to help people, but I also think there's companies out there that are trying to make millions of dollars on people before they can truly understand what's going on," he said.

"She had nothing to gain from this study," he said. "Why would a 36-year-old mother of a 5-year-old that's going to kindergarten want to participate in something just to see how safe it is on her body? Nothing adds up." (Johnson & Tanner, 2007)

Although the husband's observations may be filtered through a hindsight bias (Rachlinski, 1998), they certainly reflect a strong therapeutic misconception.

RESEARCH

Be careful with what you ask: the following 2 topics again challenge notions that more knowledge is better, and that choices lead to better results. The first looks at our efforts at breeding and selection of animals, specifically dogs. The second looks at genetic testing to prove family relations for immigration purposes.

IT'S A DOG'S LIFE

Do we really want to use genetics to breed humans as we breed other species? During discussions, some relied upon our long history of animal breeding as an example of generally positive results: there was an assumption that genetic selection resulted in getting positive traits, but not negative ones -- in other words, we can choose 'good' genes and weed out 'bad' ones with high accuracy. Recent reports from the headlines should dispel such assumptions, if one reads closely. Alas, a pervading optimism bias may selectively filter out the 'bad' news, notwithstanding long-known multiple effects of single gene manipulation.

Some discoveries grow out of government-financed research aimed at improving human health. Others are paid for by breed clubs carrying out their mission to better their breeds.

...

But because genes are often tied to multiple traits, scientists warn, deliberate selection of certain ones can backfire. The gene responsible for those silver-coated Labradors, for example, is tied to skin problems.

With the genetic curtain lifted, breeders also take on a heavier burden for the consequences of their choices. Whippet breeders who continue to mate fast dogs with one another, for instance, now do so knowing they may have to destroy the unwelcome bullies such pairings often produce.

Many breeders hope this new effort to corral nature will weed out the numerous recessive diseases that plague purebred dogs after generations of human-imposed inbreeding. But some question the wisdom of escalating intervention. Mark Derr, an author who has written about the history of dog breeding, urges everyone to reconsider the goal of genetic purity.

“I always use dogs as the example of why we don’t want to be mucking around with our own genome,” Mr. Derr said. “These people are trying to use DNA tests to solve problems of their own making.”

Still, some proponents of using the DNA palette are proposing to go even further. Dr. Neff, the University of California researcher, has proposed screening successive generations of dogs with DNA tests and breeding only those with genes for traits like stamina and scent detection to create a new breed of dogs to patrol subways and airports. It could be done within a few years, he said, instead of the centuries it took shepherds to breed the sheepdogs that patrol their flocks (Harmon, 2007).

WHO’S YOUR DADDY?

Do you really want to establish parentage through genetic testing?

But modern-day science often unearths secrets long buried. When the DNA results landed on Isaac Owusu’s dinner table here last year, they showed that only one of the four boys — the oldest — was his biological child.

Federal officials are increasingly turning to genetic testing to verify the biological bonds between new citizens and the overseas relatives they hope to bring here, particularly those from war-torn or developing countries where identity documents can be scarce or doctored.

But while the tests often lead to joyful reunions among immigrant families, they are forcing others to confront unexpected and sometimes unbearable truths.

For Isaac Owusu, a widower, the revelation has forced him to rethink nearly everything he had taken for granted about his life and his family.

It has left him struggling to accept what was once unthinkable: that his deceased wife had long been unfaithful; that the children he loves are not his own; and that his long efforts to reunite his family in this country may have been in vain.

But Mary K. Mount, a DNA testing expert for the A.A.B.B. — formerly known as the American Association of Blood Banks — estimates that about 75,000 of the 390,000 DNA cases that involved families in 2004 were immigration cases. Of those, she estimates, 15 percent to 20 percent do not produce a match.

Negative results can suggest an effort to bring in illegal immigrants or distant relatives, officials say, though they note that requests for DNA tests deter illicit activities. An official, who spoke anonymously because he was not authorized to discuss the cases, found no indication of wrongdoing by the families interviewed for this article.

Such genuinely unexpected results hit immigrant families particularly hard because DNA testing sometimes provides the best chance of reuniting with loved ones abroad.

“Sometimes these are complicated families,” said Tony Edson, a deputy assistant secretary of state. “People are learning things that they never knew about themselves.” (Swarns, 2007)

LAW

‘Though law often embodies ethical principals, law and ethics are far from co-extensive. Many acts that would be widely condemned as unethical are not prohibited by law -- lying or betraying the confidence of a friend, for example. And the contrary is true as well. In much that the law does it is not simply codifying ethical norms.’ (Cochran, 2007)

Finally, we explore legal areas where assumptions about more knowledge yields more choice yields better choice are challenged. First is the case of patent laws, and how they may actually restrict choices individuals and societies may make. Second is our fraying two parent model for those who have responsibility for choices regarding reproduction and child care, including health. Last, but not least, is our notion of ‘informed consent’ focusing on the individual, and how different cultures -- and different religious or spiritual traditions -- suggest another approach to choice.

PATENTS ENCOURAGE INNOVATION, DON’T THEY?

A number of commentators have noted the various obstacles our current patent laws might present for the expansion of genetic testing and choice. (Caruso, 2007) We now allow patenting of genes and sequencing, so that some genetic choices would need a license to complete legally. Others have noted that the patent laws may not, in fact, be geared to enhance and encourage innovation, but may instead add to impede it. One commentator has noted that China has long been an innovator, long before notions of private intellectual property developed, and that China still culturally sees many of these kinds of ‘inventions’ or innovations as collective, not individual property.

The well-known author of Jurassic Park, Michael Crichton (2007), has argued against our current patent laws, positing other scenarios:

YOU, or someone you love, may die because of a gene patent that should never have been granted in the first place. Sound far-fetched? Unfortunately, it’s only too real.

Gene patents are now used to halt research, prevent medical testing and keep vital information from you and your doctor. Gene patents slow the pace of medical advance on deadly diseases. And they raise costs exorbitantly: a test for breast cancer that could be done for \$1,000 now costs \$3,000.

Why? Because the holder of the gene patent can charge whatever he wants, and does. Couldn’t somebody make a cheaper test? Sure, but the patent holder blocks any competitor’s test. He owns the gene. Nobody else can test for it. In fact, you can’t even donate your own breast cancer gene to another scientist without permission. The gene may exist in your body, but it’s now private property. ***

The results have been disastrous. Ordinarily, we imagine patents promote innovation, but that’s because most patents are granted for human inventions. Genes aren’t human inventions, they are features of the natural world. As a result these patents can be used to block innovation, and hurt patient care.

For example, Canavan disease is an inherited disorder that affects children starting at 3 months; they cannot crawl or walk, they suffer seizures and eventually become paralyzed and die by adolescence. Formerly there was no test to tell parents if they were at risk. Families enduring the heartbreak of caring for these children engaged a researcher to identify the gene and produce a test. Canavan families around the world donated tissue and money to help this cause.

When the gene was identified in 1993, the families got the commitment of a New York hospital to offer a free test to anyone who wanted it. But the researcher’s employer, Miami Children’s Hospital Research Institute, patented the gene and refused to allow any health care provider to offer the test without paying a royalty. The parents did not believe genes should be patented and so did not put their names on the patent. Consequently, they had no control over the outcome.

In February of this year, Indonesia, in part concerned about rights to genetic material, halted provision of bird flu virus to scientists engaged in public health research (McNeil, 2007).

IT TAKES A VILLAGE TO RAISE A CHILD ... AND MAKE DECISIONS?

But yet another challenge to assumptions has arisen -- which individuals, exactly, have 'rights' with respect to a child. The basic model has been one father and one mother. With the advent of domestic couples and civil unions, this basic model is fraying. As reported recently in the New York Times, at least 2 courts have now expanded 'rights' to more than two.

On April 30, a state Superior Court panel ruled that a child can have three legal parents. The case, *Jacob v. Shultz-Jacob*, involved two lesbians who were the legal co-parents of two children conceived with sperm donated by a friend. The panel held that the sperm donor and both women were all liable for child support. Arthur S. Leonard, a professor at New York Law School, observed, "I'm unaware of any other state appellate court that has found that a child has, simultaneously, three adults who are financially obligated to the child's support and are also entitled to visitation."

The case follows a similar decision handed down by a provincial court in Ontario in January. In what appeared to be the first such ruling in any Western nation, the court ruled that a boy can legally have three parents. In that case the biological mother and father had parental rights and wished for the biological mother's lesbian partner, who functions as the boy's second mother, to have such rights as well.' (Marquandt, 2007)

The concept has been suggested for genetic issues as well:

The idea of assigning children three legal parents is not limited to North America. In 2005, expert commissions in Australia and New Zealand proposed that sperm or egg donors be allowed to "opt in" as a child's third parent. That same year, scientists in Britain received state permission to create an embryo from the DNA of three adults, raising the real possibility that they all could be granted equal legal claims to the child if the embryo developed to term.

Astonishingly, few legal experts, politicians or social commentators have considered the enormous risks these rulings and proposals pose for children. Those who have noticed tend to say they are nothing new, because many children already grow up with several parent figures. But this fails to recognize that stepchildren and adopted children still have only two legal parents (Marquandt, 2007).

So who bears responsibility for whatever risks are involved?

Supporters of the rulings argue that if two parents are good for children, aren't three better? True, some three-parent petitions are brought by adults who appear deeply committed to the child in question. In the Ontario case, the two women and the father all seem devoted to the boy. But in Pennsylvania, the sperm donor, whom the children

called “Papa,” was ordered to pay child support over his objections, and the lesbian co-mothers have already ended their relationship.

What is the harm if other American courts follow Pennsylvania’s example? For one thing, three-parent situations typically involve a couple and a third person living separately, meaning the child will get shuffled between homes, and this raises problems.

A few years ago, along with Norval Glenn, a sociologist at the University of Texas, I compiled the first nationwide study of children who grow up in so-called “good” divorces — that is, families in which both divorced parents stay involved in the child’s life and control their own conflict. We found that even these children must grow up traveling between two worlds, having to make sense on their own of the different values, beliefs and ways of living they find in each home. They have to grow up too soon. When a court assigns a child several parents, some of whom never intend to share a home, they consign that child, at best, to a “good” divorce situation.

Of course, sometimes the three adults might want to live together, which leads to a different set of concerns. As one advocate of polygamy argued in *Newsweek*, “If Heather can have two mommies, she should also be able to have two mommies and a daddy.” If more children are granted three legal parents, what is our rationale for denying these families the rights and protections of marriage? America, get ready for the group-marriage debate.

And these are merely the worries if the three parents cooperate. But, as the Pennsylvania case shows, they may not. Conflicts will undoubtedly arise when three parents confront the sticky, conflict-ridden reality of child-raising, often leading to a nasty, three-way custody battle. Even if they part amicably, they may still want to live in three different homes. In that case, how many homes should children travel between to satisfy the parenting needs of many adults?

Finally, why should courts stop at assigning children only three parents? Some situations involve a couple who wants the child, the sperm donor, the egg donor and the gestational surrogate who carries the pregnancy. If we allow three legal parents, why not five? (Marquandt, 2007)

INDIVIDUAL CHOICE IS THE RIGHT MODEL, ISN’T IT?

For example, some cultures may value consensus and harmony above individual expression, and might prefer group decision-making. This cultural view against individual choice in favor of the group may clash with American legal concepts of informed consent in medical decisions (Engelmeier, 2001, pp. 33-34).

And, of course, one assumption is that in individual choice, the individual concerned is the one who should make the choice. But that was not the case with the retarded child -- her parents made decisions for her. And as noted in the previous scenario regarding more than two parents, if there are disagreements between or among the parents or guardians, who then decides?

Assumptions about rational informed choice also fall apart in the face of persistent therapeutic misconception.

CONCLUSION

So we end near where we started. Optimistic assumptions continue to abound about the beneficence of genetic research. Many believe that scientific and technological progress will redound to the good, in part because we can make choices about when, where, and how to use knowledge, and the more known the better. Many assume allowing individual choice while protecting basic rights will ameliorate any deleterious consequences, such as those arising from past 'forced' programs of eugenics. Assumptions about the paths provided by care, choice, and knowledge are explored. On this odyssey, both God and Devil are in the details.

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