

Ethical Issues in Genetic Testing

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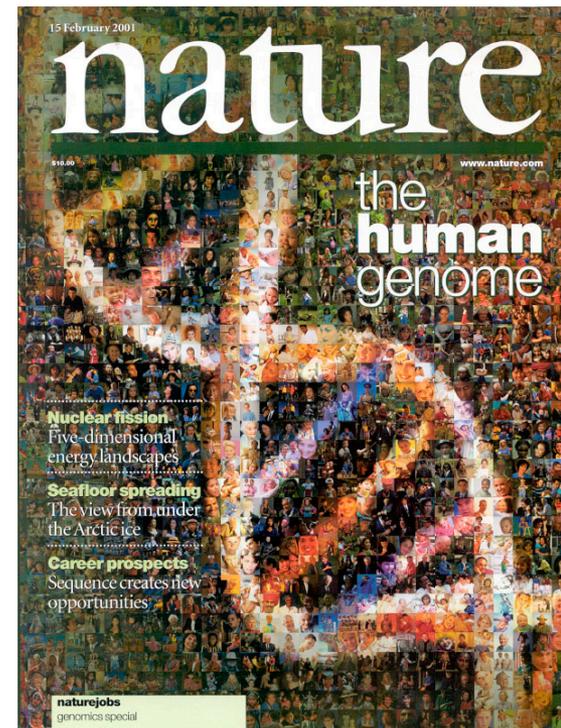
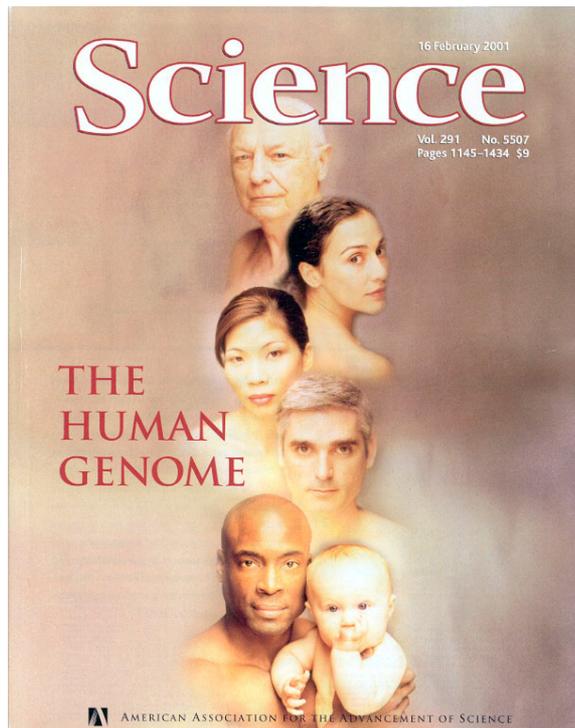


The Human Genome Project

- Thirteen year effort to map and sequence the entire human genome
- Funded by the National Institutes of Health and the Department of Energy
- Began formally in 1990 with funding of \$135 million, increased to \$3 Billion in public funding by 2000



February 2001: The “Working Draft” of the Human Genome



The Human Genome Project: Goals

- Identify all the approximate 25,000 genes in human DNA
- Determine the sequences of the 3 billion chemical base pairs that make up human DNA
- Store this information in databases
- Improve tools for data analysis



Ethical, Legal and Social Implications (ELSI) Program

Founded on the concept that the new technology of gene identification will engender problems that can be minimized if anticipated and dealt with promptly.

First time that the ethical issues of a large scientific enterprise were studied along with the enterprise itself.



What is a Genetic Test?

A genetic test is the analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes.

Task Force on Genetic Testing, 1997



What are these clinical purposes?

Clinical purposes include predicting the risk of disease, identifying carriers, and establishing prenatal and clinical diagnoses or prognoses.



Predicting the Risk of Disease

- Predictive genetic tests are tests that are performed on healthy or apparently healthy individuals with the goal of identifying their risk for developing disease in the future.
- These tests are of two types:
 - Presymptomatic testing
 - Susceptibility testing



Presymptomatic Tests

- Presymptomatic testing involves looking for genetic mutations that have a high penetrance (usually autosomal dominant)
- Tests need to be highly sensitive and specific (few false negatives or false positives)
- Examples include genetic testing for Huntington Disease and early-onset Alzheimer disease



Woody Guthrie

- The folk singer, Woody Guthrie is probably the most famous person to be affected with Huntington disease



Presymptomatic Testing

We can identify healthy individuals who we now know are very likely (virtually 100%) to develop devastating and debilitating diseases at some point in the future which, at this time, have no treatment or cure.



Testing Protocols

- Neurological examination
- Pretest counseling
- Informed Consent
- Results in person
- Follow-up available



Ethical Issues in Presymptomatic Testing

1. Are we better off knowing our fate?
2. Respect for personal autonomy
 - Informed consent
 - Right “not to know”
3. Reluctance to test children
4. Psychological costs for those tested
5. Prenatal testing for late onset disorders



Susceptibility Testing

- Susceptibility testing involves looking for genetic mutations that confer a higher risk for developing disease
- Disorders are usually multifactorial
- Tests have variable sensitivity and specificity
- Examples include testing for Apo-E4 (Alzheimer disease) and BRCA1 and BRCA2 (breast cancer)



Susceptibility Testing

- Test results of this type do not mean that disease will inevitably occur or remain absent; they replace an individual's prior risk based on population data or family history with risks based on genotype.



Ethical Issues in Susceptibility Testing

1. Education and counseling for those at risk
2. Test interpretation can be complex
3. Potential for increased monitoring and possible treatment
4. What counts as “useful information”



The Angelina Jolie Effect

- When Angelina Jolie went public with her genetic test results and subsequent double mastectomy, interest in genetic testing for breast cancer spiked considerably



Carrier Identification

Identifies individuals who do not themselves have a particular disease but who are at risk for having a child with a particular disease

Carrier testing involves individuals known to be at high risk because of family history (testing a woman whose sister has a son with cystic fibrosis)

Carrier screening involves testing individuals with no family history (testing all Caucasian women of child bearing age for cystic fibrosis)



Examples of Carrier Screening

- Tay Sachs disease in Ashkenazi Jewish populations (1/27)
- Sickle cell anemia in African American populations (1/13)
- Cystic fibrosis in Caucasian populations (1/25)



Ethical Issues in Carrier Screening/Testing

1. Respect for individual's/couples' beliefs and values concerning tests taken for assisting reproductive decisions
2. Mutations for certain diseases may have a higher prevalence in certain ethnic populations raising the issue of stigmatization
3. Few choices available to those identified as carriers (refrain from childbearing, donor egg or sperm, PGD)
4. Obligation to offer education and counseling



Prenatal Genetic Testing

- Testing of the fetus prior to birth in order to identify genetic mutations that may cause disease.
- Aim is to enable parents to have children they otherwise would not have been willing to have because of a fear of birth defects or genetic disease.



Examples of Common Prenatal Tests

Approximately 2.5 million pregnant women are screened each year to see if their fetuses are at high risk for Down syndrome or neural tube defects.



Ethical Issues in Prenatal Testing

1. Respect for individual's/couples' beliefs and values is crucial
2. Ideology of non-directiveness is compromised by the fact that you are offering a test for a specific disorder
3. Potential for increased pressure on couples not to have children who deviate from normal.
4. Possibility of decreased tolerance and fewer resources for those with disabilities
5. Possible termination of fetus based on ambiguous information





*"The good news is that you will have a healthy baby girl.
The bad news is that she is a congenital liar."*

Newborn Screening

- Screening newborns shortly after birth to identify genetic conditions
- The aim is to identify conditions that are treatable in order to begin treatment as soon as possible to prevent serious mental or physical handicaps.



Criteria for Effective Newborn Screening Programs

- Treatment is available.
- Early treatment can reduce or eliminate permanent damage
- Disorder would not be revealed in newborn without a test
- Rapid and economical laboratory test is available that is highly sensitive and reasonably specific
- Condition is frequent and serious enough to justify the expense of screening
- Societal infrastructure is in place to inform the newborn's parents and physicians of the results, confirm the results, begin treatment and offer counseling



Changing Criteria for the Justification of Newborn Screening Programs

- Traditionally, the major justification for all newborn screening programs was for the benefit of the child
- 2005 guidelines from the ACMG expanded that justification to include a benefit to the family as well as a benefit to the public, such as contributions to the advancement of science
- This expanded justification could include any test
- Somewhat concerning as in most states, newborn screening is mandatory and parental permission is not sought
- <http://mchb.hrsa.gov/screening>



Mixed Responses

- 2008 President's Council on Bioethics reiterates that screening should follow classic criteria
 - President's Council on Bioethics (2008) *The Changing Moral Focus of Newborn Screening*
- 2013 American Academy of Pediatrics policy statement reaffirms that screening decisions be based on child's best interest
 - American Academy of Pediatrics (2013) *Ethical and Policy Issues in Genetic Testing and Screening of Children*



Ethical Issues in Newborn Screening

1. Voluntary vs mandatory testing
2. Lack of informed parental consent
3. Lack of education and counseling of parents
4. Technology creep-tests often added to panel without assessing benefit to child
5. Necessity for treatment and follow-up to prevent damage
6. Increasing pressure to use residual samples for population based research raising issues of informed consent for research



Ethical Issues in Newborn Screening

7. Parental anxiety about false positive results
8. Harm to parent child relationship by parental misperceptions about meaning of child's carrier status
9. Possibility that children will be subjected to needless and potentially risky, medical interventions or monitoring



Genetic Libertarians

- Genetic libertarians who feel that patients have a right to a full and complete accounting of all possible risks conveyed by both established and novel variants found through genetic testing, or even variants of unknown significance in disease genes



Genetic Empiricists

- Genetic empiricists who believe that there is insufficient evidence about the penetrance of most pathogenic variants in the general population to warrant the sharing of incidental findings and that it is irresponsible to create the psychological burdens of being a “patient in waiting” or to expose patients to unnecessary surveillance or diagnostic testing



General Ethical Issues Related to Genetic Testing

- Lack of knowledge
- Direct marketing of tests to consumers
- Fear of discrimination



Lack of Knowledge

Consumers

A recent poll indicated that only 26% of a population-based sample knew what DNA was.

Christensen KD, Jararatne TE, Roberts JS, Kardia SLR, Petty EM (2010) Understandings of basic genetics in the United States: Results from a national survey of black and white men and women. *Public Health Genomics* 13:467-4.

Physicians

A 2012 study in *The Cancer Journal* reviewed dozens of cases in which doctors ordered wrong or unnecessary genetic tests, misinterpreted the results of correct tests, or failed to refer a patient to a genetic counselor despite a strong family history of a genetic condition

Brierley KL, Blouch E and Cogswell W (2012) Adverse events in cancer genetic testing: Medical, Ethical, Legal and Financial Implications. *The Cancer Journal* 18: =



Lack of Knowledge

- In a study funded by the National Human Genome Research Institute 74% of more than 200 internists said their knowledge of genetics was “very to somewhat poor”, yet 44% admitted to going ahead and ordering genetic tests anyway
- Klitzman R, Chung W, Marder K et al. (2013) Attitudes and practices among internists concerning genetic testing. *J Genet Couns* 22:90-100.



Direct Marketing

- In July of 2001, Myriad Genetics, based in Salt Lake City, Utah announced that it was preparing to market genetic tests directly to consumers
- Primarily genetic tests to identify risks for certain familial cancers (breast and ovarian cancer) which are only appropriate for a relatively small number of individuals but for which Myriad held the patents
- This decision was made primarily because the sales of these tests were not up to projections





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Helen Mendel
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Discrimination

- Insurance
- Employment
- Law Enforcement





"Unfortunately, you have what we call 'no insurance.'"

Genetic Information Nondiscrimination Act- GINA

- Signed into law on May 21, 2008
- Protects consumers from discrimination by health insurers and employers on the basis of genetic information
- Health insurance regulation took effect in May 2009 and employment regulation in November 2009
- Does not apply to those in the military



Affordable Care Act

- Prohibits insurers from discriminating against persons with pre-existing conditions





"Very nice résumé. Leave a sample of your DNA with my secretary"



Employment

- Between 2000 and 2014, the cost to employers of providing medical and dental insurance increased 10 – 15% per year
- By 2013, health insurance benefits comprised 11.7% of employee wages and benefits
- Employers have a major incentive to have a healthy workforce



Law Enforcement

- The greatest advance in forensic science in the past decade has been in the application of DNA analysis
- The ability of DNA analysis to exclude suspects with virtually 100% certainty may be the single largest cause for a major shift in attitudes towards the death penalty in this country



Function Creep

- Example: In 1930 the social security number was invented to be used only as an aid to access the new retirement program, it is now a universal identifier
- DNA banks established by the military to identify the remains of soldiers have been accessed in criminal cases occurring on or around military bases



Sample Collection

- In less than a decade sample collection for forensic data bases has gone from:
 - Convicted sex offenders
 - All violent offenders
 - All persons convicted
 - Juvenile offenders in 28 states
 - All persons arrested





*"Please accept the apologies of this court. You're free to go now,
and, by the way, here's your DNA back."*

Summary

- The completion of the Human Genome Project in 2003 will provide a wealth of genetic information and an ever increasing array of genetic tests
- Results of testing can help individuals make important decisions about their own health and about reproductive decisions in the face of genetic risk
- There is a lack of education about genetics in general and the proper use of genetic testing on the part of consumers and health care providers



Summary

- The use of genetic test results by third parties- insurers, employers, law enforcement- may be cause for concern
- It remains to be seen whether recent laws passed to prevent discrimination in employment and health care actually do so



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