

Ethical and Social Implications of Genetic Testing for Communication Disorders

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Topics for this Discussion

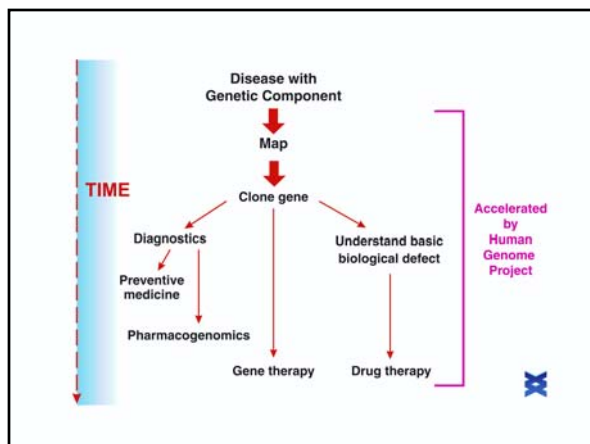
- The Human Genome and Ethical Considerations – A Model
- Ethical Complexities of Genetic Information at the Individual and Societal Levels
- Examples from Genetic Hearing Loss

Ethical Concerns of Genetic Information

- Individual and family concerns – privacy, discrimination, family health data, reproductive options
- Societal concerns – race, ethnicity, group identity
- Translation of genetic tests to clinical practice
- intellectual property and commercialization
- Non-medical uses of genetic testing

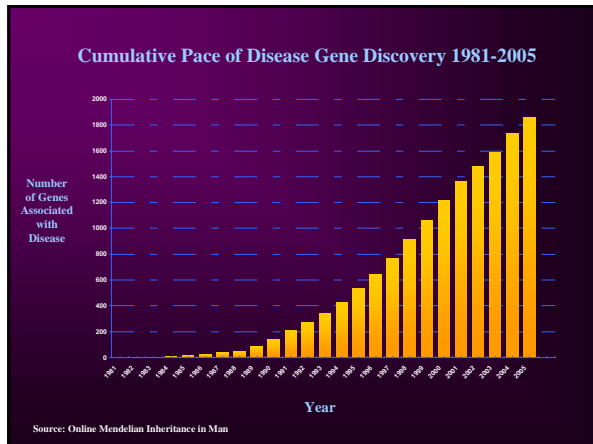
Ethics and the Human Genome

- How have studies of the human genome help define and address ethical, legal and social implications of testing for genes?
- Can these lessons be applied to addressing these issues as applied to communication disorders?



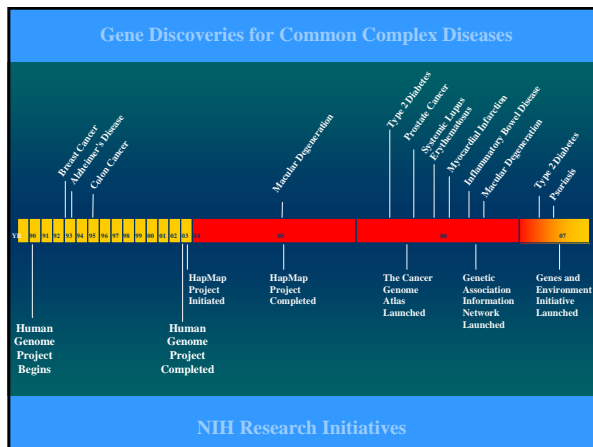
Modes of Inheritance

- Mendelian Inheritance
 - caused by mutations in a single gene
- Multifactorial, Complex or Non-Traditional Inheritance
 - caused by several genes and environmental factors, each of which may have only a small, additive effective on causing the trait



Progress in Characterizing the Human Genome

- Technological developments made possible through the Human Genome and other publically and privately-funded projects have accelerated gene discovery for both Mendelian and complex traits
- Several of the publically-funded genome projects have also included an ethics component



Goals of the Human Genome Project (HGP)

- Mapping and sequencing the human genome
- Mapping and sequencing model organisms
- Publicly available computerized data collection, storage, and analysis
- Technology development and training
- Ethical, legal, and social issues (ELSI)

Current Focus of the National Human Genome Research Institute

- Identification of the full complement of human proteins
- Exploration of the relationship between genetic sequence and phenotype
- Study of the interaction of proteins with each other
- ELSI studies and education



Current Focus of the National Human Genome Research Institute

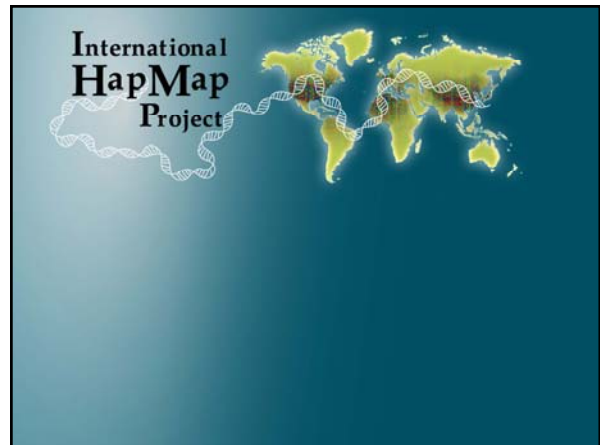
- ELSI component
 - Intellectual property
 - Translation of genetic information to improved human health
 - Use of genetic information in non-health situations
 - Impact of genomic research on the concepts of race, ethnicity and group identity

The Enduring Ethical Issues of Genetic Information

Genetic information can disclose essential secrets about:

- **F**amilial role
- **A**ncestral origins
- **C**ommunity memberships
- **E**thnic affiliations

Juengst ET (2004). FACE facts: why human genetics will always provoke bioethics. *J Law Med & Ethics* 32(2): 267-275.



International HapMap Project

- Conducted from 2003 – 2005
- The HapMap is a catalog of linked genetic variants that occur as part of haplotypes.
- Haplotypes were examined to determine how they are distributed within and among different populations of the world.
- Many haplotypes have been found which contain DNA variants that are useful in identifying disease-causing genes.

The International HapMap Project: Ethical, Social, and Cultural Issues

- The goal of the HapMap project was to develop a resource to facilitate future studies that relate human genetic variation to health and disease.
- Because the HapMap facilitated comparisons among both individuals and groups, the ethical issues were especially challenging.

HapMap - Populations Included

- Yoruba (Ibadan, Nigeria)
- Han Chinese (Beijing, China)
- Japanese (Tokyo, Japan)
- Utah residents with Northern & Western European ancestry

Concerns Raised by Labeling Populations

- Group stigmatization, discrimination (if a higher frequency of a variant associated with a stigmatizing disease is found in one population and the results are improperly over-generalized)
- Population history studies (challenge to religious convictions, established legal or political claims)
- Reification of race (a mostly social construct) as a highly meaningful biological construct

Other Concerns

- Too much focus, money spent on genetic research, not enough on ensuring access to basic health care
- Too much focus on genetics, not enough on environment, as contributor to disease risk
- Intellectual property, commercialization (and no immediate benefit to participating communities)

Addressing Group Concerns Through Community Engagement

- Also called community consultation, public consultation, community review
- A chance for communities to share their views about the ethical, social, and cultural issues the Project raises, provide input on how their samples should be collected and described, and identify any other relevant community concerns

Methodologies for Community Engagement

- Individual interviews
- Focus groups
- Community surveys
- Town meetings

Why is genetic information ethically complex?

- Family health data
- Parentage
- Reproductive options
- Future health risks
- Who/What we are – community, racial and ethnic identities

Why is genetic information ethically complex?

Non-medical uses of genetic information:

- insurance
- employment
- criminal law
- litigation
- domestic relations
- immigration
- settle estates
- paternity
- kinship



Ethical Considerations of Genetic Testing

- The availability of genetic tests does not mean that their routine use is appropriate.
- Each genetic test has risks and benefits.
- Information obtained through genetic testing can be empowering.
- Information obtained through genetic testing can disrupt family relationships, can be used as the basis for discrimination or can be psychologically harmful.

Ethical Concerns of Genetic Information

- Additional concerns related to the identification of genes for complex traits:
 - Overhype by the media and health care providers about the causality of genetic variants
 - Patient misunderstandings regarding the predictive power of tests for genetic variants
 - Should testing for genetic variants which may confer only a small risk for a disorder be used for reproductive decision making?

Potential Ethical Considerations Related to Communication Disorders

- Is it ethically responsible to offer prenatal diagnosis for a genetic variant that may predispose to a communication disorder?
- Could genetic screening to identify individuals who are predisposed to communication disorders lead to psychological harm, stigmatization and discrimination?

Ethical Considerations of Genetic Testing

- Some individual concerns regarding genetic testing:
 - Informed consent
 - Privacy/confidentiality issues
 - Discrimination
 - Access to the test results

Ethical Considerations of Genetic Testing

- Informed Consent:
 - The benefits as well as the risks of a genetic test must be fully disclosed.
 - Psychological burden
 - Impact of the information on employment, insurance coverage, and family relationships
 - These risks are especially applicable to later-onset conditions (heart disease, cancer, Alzheimer's disease, etc.).

Ethical Considerations of Genetic Testing

- Privacy/Confidentiality:
 - Confidentiality of medical records (is privacy possible in the era of electronic databases?)
 - Who has access to the results of genetic testing (employers, insurance companies, relatives)?
 - Genetic data are family data.
- Discrimination
 - Can employers and insurance companies deny jobs and insurance coverage based on the results of a genetic test?

Role of State and Federal Laws

- State laws on genetic privacy (40 – insurance, 27 – employment)
 - <http://www.nhgri.nih.gov/11510227>
- HIPAA (Health Insurance Portability and Accountability Act of 1996)
- Federal legislation has been enacted to protect federal workers from genetic discrimination.

Ethical Considerations of Genetic Testing

- Is adequate genetic counseling provided pre- and post-testing?
- Are primary care physicians likely to know how to interpret genetic tests or have the time to counsel families about using (or not using) the information?

Genetics and Medicine



Types of Genetic Testing

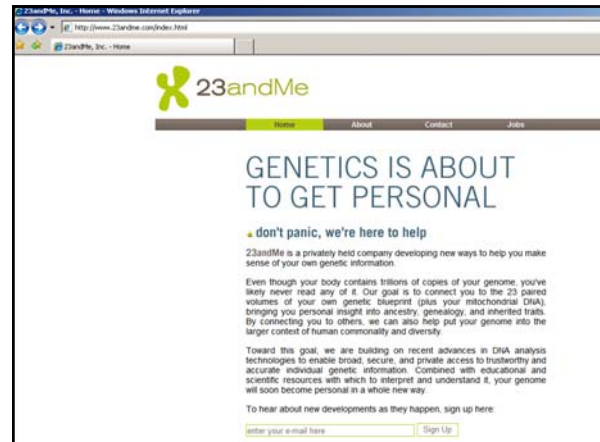
- Carrier screening
- Diagnostic screening
- Newborn screening
- Predictive (presymptomatic) testing
- Prenatal Diagnosis

Some are routinely offered through commercial laboratories, some are available only through carefully controlled research or clinical protocols, some are directly marketed to consumers.

Direct-to-Consumer Genetic Testing

- *BRCA1* & *BRCA2*
- Hemochromatosis
- Cystic fibrosis
- Paternity tests
- Geneologic testing
- Non-medical tests: nutrition, aging, behavior

- Marketing directly to consumers and “home testing” kits available on the Internet



Misunderstandings about the Clinical Power of Genetic Tests

- Example from research on autism:
 - Autism is an extremely heterogeneous disorder that occasionally (about 10% of cases) has a single gene or chromosomal etiology (e.g. fragile X or Rett syndrome, tuberous sclerosis, chromosome 15q11 – q13 duplication).
 - Autism is largely a multifactorial disorder with a strong genetic component, caused by susceptibility genes and environmental factors that remain largely unknown.

Tabor HK, Cho MK (2007). Ethical implications of array comparative genomic hybridization in complex phenotypes: points to consider in research. *Genet Med*, 9(9): 626-631

- Examined recent literature describing research using microarray and other technologies to identify genetic variants associated with autism.
 - There was substantial variation and inconsistency in criteria used to determine if genetic variants were causal.
 - The language used in scientific publications tended to overestimate the clinical relevance of causal relationships.
 - Results tended to be over generalized for the general population.
 - All of these factors were thought to lead to media hype and patient misunderstandings about the clinical power of these tests.

Genetic Counseling

- In any genetic testing, pre- and post-counseling by a qualified professional is critical.

- As genetic testing moves into the hands of primary health care providers and direct to consumer, the chance that adequate pre- and post-counseling will occur is diminished.

Ethics and Public Policy

Unfortunately, decisions to introduce genetic tests into clinical practice are based on:

- consumer demand
- professional practice
- legal forces

rather than.....

Ethics and Public Policy

... a thoughtful evaluation of:

- accuracy and reliability
- provisions for consumer and professional education and
- public participation in evaluation issues related to testing.

What Often Drives the Use of New Genetic Tests

- Gene discovered
- Gene patent issued/licensing agreement(s) (single or multiple which may increase or decrease competition and pricing)
- Company(ies) develops commercially available genetic test (rarely for rare diseases)
- Company markets genetic test (to doctors and increasingly directly to consumers)
- Test is used in clinical care appropriately and sometimes inappropriately

Evidence-Based Practice

- Also known as outcomes-based or translational research.
- Professionals in the fields of genetics and speech, language and hearing sciences increasingly recognize the importance of the use of evidence-based practice to guide the introduction of new technologies, tests and practice to the clinical realm.

Evidence-Based Practice

An Example from Hereditary Hearing Loss:

- A1555G Mutation in the mitochondrial 12S rRNA gene, *MTRNR1*
- mutation in combination with exposure to aminoglycosides results in rapid onset of hearing loss
- prevalent in Spanish, Chinese and other oriental ethnic groups but has also been found in Caucasians, Greeks, etc.
- testing for this mutation has been clinically available for several years

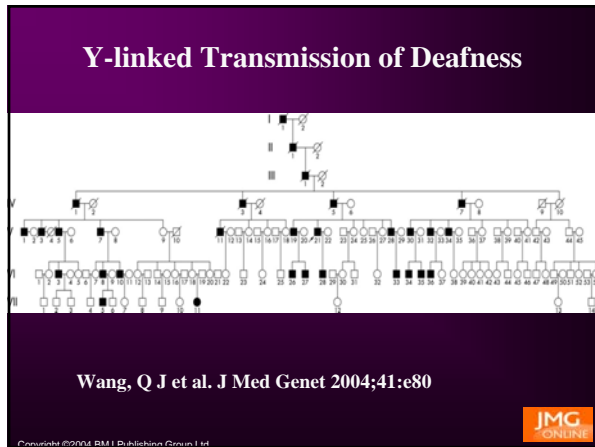
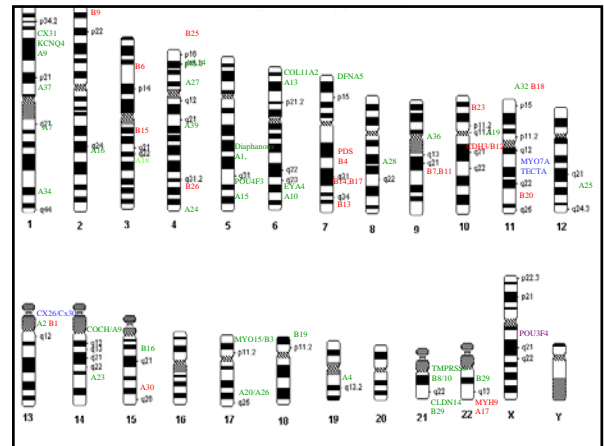
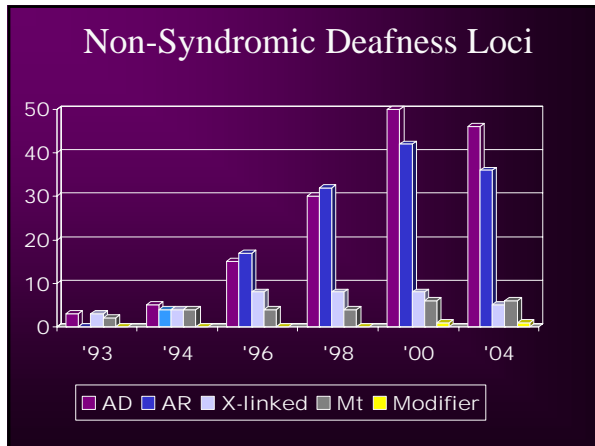
Evidence-Based Practice

- The incremental cost-effectiveness of screening for the A1555G variant was examined in a hypothetical population of patients with cystic fibrosis
- This model predicted small improvements in patient outcomes, counteracted by a lack of cost-effectiveness and the possibility of worse patient outcomes due to avoidance of antibiotic therapy.

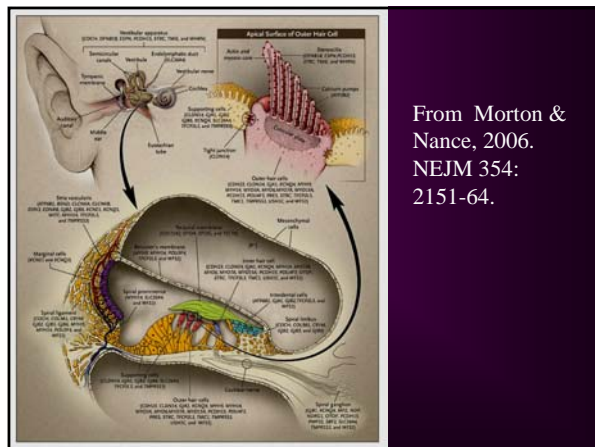
Veenstra et al. (2007). Pharmacogenomic testing to prevent aminoglycoside-induced hearing loss in cystic fibrosis patients: potential impact on clinical, patient, and economic outcomes. *Genet Med*, 9(10): 695-704.

Ethics and Genetics - Examples from Hereditary Hearing Loss

- Mendelian Inheritance
 - 30 syndromic loci mapped
 - 80 nonsyndromic loci mapped
 - DFNA – a. dominant (20 genes cloned)
 - DFNB – a. recessive (21 genes cloned)
 - DFN – X-linked recessive (1 gene cloned)
 - DFNM – 2 modifier genes mapped



- ### Examples of Mendelian Forms of Hearing Loss
- *GJB2* (connexin 26)
 - *MYO7A* (Usher syndrome)
 - *PAX3* (Waardenburg syndrome, Type 1)
 - *SLC26A4* (Pendred syndrome)



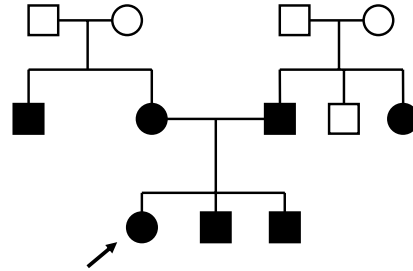
From Morton & Nance, 2006. NEJM 354: 2151-64.

- ### Examples of Complex Inheritance of Hearing Loss
- Presbycusis
 - Noise-induced hearing loss
 - Modifier genes
 - Genetic susceptibility to hearing loss caused by aminoglycoside antibiotics
 - *MTRNR1* (mitochondrial gene encoding 12S rRNA)
 - A1555G mutation

Ethical Issues Related to Gene Identification for Hearing Loss

- Prenatal Diagnosis
- Molecular Newborn Screening
- Genotypic Mate Selection

Assortative Mating in the Deaf Community



Contemporary Attitudes Towards Genetics Among the Deaf

- Attitudes towards
 - genetic testing for deafness in general
 - prenatal diagnosis for deafness
 - the use of genetic testing for partner selection
 - newborn hearing screening and newborn screening for deafness genes

Attitudes Surveys

- Middleton, Hewison & Mueller (1998). Attitudes of deaf adults toward genetic testing for hereditary deafness. *AJHG* 63: 1175-1180.
- Middleton, Hewison & Mueller (2001). Prenatal diagnosis for inherited deafness – what is the potential demand? *J Genet Counsel* 10:121-131.

Middleton et al., 2001

- 644 deaf, 143 hard of hearing and 527 hearing individuals with either a deaf parent or a deaf child
- 21% of deaf, 39% of hard of hearing and 49% of hearing said they would consider prenatal diagnosis for deafness
- 2% of deaf participants said they would consider a therapeutic abortion of a hearing baby

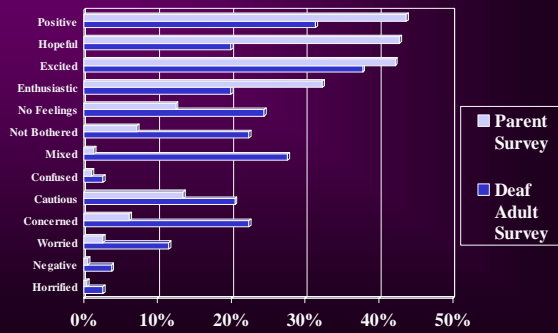
Attitudes Surveys

- Brunger et al. (2000). Parental attitudes toward genetic testing for pediatric deafness. *AJHG* 67:1621-1625.
 - 96 hearing parents of deaf children who had undergone genetic testing
 - the majority had a positive attitude towards genetic testing including prenatal diagnosis, but none said they would use the information to terminate the pregnancy

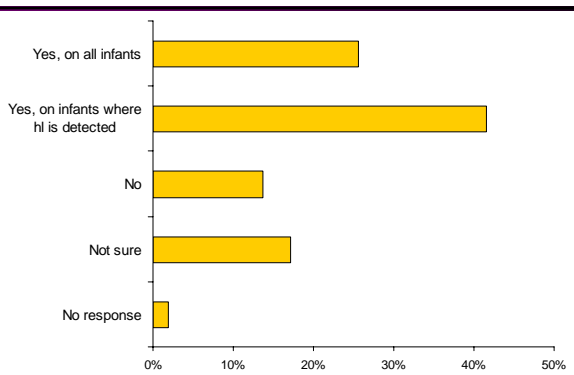
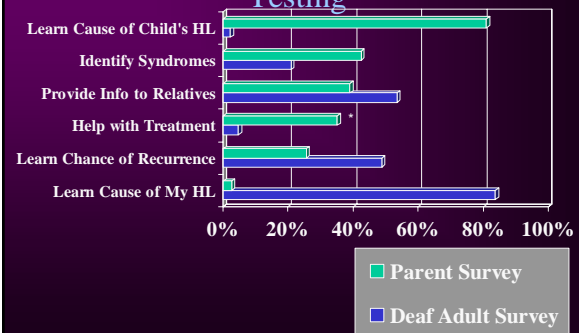
Attitude Surveys

- Stern et al. (2002). Attitudes of deaf and hard of hearing subjects towards genetic testing and prenatal diagnosis of hearing loss. *J Med Genet* 39:449-453.
- Taneja et al. (2004). Attitudes of deaf individuals towards genetic testing. *Am J Med Genet* 130A:17-21.
- Burton et al. (2006). A focus group study of consumer attitudes toward genetic testing and newborn screening for deafness. *Genet Med* 8(12): 79-783.

Feelings about Advances in Genetics of Hearing Loss

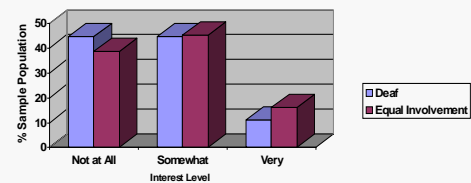


Motivations for Pursuing Genetic Testing

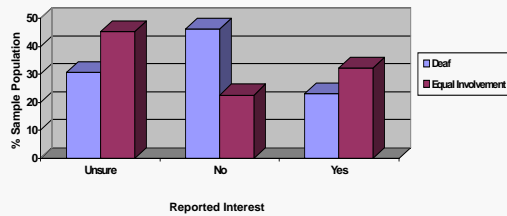


Do you think that genetic testing should be performed on newborn infants to detect genes for deafness/hearing loss?

Interest in Using Genetic Test Results for Partner Selection



Reported Interest in Selecting a Partner Specifically for Having a Child of a Desired Hearing Status



Ryan, Miedzybrodzka, Fraser, Hall (2003). Genetic information but not termination: pregnant women's attitudes and willingness to pay for carrier screening for deafness genes. *J Med Genet* 40:e80.

- 104 non-deaf pregnant women from Scotland were surveyed
- 72% would want to know if they were a carrier of a deafness gene
- 74% would have prenatal diagnosis to determine the fetus' hearing status
- 7% would have a termination if the test indicated the baby would be deaf

Conclusions

- Genetic testing, including testing for genes associated with communications disorders, is ethically complex and an individual and societal level.
- Testing for disorders with complex (multifactorial) inheritance brings additional concerns.
- Evidence-based practice is essential to guide the introduction of new technologies, tests and practice to the clinical realm so that benefits are maximized and risks are minimized.