

Final Progress Report

The Human Genome Project and Mental Retardation: An Educational Program

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Progress

The Arc, a national organization on mental retardation, was funded in February 1996 to conduct an educational program for our members, many of whom are families having a member with a genetic condition causing mental retardation. The project was designed to make our members aware of this scientific undertaking, the Human Genome Program, and to examine critical issues related to genetic discoveries affecting people with mental retardation and their families.

The project focused on three topics where issues affecting families were identified:

- Insurance and employment discrimination based on a person's genes.
- Decisions involving genetic testing, screening and counseling (including prenatal and newborn testing).
- Ethical issues involving genetic therapies that may eventually "cure" mental retardation.

The scope of the original proposal changed as a result of negotiations to reduce the budget. The Arc's remaining three primary aims or objectives are described below followed by a description of the work accomplished.

Objective I. Develop and disseminate educational materials for members/leaders of The Arc to inform them about the Human Genome Project and mental retardation.

We developed a total of eight issues in a series of reports titled Genetic Issues in Mental Retardation and four two page fact sheets (**Appendix A**).

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Reports:

Issue 1 - *An Introduction to Genetics and Mental Retardation*

The first report gives an explanation of the HGP, The Arc's purpose for being involved in ELSI issues and explains the genetic causes of mental retardation.

Issue 2 - *Genetic Discrimination*

Genetic discrimination is one of the most feared results of not having genetic privacy. This report explores what genetic discrimination is, how often it seems to be happening and state/federal legislation that is attempting to prohibit this type of discrimination.

Issue 3 - *Genetic Testing, Screening and Counseling - An Overview*

Deciding whether or not to be tested for a genetic disorder can be one of the more confusing aspects resulting from genetic research. Our report answers the questions many people have about this topic, such as who needs testing, is it harmful or helpful, what are the different types of genetic testing, what is informed consent, how reliable are the results of a test and should children be tested?

Issue 4 - *Protecting Genetic Privacy*

Many people do not know how to protect their genetic information, or realize the need for such protections. This issue gives readers practical guidance on protecting their genetic privacy and explains the importance of doing so.

Issue 5 - *Fragile X Syndrome*

This report was prepared by Don Bailey, Ph.D., the Director of the Frank Porter Graham Child Development Center of the University of North Carolina at Chapel Hill. It gives an easy-to-understand explanation of what fragile X syndrome is, how it is inherited, effects of the syndrome and the challenges facing parents and professionals in identifying educational and therapeutic strategies for people with the syndrome.

Issue 6 - *Gene Therapy and Mental Retardation*

This report explains what gene therapy is, basic gene therapy techniques and discusses ethical issues related to gene therapy. For example, the questions of whether or not gene therapy should be used to treat or cure mental retardation, and should genetic enhancement be used to improve cognitive abilities are examined.

Issue 7 - *Participating in Genetic Research: Considerations for People with Mental Retardation and Their Families*

This report presents information to help families make decisions about whether they should participate in genetic research. Types of genetic research and the risks of participation are discussed, along with issues related to informed consent.

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Issue 8 - Mental Retardation & Developmental Disabilities Research Centers: An Overview of Current Genetic Research

The final report gives readers current information about the latest genetic research involving conditions associated with mental retardation. Five Mental Retardation Developmental Disability Research Centers and their areas of research are highlighted.

Fact Sheets:

Genetic Causes of Mental Retardation - includes easy-to-understand facts and information from the project's first report, *An Introduction to Genetics and Mental Retardation*.

Facts About Genetic Discrimination - provides a brief overview of the information found in the project's second report, *Genetic Discrimination*.

Prader-Willi Syndrome - provides a clear description of the syndrome, explains why it occurs, how common it occurs in families and effects of the syndrome. This fact sheet was reprinted with permission from the Prader-Willi Syndrome Association.

PKU - defines PKU, explains how it is inherited and diagnosed. The fact sheet also points out when babies should be tested and how people with the condition can be treated through the use of a regimented diet.

Evaluation of Materials

Project materials received considerable review from the scientific advisory panel (**Appendix B**). Reports with highly scientific or complex information needed additional review. These reviewers included experts in the field of genetic therapy and genetic privacy issues, a team of genetic counselors from The Children's Medical Center of Dallas and some members of The Arc who are parents of children with conditions associated with mental retardation. The report on fragile X syndrome was actually written by an expert, Don Bailey, Ph.D.

All materials were disseminated to the executive directors and presidents of The Arc's 1,100 state and local chapters, to the national board of directors and to national committee chairpersons. Availability was announced in The Arc's newspaper, which goes to 140,000 members. All materials are now placed on The Arc's Home Page on the World Wide Web. The materials have been added to The Arc's publications catalog. In addition, we continue to respond to other individuals interested in genetic issues. In doing so, we have broadened our audience to include other disability organizations.

Other Information Dissemination within The Arc:

Articles in The Arc's Newspaper (Appendix C).

Four articles were written on topics related to The Arc's Human Genome Education project in the organization's paper, The Arc Today. They include:

- *The Arc undertakes human genome project* (Spring 1996)

- *Genome Project yields publication, discussion* (Winter 1996)
- *Sheep cloning: Good or baaaaad for humans?* (Summer 1997)
- *Clinton recognizes need for anti-discrimination law* (Winter 1997)

Chapter Dissemination

- Some state and local chapters of The Arc advertised the availability of The Arc's reports, including The Arc of Bergen and Passaic Counties (NJ) and The Arc of New Jersey.
- Some chapters reprinted information directly from The Arc's reports and fact sheets in their chapter newsletters, including Tulsa Arc, The Arc of Texas, Arc/Muskegon (MI) and The Arc of Bay County (MI) and The Arc of California.
- Some chapters wrote articles on the project for their chapter newsletter, including The Arc of New Mexico and Parc (Peoria, IL). The Arc of California wrote a three-part series titled, "The Mystery of Genetics."
- Some chapters/organizations requested project staff to author articles for their chapter newsletters, including The Arc of Maryland and The National Conference of Executive Directors of The Arc.

Objective II. Conduct training on the scientific and ethical, legal and social aspects of the HGP and mental retardation using The Arc's existing training vehicles.

Training Materials

Project staff developed a script, overheads and an edited video for an overview presentation on the Human Genome Project and mental retardation which was used by The Arc's staff and national volunteer leaders to conduct workshops nationwide. The training package included a manual with a script, overhead masters, a video introducing the Human Genome Project and handouts. Small group sessions were used to guide participants into discussing three case scenarios that dealt with 1) genetic discrimination in insurance, 2) genetic testing and 3) gene therapy to "cure" mental retardation.

The workshop was piloted with The Arc's Board of Directors and revised based on members' feedback. A second pilot was conducted with The Arc's national Health Promotion & Disability Prevention Committee. The final version of the workshop package was based on this committee's feedback. (The workshop script and overheads are in **Appendix D.**)

Training Events

The Arc proposed to conduct training for its leaders and members at large. The following educational activities were accomplished:

Training for Board of Directors (24 members):

- A Human Genome Project educational activity was placed on the agenda of each Board meeting in 1996 and 1997 (eight meetings).

- The Board participated in the pilot of the workshop package. Fifteen volunteered to conduct the workshop in their local chapter of The Arc. (With no enforcement policy for these volunteers, only two are known to have conducted the workshop. However, one conducted it several times.)

National Level Training

The Arc's National Convention

- Nov. 1996 – Round Table: Genetic Discrimination: Issues for Families – Principal Investigator – 7 participants
- Nov. 1996 – Workshop: Gene Therapy Research and Ethical Issues – Mark Batshaw, M.D. and Principal Investigator– 197 participants
- Nov. 1997 – Round Table: Gene Therapy to Cure Mental Retardation – Ethical Issues, Principal Investigator – 10 participants
- Nov. 1997 – Workshop: Facts and Issues in Genetic Discrimination, Paul Billings, M.D., Ph.D. – 30 participants
- Nov. 1997 – Workshop: The Human Genome Project and Ethical Issues, Deborah Cohen, Ph.D. and Maxine O'Kelley, Co Chairmen, The Arc's Health Promotion and Disability Prevention Committee – 80 participants
- Nov. 1998 – Workshop: The Human Genome Project and Ethical Issues, Deborah Cohen, Ph. D. – 22 participants

Total Participants - 346

Summer Leadership Training

- July 1996 – Luncheon presentation by principal investigator reviewing ethical, legal and social issues related to HGP of concern to members of The Arc – 100 participants
- July 1997 – Workshop, The Human Genome Project and Ethical Issues, Principal Investigator – 60 participants

Total Participants - 160

State Conventions – Sessions Conducted by Principal Investigator

- June 1996 - Luncheon address, The Arc of Michigan – 70 attendees
- April 1997 – Workshop, The Arc of New Mexico – 12 attendees
- April 1997 – Plenary session, The Arc of Indiana – 140 attendees
- May 1997 – Two workshops, The Arc of Oregon – one for chapter executive directors, one for families – 24 attendees
- May 1997 – Plenary session and workshop, The Arc of Maryland – 90 attendees at plenary; 15 at workshop
- June 1997 – Workshop, The Arc of the District of Columbia – 18 attendees
- October 1997 – Workshop, The Arc of Colorado – 15 attendees
- October 1997 – Workshop for local chapter executive directors sponsored by The Arc of Massachusetts – 14 attendees
- May 1998 – Workshop, The Arc of Illinois – 20 attendees
- October 1998 – Workshop, The Arc of Wyoming – 60 attendees (Joint conference with other disability groups)

Total participants - 463

Workshops by National Leaders using The Arc's Workshop Package

- 1997 – Four workshops, The Arc of North Carolina state convention and three local chapters, conducted by national board member of The Arc – 200 total participants
- 1997 – Workshop, The Arc of Wood County, WV, conducted by member of Health Promotion and Disability Prevention Committee – 12 participants
- 1997 – Workshop, The Arc of Washington County, OR, conducted by national board member – 12 participants
- 1997 – Eight workshops, NJ, conducted by member of the Health Promotion and Disability Prevention Committee – 200 participants

Total Participants - 424

Objective III. Disseminate education materials to other disability organizations and the general public as appropriate.

In order to make the project's information available beyond chapters and members of The Arc, the following activities were conducted:

Published Articles (Appendix E).

- Two articles were written in The Fort Worth Star Telegram (TX), on The Arc's Human Genome Educational Project and ethical issues of the HGP (April 1996).
- Project staff authored a story in Exceptional Parent, a magazine for parents of children with disabilities. The story titled, *The Danger of Knowing Too Much*, gave an overview of some of the ethical dilemmas families with disabilities face given the advancements of genetic research brought about by the HGP (Nov. 1997).
- The Lansing State Journal (MI) wrote a story titled, *New Discoveries Bring New Forms of Discrimination*, which was a reprint from The Arc's fact sheet titled *Genetic Discrimination* (Feb. 1998).
- A brief article titled, *Mental Retardation Organization Viewpoint*, was published in Human Genome News (Vol.9, No. 3, July 1998).

Presentations Outside The Arc by the Principal Investigator

- May 1997 – Seminar at Oregon Health Sciences University organized by The Arc of Oregon and the University Affiliated Program at OHSU – 25 attendees
- October 1997 – Presentation to the Founders Club (major donors) of The Arc of Massachusetts – 35 attendee
- November 1997 – Presentation at DOE's Human Genome Program Contractor-Grantee Workshop VI. The presentation was placed on The Human Genome Project's web site, found at <http://ornl.gov/hgmis/resource.arc.html> (Appendix F).
- May 1998 – Workshop at the American Association on Mental Retardation's annual meeting – 30 attendees

Dissemination of Project Materials to Broader Audience

- All project genetic issues reports were disseminated to the 85 members of the American Association of University Affiliated Programs (71 University Affiliated Programs, 14 Mental Retardation and Developmental Disability Research Centers).
- The genetic issues reports were sent to a list of 500 of The Arc's major donors and corporate contacts.
- Materials as produced were sent to 167 individuals who requested to be added to the mailing list (many of whom were not directly affiliated with The Arc).
- The workshop package developed by The Arc was furnished to the University of Minnesota for its training program.

Information was, and continues to be, provided to any person who contacts The Arc for materials on the project. Examples of inquiries include: university professors interested in passing the information on to their students, families not affiliated with The Arc who want to learn more about the risks of genetic testing and counseling, medical schools updating patient information files for genetic counseling patients, individuals who want to have children but are carriers of fragile X syndrome and other syndromes, and psychologists interested in volunteering to assist The Arc in developing an understanding of and positions of the ethical questions involved in the HGP.

Other Outreach Activities

State Legislative Advocacy. Some of The Arc's state chapters have attempted to influence law makers regarding the HGP's ethical issues. Using the training materials from this project, a national Board of Directors member from Maryland testified on a genetic discrimination bill before her state's legislature. New Mexico's legislature also requested similar information from The Arc (April 1997).

National Board Resolution. As a result of The Arc's efforts to educate the board about the ethical, legal and social issues of The Human Genome Project, the board of directors passed a resolution on genetic discrimination that states:

WHEREAS, Genetic discrimination means that individuals are treated differently based on actual or perceived genetic differences; and
WHEREAS, We all have several defective genes that place us at risk of genetic discrimination, even though we may never get the disease; therefore, be it
RESOLVED, The Board of Directors of The Arc of the United States supports the enactment of laws banning genetic discrimination.

Adopted by The Arc of the United States' Board of Directors, October 1996

The Arc's Web Site. All the materials developed through The Arc's Human Genome Education Project can be found on The Arc's web site, TheArc.org, under the Department of Research and Program Services. We will continue to maintain this site and develop links to other relevant sites. We recently linked to a site in Japan that requested our assistance. That organization is soliciting views on genetic therapy issues through a series of case vignettes.

The Arc's Publication Catalog. All project materials are advertised in The Arc's Publications Catalog. Single copies are free to those who send in a self-addressed stamped envelope. A flyer was produced to continue to promote the materials (**Appendix G**).

Continued plans for 1999

Although the project has ended, the Arc will continue to stay current with issues related to the Human Genome Program and genetic research findings. The Arc will also continue to participate in the dialogue related to ethical, legal and social implications as appropriate. Known plans for 1999 include:

- April – The principal investigator will speak at a Human Genome Project Conference sponsored by Zeta Phi Beta Sorority National Educational Foundation at Xavier University of Louisiana. Her topic is “Genetics and Mental Retardation.”
- May – The principal investigator will present at the American Association on Mental Retardation's annual convention on a panel titled “Ethical Challenges in Conducting Research with Persons with Mental Retardation.” Her topic will be “Deciding to Participate in Genetic Research: Ethical, Legal and Social Issues for Families.”
- The principal investigator has been invited to author a chapter on “Genetic Privacy and Ethics” in a book titled “Handbook of Genetic Communicative Disorders.”

Assessment of Project Results

This section briefly summarizes the outcomes of the project.

Outcome 1. Families who may be directly affected by the findings of the Human Genome Project will gain information to help them make decisions about genetic testing, counseling and therapies.

The project produced written information targeted to families on each of these topics. All publications were disseminated to The Arc's 1,000 chapters for use by their members. These publications will remain available in The Arc's Publications Catalog as long as the information remains current.

In addition, many family members participated in national or state workshops and gained information from the training offered. They were also able to discuss issues related to genetic testing and counseling, genetic discrimination and gene therapies with a supportive group.

Another example of dissemination to families is the article published in Exceptional Parent magazine, *The Danger of Knowing Too Much*. Its audience is families of children with disabilities.

Finally, one of the reasons for collaborating with the American Association of University Affiliated Programs (UAP) for Persons with Developmental Disabilities is to help reach families. The UAPs in each state offer services to families who have children with disabilities. All materials were disseminated to the UAPs.

Outcome 2. The Arc's leadership (board of directors and national committees) will have sufficient information and knowledge to develop policies to guide the organization as it relates to ethical, legal and social aspects of the Human Genome Project.

Board members were trained on the basics of the HGP at board meetings and by participating in a pilot of the project's workshop, gaining general knowledge of the issues. Several of them volunteered to become project trainers and to offer the workshop to their own local chapters. The Arc's Health Promotion and Disability Prevention Committee also participated in the project by being trained as trainers. Three of the four members went on to conduct training with chapters in their home states. During this process, the Health Promotion and Disability Prevention Committee recommended to the board of directors that they formally recognize The Arc's opposition to genetic discrimination in health insurance. The board passed such a resolution as mentioned earlier.

To help the board of directors gain a sense of members' views on ethical, legal and social implications of the HGP, individual members participating in training across the country were invited to respond to an opinion survey. The survey solicited their views on selected issues related to genetic testing, genetic discrimination and gene therapy after they completed the workshop. They were asked to indicate whether they strongly agreed, agreed, disagreed, strongly disagreed or did not know to a list of 12 statements. The number and percentage of responses of participants who turned in their survey instruments are summarized in **Appendix H**. Table 1 shows the percentage of responses in agreement, disagreement or unknown opinion.

The table reveals that members' views are in close agreement on a number of issues. In the area of genetic testing, 90 percent agree or strongly agree that people should tell their husbands/wives the results of their own genetic tests. There was somewhat less agreement on whether people with a genetic condition in the family should be tested before having children (73% agreed or strongly agreed) and on whether people should tell blood relatives about genetic test results (68% agreed or strongly agreed). There was little agreement on whether infants and children should be tested for genetic conditions if there is no benefit to the child through treatment.

Members of The Arc were more united in being opposed to genetic discrimination. More than 85 percent believe that insurance companies should not deny medical benefits based on an individual's genes; that health insurers should not be able to get genetic information; that employers should not deny employment based on genes and that The Arc should support legislation banning genetic discrimination.

TABLE 1
The Arc's Members' Opinions Issues

Genetic Testing Issues

	<u>Agree</u>	<u>Disagree</u>	<u>Don't Know</u>
Newborns should be tested for genetic conditions even if no treatment exists.	57%	34%	9%
People who have a genetic condition in the family should be tested before having children.	73%	19%	7%
People should tell their husbands/wives the results of their own genetic tests.	90%	5%	4%
People should tell their blood relatives about the results of their own genetic tests.	68%	24%	8%
Children should be tested for genetic conditions even if there is no clear benefit to the child.	39%	47%	14%

Genetic Discrimination Issues

It is fair for insurance companies to deny medical benefits based on an individual's genes alone, including those who show no outward signs of having a disability.	4%	95%	1%
Health insurers should be able to get genetic information if they pay for the tests.	11%	87%	2%
Employers should be allowed to deny employment to people based on having genes with the potential to cause future disease or disability.	3%	96%	2%
The Arc should support legislation banning genetic discrimination in health insurance and employment.	91%	6%	3%

Gene Therapy Issues

Gene therapy is a proven form of treatment for some conditions causing mental retardation.	41%	32%	26%
Advocating for a cure for mental retardation does not devalue those who have the condition.	89%	6%	5%
Based on my current knowledge, I believe The Arc should advocate for more funding for research to cure genetic conditions.	86%	5%	8%

Members were divided on whether or not gene therapy is a proven form of treatment for some conditions causing mental retardation. This is probably due to the way the question is worded, because the training made clear that no one had yet been cured of a mental retardation condition through gene therapy. Yet, gene therapy research is underway for several conditions. On the other hand, most members (89%) believe that advocating for a cure does not devalue those who have the condition, and 86 percent believe The Arc should advocate for more funding for research to cure genetic conditions.

This information will serve as background information for the organization's leaders as they ponder issues that arise, such as whether or not to support legislation or advocate for funding at the national level or in a particular state on issues related to genetic testing, counseling, discrimination and therapy.

Outcome 3. The members at large will have general knowledge about the Human Genome Project and the social, legal and ethical aspects that apply to genetic conditions that cause mental retardation.

Members at large were invited to participate in national and state level training. Over the course of the project, 32 training events conducted by staff and volunteers engaged nearly 1,400 members in discussions of The Arc's issues related to the HGP. All members were informed of available educational materials by articles in The Arc's national newspaper. The series of Genetic Issues in Mental Retardation reports and fact sheets were disseminated to 2,200 chapter leaders, including presidents, executive directors, committee chairpersons, and national board members. In turn, chapters disseminated information to their members via newsletters or handouts. At the national level, The Arc can track the number of reports printed and disseminated. For example, a recent check on the *Fragile X Syndrome*, Genetic Issues in Mental Retardation report, revealed 4,500 had been printed, and 12 remained in inventory. As mentioned before, all reports will continue to be reprinted and maintained in The Arc's Publications Catalog. Single copies are free with a self-addressed stamped envelope. They are all available on The Arc's web site as well.

APPENDICES

Appendix A: Project Reports and Fact Sheets

Genetic Issues in Mental Retardation Reports

- *An Introduction to Genetics and Mental Retardation*, Vol. 1, No. 1, Oct. 1996 – Rev. Dec. 1996
- *Genetic Discrimination*, Vol. 1, No. 2, Oct. 1996
- *Genetic Testing, Screening and Counseling – An Overview*, Vol. 1, No. 3, Jan. 1997
- *Protecting Genetic Privacy*, Vol. 2, No. 1, June 1997
- *Fragile X Syndrome*, Vol. 2, No. 2, Oct. 1997
- *Gene Therapy and Mental Retardation*, Vol. 2, No. 3, Jan. 1998
- *Participating in Genetic Research: Considerations for People with Mental Retardation and Their Families*, Vol. 3, No. 1, Dec. 1998
- *Mental Retardation & Developmental Disabilities Research Centers: An Overview of Current Genetic Research* Vol. 3, No. 2, Jan. 1999

Fact Sheets

- *Genetic Causes of Mental Retardation*, Dec. 1996
- *Facts About Genetic Discrimination*, Dec. 1996
- *Prader-Willi Syndrome*, Mar. 1997
- *Pyhenylketonuria (PKU)*, July 1997

Appendix B: List of Scientific Advisory Panel

Appendix C: Newspaper Articles

- *The Arc undertakes human genome project* (Spring 1996)
- *Genome Project yields publication, discussion* (Winter 1996)
- *Sheep cloning: Good or baaaaad for humans?* (Summer 1997)
- *Clinton recognizes need for anti-discrimination law* (Winter 1997)

Appendix D: Workshop Script/Overheads

Appendix E: Published Articles

- *The Fort Worth Star Telegram* (TX), April 1996
- *The Danger of Knowing Too Much*, Exceptional Parent, Nov. 1997
- *New Discoveries Bring New Forms of Discrimination*, The Lansing State Journal (MI), Feb. 1998
- *Mental Retardation Organization Viewpoint*, Human Genome News, July 1998.

Appendix F: Principal Investigator's presentation on Department of Energy ELSI Web site

The Human Genome Project: Examining The Arc's Concerns Regarding the Project's Ethical, Legal, and Social Implications

Appendix G: Order Form for Project Publications

Appendix H: Responses to Participant Survey

Appendix A

The Genetic Issues In **Arc** Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 1, No. 1

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

An Introduction to Genetics and Mental Retardation

The Human Genome Project

The Human Genome Project (HGP) is an international effort involving hundreds of scientists who are attempting to map all 60,000 -- 100,000 human genes. Doing so would be the first step to unlock the nature of human life, shining light on its secrets and mysteries. The project, which is being directed by the National Institutes of Health (NIH) and the Department of Energy (DOE), began in 1990. Its ambitious goal is to identify all genes within the human body by the year 2005. Aside from gene identification, the project is also attempting to identify and answer specific ethical questions related to the consequences of new genetic findings within society. The hope is to begin developing policy options which can address the ethical questions sparked by the project.

The Arc's Human Genome Education Project

Imagine being able to pinpoint the source of every genetic disorder affecting mankind. For The Arc, the secrets of genetic disorders related to mental retardation could be uncovered. The Human Genome Project could provide a possible future of treatments and cures of some forms of mental retardation.

The Arc received funding from DOE to educate its members and leaders about the ethical, legal and social implications of genetic knowledge and use. As a result, issues can then be evaluated and discussed, and positions developed, based on adequate understanding.

The Arc's involvement stems from the fact that many mental retardation disorders have a genetic cause. As genes causing mental retardation are discovered, the possibility of treatments, cures and genetic testing for inherited conditions raise ethical dilemmas regarding such areas as privacy, fairness and discrimination.

To address these issues, three percent of DOE's overall Human Genome budget is devoted specifically to funding research focusing on the impact of Ethical, Legal and Social Implications (ELSI) of new genetic findings within society. The ELSI program seeks to involve concerned individuals and groups -- like The Arc -- who are directly affected by genetic research. Specific ELSI issues addressed by The Arc's project include:

- Discrimination in insurance and employment
- Genetic testing, screening and counseling
- Genetic therapies to "cure" mental retardation

Ethical, Legal and Social Concerns Arising from New Genetic Findings

Why should The Arc become involved in ethical discussions about genetics? Many mental retardation disorders have genetic causes, with Down syndrome and fragile X syndrome being the most common. (See "Genetic Causes of Mental Retardation" for other mental retardation disorders with genetic causes.) More than 350 inborn errors of metabolism have been identified, most of which lead to mental retardation. Specific genes have already been discovered for a number of single gene conditions, including fragile X syndrome, for which a treatment may be a possibility in the future.

There is a long history of discrimination against people with mental retardation, ranging from the eugenics movement resulting in involuntary sterilization, to the practice of allowing infants born with Down syndrome to die from lack of medical treatment, to the current call to harvest organs of babies born with anencephaly for transplant purposes, even though the infant has not been declared dead.

The Arc's mission is to carry out the following objectives:

- Develop and disseminate educational material for members and leaders of The Arc to inform them about the HGP and mental retardation.
- Conduct training for The Arc's leaders on the scientific, ethical, legal and social aspects of the HGP and mental retardation who can, in turn, provide training to their state and local chapter's membership.
- Disseminate educational material to other disability organizations and the general public as appropriate.

With this history of discrimination, it is imperative that the scientific and medical community hear the views of consumers and families regarding ethical issues involving new genetic findings. We will prepare educational materials and offer training and opportunities for our association to consider such questions as:

- Must a physician offer prenatal genetics screening to all pregnant women (or risk medical malpractice liability if he or she doesn't)? Does a woman have a right to refuse prenatal screening?
- Should genetic testing be offered when there is no treatment? What about access to testing for poor people?
- What rights does a child have to agree to or refuse testing? Who has rights to the test results? Are parents endangering their child's future employability and insurability? What about psychological harm to the child? (Your young teenage daughter learns she's a carrier for fragile X syndrome, for example.)

- How can the confidentiality of test results be maintained to prevent insurers from discrimination? Can employers discriminate on the basis of a person's genes?

- Should therapies for genetic conditions causing mental retardation even be considered? Is there positive value in diversity? How can we avoid stigmatizing those living with a genetic condition while trying to eliminate the condition in others? Are some conditions so destructive to the individual that if a therapy is possible it should be undertaken?

- Should you include your newborn child in experimental gene therapy research? Do any guidelines exist to help you make this difficult decision?

These are some examples of the challenging issues The Arc will be addressing throughout the two-year project. With the scientific community often basing their decisions on their beliefs about quality of life of a person with mental retardation, The Arc must participate in the discussions on the ethical, legal and social issues regarding use of genetic knowledge.

Genetics: An Introduction

Children resemble their parents and relatives, and these traits are passed on for generations. In other words, a child may have his father's nose, her mother's eyes, and those traits might be passed along to that child's child and so on for generations. Biologically this is called inheritance, and genetics is the biology of inheritance. Geneticists study the mechanisms of hereditary transmission -- and sometimes the variations -- of human characteristics.

The characteristics we inherit and pass on are contained within the nucleus of our cells, and the human body is composed of 100 trillion cells. The cell's nucleus carries a blueprint for life composed of contributions of the ancestors who preceded us. That blueprint is in our chromosomes -- our genetic code. The genes on our chromosomes determine our physical and biochemical properties; in effect, our genetic inheritance.

The tens of thousands of genes carried on our chromosomes determine everything from what an individual cell's job is -- whether the cell is a skin cell, a heart muscle cell or a brain cell -- to our physical and developmental characteristics. This complete set of 46 chromosomes is called the cell's genome.

Genetic Disorders Associated with Mental Retardation with an Estimated Incidence in Excess of 1:100,000

Diagnosis	Type of disorder	Genetics	Incid./1,000
Down syndrome	Chromosomal		1.30
Fragile X	Single gene	Triplet repeat*	0.60
Duchenne muscular dystrophy	Single gene	X-linked recessive	0.15
Trisomy 13	Chromosomal		0.125
Tuberous sclerosis	Single gene	Autosomal dominant	0.1
Phenylketonuria (PKU)	Single gene	Autosomal recessive	0.067
Cri du chat	Chromosomal		0.05
Galactosemia	Single gene	Autosomal recessive	0.017
Hunter syndrome	Single gene	X-linked recessive	0.01

*Triplet repeat diseases are inherited in a unique way. The genetic defect can worsen as the gene is passed from one generation to the next. Triplet repeat is named by the three-letter sequences of DNA code which are repeated too many times in the genes causing disorders.

SOURCE: Moser, H.W. (1995), "A Role for Gene Therapy in Mental Retardation," *Mental Retardation and Developmental Disability Research Reviews*. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

Genetic Causes of Mental Retardation

With up to 100,000 genes encoded in each cell and 100 trillion cells making up the human body, people are a mind bogglingly complex organism. Add to that the constant division and replication of those cells as part of their natural life spans and it is amazing that more things don't go wrong.

Because of this complexity, there are no easy answers to the question of what causes mental retardation. It is attributable to any condition that impairs development of the brain before birth, during birth or in the childhood years. It is caused not only by the genotype or genetic make-up of the individual, but also by the possible influences of environmental factors. Those factors can range from drug use or nutritional deficiencies to poverty and cultural deprivation. As many as 50 percent of people with mental retardation have been found to possess more than one causal factor.

In 30 percent of people with severe mental retardation, the cause of mental retardation remains unknown. When compared to those severely affected, identifying the cause of mental retardation in children mildly affected is much more difficult. Roughly 90 percent of all cases of mental

retardation fall within the mild range. Some research has determined that in 75 percent of children with mild mental retardation the cause is unknown.

Most identifiable causes of severe mental retardation originate from genetic disorders. Since the brain is such a complex organ, there are many genes involved in its development. Therefore, there are many different genetic causes of mental retardation. Up to 60 percent of severe mental retardation can be attributed to genetic causes making it the most common cause. (See table for an overview of the more common genetic disorders associated with mental retardation.)

Genetic disorders are generally associated with mental retardation, chronic health problems and developmental delay. In order to have a better understanding as to how genetic disorders occur, they are typically broken down into three types: Chromosomal, single-gene and multifactorial. Two of the most common genetically transmitted forms of mental retardation include Down syndrome (chromosomal disorder) and fragile X syndrome (single-gene disorder).

Chromosomal disorders affect approximately 7 out of every 1,000

infants. The disorder is caused by a person having too many or too few chromosomes, or when there is a change in the structure of a chromosome. Half of all first-trimester miscarriages or spontaneous abortions occur as a result of a chromosome abnormality. If the child is born, he or she usually has multiple birth defects and mental retardation.

Most chromosomal disorders happen sporadically. They are not necessarily inherited (even though they are considered genetic disorders). Only a few specific types are inherited in the same way single-gene disorders are inherited. In order for a genetic condition to be inherited, the disease-causing gene must be present within one of the parent's genetic code. In chromosomal disorders, each of the parent's genes is normal. However, during cell division an error in separation, recombination or distribution of chromosomes occurs. Examples of chromosomal disorders include Down syndrome, Trisomy 13, Trisomy 18 and Cri du chat.

Single-gene disorders (sometimes called inborn errors of metabolism or Mendelian disorders) are caused by non-working genes. These disorders of metabolism occur when cells are unable to produce proteins or enzymes needed to change certain chemicals into others, or to carry substances from one place to another. The cell's inability to carry out these vital internal functions often results in mental retardation.

Although many conditions are generally referred to as "genetic disorders," single-gene disorders are the most easy to identify as true genetic disorders since they are caused by a mutation or change within a single gene. Single-gene disorders are considered to be potentially the most responsive to gene therapy since they are caused by a mutation within a single gene, as opposed to being caused by mutations within several different genes.

Approximately 1 in 1,500 children are born with defective enzymes resulting in inborn errors of metabolism. Over 7,000 genetic disorders have been identified and catalogued, with up to five new disorders being discovered every year. Though rare, there is a one in 500 chance for a child inheriting this type of disorder.

Single-gene disorders are inherited in one of three ways:

1) **Dominant Inheritance.** This occurs when a person has a dominant, disease-causing gene which causes abnormalities even if coupled with a "normal" gene. An example associated with mental retardation is tuberous sclerosis.

2) **Recessive Inheritance.** This occurs when there are two copies of a non-working gene. Parents of children with autosomal recessive conditions are called "carriers" since each parent carries one copy of a disease gene. They show no symptoms of having a disease gene and remain unaware of this until having an affected child. Single-gene disorders are usually classified as autosomal recessive disorders and can be discovered prenatally if the mother is at risk for this genetic condition. Examples associated with mental retardation include phenylketonuria (PKU) and galactosemia.

3) **X-linked disorders.** These affect those genes located on the X chromosome and can be either X-linked recessive or X-linked dominant. Because there are so few X-linked dominant disorders, more attention is generally paid to X-linked recessive disorders.

The X-linked recessive disorder is also referred to as a sex-linked disorder since it involves genes located on the X, or female, sex chromosome. Since females have two X chromosomes, they are usually unaffected carriers and are less likely than males to show any symptoms of the disorder. On the other hand, males have only one X chromosome and, therefore, cannot be carriers of X-linked recessive disorders. If a male inherits an X-linked recessive disorder, he is affected. Some examples associated with mental retardation include fragile X syndrome, Hunter syndrome, Lesch Nyhan syndrome and Duchenne muscular dystrophy.

Combinations of multiple gene and environmental factors leading to mental retardation are called *multifactorial disorders*. They do not follow a normal inheritance pattern and no one knows exactly why they occur. They are inherited (passed on throughout family generations) but do not share the same characteristic inheritance patterns of single-gene disorders.

Their inheritance patterns are usually much more complex than those of single-gene disorders because their existence depends on the simultaneous

presence of several heredity and environmental factors. For example, weight and intelligence are inherited in this way. These disorders are very common and cause a majority of birth defects. Examples of multifactorial disorders include heart disease, diabetes, some cancers, spina bifida, anencephaly, cleft lip and cleft palate, clubfoot and congenital heart defects.

Becoming familiar with the genetic causes of mental retardation paves the way for more thorough discussions of ethical issues involving genetic research. For example, how will the discovery of new genes associated with mental retardation impact those individuals who have mental retardation? How will individuals who carry a gene for mental retardation, but who show no symptoms of a disorder, be affected?

Knowing how mental retardation is genetically inherited opens the door for a clearer understanding and more educated discussions about the ethical issues involved with genetic research. Upcoming reports will address these issues in greater depth by highlighting some of the more common genetic disorders associated with mental retardation.

By focusing on these specific disorders, those ethical questions most applicable to The Arc's membership can be defined and discussed. Ultimately, these discussions prepare The Arc to confidently tackle genetic and ethical issues by developing carefully thought out positions related to the use of innovative genetic research.

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The following resources can be helpful for those seeking additional information on the Human Genome Project and other topics related to genetic research.

Alliance of Genetic Support Groups
35 Wisconsin Circle, Suite 440
Chevy Chase, MD 20815
301-652-5553
1-800-336-4363 (1-800-336-GENE)
Contact: Mary Davidson, Executive Director

Provides information for individuals affected by genetic conditions and their families, as well as the public or media and professionals. They provide peer support, professional counseling, crisis intervention, referrals for non-medical services and genetic counseling. Technical assistance is offered to those interested in forming a group or chapter and in fundraising. They maintain a database of support groups on specific genetic disorders and publish a *Directory of National Genetic Voluntary Organizations*.

National Organization for Rare Disorders (NORD)
P.O. Box 8923
New Fairfield, CT 06812
203-746-6518
1-800-999-6673 or 1-800-999-NORD
Contact: Abbey S. Meyers, President
<http://www.w2.com>

Provides information about symptoms, causes, treatments for those affected by a genetic disorder and research on more than 5,000 rare disorders. Also provides assistance in forming support groups or chapter bylaws and fundraising, and referrals to appropriate organizations. Maintains a registry of affected individuals and research grants (linking researchers with families).

Council of Regional Networks for Genetic Services (CORN)
Emory University
Pediatrics/Medical Genetics
2040 Ridgewood Drive
Atlanta, GA 30322
404-727-1475
Contact: Cynthia Hinton, M.S., M.P.H., CORN's Project Coordinator

CORN is a consortium of genetic service providers whose goal is to improve access to genetic services and enhance the quality of these services. There are ten regional networks nationwide which provide opportunities for consumers and professionals to communicate and become active in shaping genetic services in their region and nationally.

National Center for Human Genome Research
Building 31, Room B1C35
9000 Rockville Pike
Bethesda, MD 20892
301-402-4570
Contact: Leslie Fink
<http://www.nchgr.nih.gov>

Provides timely information about the progress of the Human Genome Project, as well as numerous written materials and other resources.

Human Genome Management Information System (HGMIS)
Oak Ridge National Laboratory
1060 Commerce Park, MS 6480
Oak Ridge, TN 37830
423-576-6669
<http://www.ornl.gov/hgmis/>

Facilitates genetic research and education for the U.S. Department of Energy (DOE) Human Genome Program Task Force. Staff answer questions about the genome project and provide general information through an information clearinghouse. Produces numerous publications on the project, including a newsletter and the Primer on Molecular Genetics.

Primer on Molecular Genetics
by Denise Casey
1991-1992 DOE Human Genome Report
Contact: HGMIS (above)
<http://www.gdb.org/Dan/DOE.intro.html>

A good overview of genetics, including the basics of DNA, genes and chromosomes, is clearly explained in this document, especially as this information relates to genetic research being conducted by the Human Genome Project. It is a popular resource for teachers, genetic counselors and educational organizations.

Additional Genetic Information Available on the Internet

DOE Office of Health and Environmental Research (OHER) Home Page for the DOE Human Genome Program
<http://www.er.doe.gov/production/ohher/ohher-top.html>

Provides information on DOE's Human Genome Project and other OHER projects and links to other program-related sites.

National Center for Genome Resources (NCGR)
<http://www.ncgr.org>

NCGR's Genetics and Public Issues program covers a wide array of genetic information.

For more information, contact:
The Arc of the United States
500 E. Border St., S-300
Arlington, Texas 76010
(817) 261-6003
TDD (817) 277-0553
[Http://TheArc.org/welcome.html](http://TheArc.org/welcome.html)

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The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 1, No. 2

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Genetic Discrimination

Why Should We Care?

Discrimination based on the presence of a disability has always been an issue of great concern to The Arc. People with mental retardation have, for example, long been discriminated against in both insurance and employment. Now a different type of discrimination is emerging due to the increasing use of genetic testing for the purpose of exposing the presence of any abnormal or defective genes. This new phenomenon is called genetic discrimination.

Discrimination based on genetic characteristics includes those individuals who have a gene or genes predisposing them or their offspring to developing diseases, conditions or late-onset disorders. Late-onset refers to disorders which may not show visible signs until later in the individual's life. One example is Huntington disease, a progressive genetic disorder characterized by late-onset neurological symptoms typically arising in the third to fourth decade of life.

Genetic discrimination occurs when someone is treated differently, not based on having a disability, but based on having a gene that may (or may not) cause the person to show symptoms of a disability sometime in the future. In other words, genetic discrimination occurs when people are treated differently because they have the gene or genes, even when they show no symptoms of disease. Men and women who are carriers for a genetic condition (who show no signs of disease) may also be discriminated against because of their potential to have a child with a genetic condition.

With the passage of the Americans with Disabilities Act (ADA) in 1990, discrimination based on the presence of a disability is now against the law. The ADA may protect against genetic discrimination as well since the law applies not only to people with a

disability, but also to people regarded as having a disability. People who experience genetic discrimination are often regarded as having a disability (because they have an abnormal gene), even though they may not. The Equal Employment Opportunities Commission (EEOC) ruled in 1995 that genetic discrimination in employment is prohibited. However, the ADA does not prohibit insurance companies from denying coverage to people who carry defective genes if, based on state law, they have evidence to determine the risk of covering an individual.

The Arc's Human Genome Education Project is promoting education and discussion of the ethical, legal and social concerns resulting from new discoveries about the human genome. One aspect of the project focuses on genetic

discrimination, especially as it relates to the ability to obtain and keep health insurance and employment. Because people with mental retardation experience discrimination based on having a disability rather than discrimination based on having disease-causing genes, these issues do not directly impact them. However, family members of a person with mental retardation, or carriers of a genetic condition associated with mental retardation, need to be aware of the possibility of being discriminated against based on their genetic make-up.

This volume of *Genetic Issues in Mental Retardation* covers information related to genetic discrimination, including an explanation of its effects and information that may help protect you and your family from being the target of discrimination.

Key Points Related to Genetic Discrimination

- Genetic discrimination means that individuals are treated differently based on actual or perceived genetic differences, as distinguished from being discriminated against based on actually having a disease or condition that is genetically caused.
- A recent study noted more than 200 instances of genetic discrimination in areas such as health insurance, employment and adoption.
- The scientific community's ability to test for disease-causing genes is advancing rapidly, much faster than our ability to treat the disease condition.
- We all have several defective genes that place us at risk of genetic discrimination. Some members of The Arc learned of their gene-carrying status when they had a child who inherited a gene that caused mental retardation.
- Just because we have a gene or genes predisposing us to a genetic disease does not mean we will get the disease. A variety of environmental factors (such as geographic location, general nutritional state, personal health habits, socioeconomic level, access to health care and exposure to pollutants and chemicals) also play a major role.
- States and the federal government have begun to enact laws prohibiting genetic discrimination. The Americans with Disabilities Act (ADA) may offer protection to people regarded as having a disability because they have a defective gene. Guidelines for policymakers to ban genetic discrimination have been proposed.

Facts About Genetic Discrimination

What is genetic discrimination?

Genetic discrimination describes the differential treatment of individuals or their relatives based on their actual or presumed genetic differences as distinguished from discrimination based on having symptoms of a genetic-based disease (Geller, et al, 1996). Genetic discrimination is aimed at people who appear healthy or whose symptoms are so mild that their functioning and health are not affected. Such individuals may include people who carry the gene for fragile X, the most common inherited cause of mental retardation. Twenty percent of people with this gene will never display any form of mental retardation. Yet, because they carry the gene for fragile X, they could be treated as though they had mental retardation even though they do not (Boyle, 1995).

Why is concern about genetic discrimination increasing?

The Human Genome Project, a collaboration of scientists worldwide, is conducting research to find the location of the 100,000 or so human genes by the year 2005. Understanding the complete set of genes, known as the human genome, will lead to precise new approaches to the diagnosis, treatment and prevention of disease. Errors in our genes are responsible for an estimated 3000 to 4000 clearly hereditary diseases and conditions. They play a part in cancer, heart disease, diabetes and many other common conditions, such as mental retardation. Within the next five to ten years we may be able to discover almost all of the diseases we are at risk of inheriting.

Genetic testing can be harmful if the information is used to deny jobs or insurance or if it leads to other forms of discrimination. According to Francis S. Collins, Director, National Center for Human Genome Research (1995), "all of us carry probably four or five really fouled-up genes and another couple of dozen that are not so great and place us at risk for something (p. 16)." However, although everyone has a few defective genes, not everyone will be affected. Multiple factors within the environment have a significant impact

Legislation on Genetic Discrimination Within the United States*

State	Enacted Bills	Pending Bills	Defeated Bills
Alaska			Health Insurance
California	Health Insurance	Employment	
Colorado	Health Insurance & Group Disability		
Connecticut			Health Insurance & Employment
Florida			Health and Life Insurance
Georgia	Health Insurance		
Hawaii		Health, Life Insurance & Employment	
Iowa	Employment		
Illinois		Employment	Health Insurance
Indiana			Health Insurance
Kansas			Health Insurance & Employment
Maryland	Health Insurance		
Massachusetts		Health, Life & Disability Insurance	
Michigan		All Insurance & Employment	
Minnesota	Health Insurance		
Nebraska			Health Insurance
New Hampshire	Employment		
New Jersey	Health Insurance & Employment		
New York	Employment	Health Insurance	
Ohio	Health Insurance		
Oklahoma			Health Insurance & Employment
Oregon	Health Insurance & Employment		
Pennsylvania		Health Insurance	
Rhode Island	Employment		
Texas			Health Insurance & Employment
Virginia	Health Insurance		
Wisconsin	Health Insurance & Employment		

* This information was taken from "Genetic Discrimination Legislation: Enacted, Pending, and Defeated State Legislation (July 1996)." Contact the Council for Responsible Genetics (CRG) for detailed, up-to-date information within your state.

on a person's health. These factors, either alone or combined with a disease-causing gene, can increase or decrease an individual's risk of developing a disease (Nelson-Anderson & Waters, 1995).

Where is genetic discrimination happening?

A recent study which questioned people with defective genes that could lead to a disease, but who had no symptoms, found that genetic discrimination occurred in many settings (Geller, et al, 1996). As a result, people who fear potential genetic discrimination may be discouraged from obtaining genetic

information that could bring health benefits to them and their families.

One of the most common forms of discrimination is denial of health insurance based on a person's genes. Insurance companies gather and use medical information to predict a person's risk of illness and death. They use this "risk" information to determine which individuals and groups they will insure and at what price. That information plays a critical role for people in determining access to health care.

Employment is another area with reported cases of discrimination. Many individuals believe they were not hired or were fired because they were at-risk for genetic conditions. In other cases, individuals who were employed were reluctant to change jobs because they feared losing health insurance coverage (Geller, et al, 1996). Having a defective gene could be considered a pre-existing condition by insurance companies who, on that basis, may deny coverage. Recently passed federal legislation places limitations on the exclusion period for pre-existing conditions when people change jobs (The Health Insurance Portability and Accountability Act of 1996).

Discrimination has also occurred when medical professionals counseled individuals about child bearing by urging prenatal diagnostic testing or telling them they should not have children. Similarly, some adoption agencies have unfairly treated prospective parents with a genetic condition by refusing adoption or assuming they should adopt only children at risk of inheriting a disability (Geller, et al, 1996).

Doesn't the ADA protect people against genetic discrimination?

The Americans with Disabilities Act (ADA) offers protection from discrimination to individuals *currently affected* by a genetic condition or disease. It also applies to individuals who are *regarded* as having a disability. The Equal Employment Opportunities Commission, which oversees enforcement of nondiscrimination in employment, has ruled that ADA applies specifically to individuals who are subjected to discrimination on the basis of genetic information relating to illness, disease, condition or other disorders (EEOC, 1995). This

interpretation extends coverage to people who have genes making them predisposed to a disease-causing disability or who have genes for a late-onset disorder. However, it may not protect carriers of genetic disorders who do not yet manifest symptoms of a disease (the "unaffected carrier"). They may be discriminated against based on concerns about health costs of future affected dependents.

The Americans with Disabilities Act does not cover the insurance industry. Insurance companies may deny health, life, disability and other forms of insurance to people with defective genes if there is a sound basis for determining risks consistent with state law. Health maintenance organizations can also refuse to cover an individual with a genetic diagnosis even if the individual has no symptoms of the genetic disorder, provided there is a sound basis for the decision based on actual risk experience (Alper and Natowicz, 1993).

What are the implications of genetic information for family members?

When people learn that they have a gene that places them at increased risk for certain diseases, they face the dilemma of whether or not to tell other family members about their potential susceptibility to disease. This information is directly relevant to their biological relatives, for other family members may also have the gene and be at increased risk. It also has implications for family members being at risk of genetic discrimination, since genetic information about an individual is also information about that person's family.

Genetic information may profoundly affect people's decisions about having children. There is also evidence that some individuals who have defective genes are stigmatized, suffering a loss of social and economic opportunities (NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research, 1993).

What steps are being taken to eliminate genetic discrimination?

In addition to federal law and regulations, several states have developed and adopted legislation banning discrimination in health insurance and employment. Currently

eleven states have laws prohibiting health insurers from denying health care coverage because of a genetic condition. Seven states prohibit employers from requiring genetic tests or using genetic health predictions in employment decisions. Seven other states have bills pending to protect individuals from discriminatory use of genetic information in employment practices or for insurance purposes (Council for Responsible Genetics, 1996). Refer to the table "Legislation on Genetic Discrimination within the United States" for a brief overview of state legislation.

As noted earlier, the Federal Health Insurance Portability and Accountability Act of 1996 offers protections against discrimination in health insurance by limiting pre-existing condition exclusions. It also prohibits discrimination against individuals based on health status, including their genetic information.

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- The Health Insurance Portability and Accountability Act of 1996, Pub.L. No. 104-191, Title 1, Sec. 101 and 102, 104th Cong. (1996).

Guidelines for Developing Policies to Ban Genetic Discrimination

The following guidelines were developed by the NIH-DOE Working Group on the Ethical, Legal, and Social Implications of the Human Genome Project and the National Action Plan on Breast Cancer to assist policy makers in developing legislation to protect individuals from genetic discrimination in insurance. They have been endorsed by the National Advisory Council on Human Genome Research.

1. Insurance providers should be prohibited from using genetic information, or an individual's request for genetic services, to deny or limit any coverage or to establish eligibility, continuation, enrollment, or contribution requirements.

2. Insurance providers should be prohibited from establishing differential rates or premium payments based on genetic information or an individual's request for genetic services.

3. Insurance providers should be prohibited from requesting or requiring collection or disclosure of genetic information.

4. Insurance providers and other holders of genetic information should

be prohibited from releasing genetic information without prior written authorization of the individual. Written authorization should be required for each disclosure and include to whom the disclosure would be made.

Case Examples of Genetic Discrimination

What Would You Do?

• A mother suspects her young son may have a learning disability. She consults her doctor. Her doctor performs some genetic tests and discovers that the child has fragile X syndrome, the most common genetic cause of mental retardation. Her insurance company eliminates the boy's coverage, claiming that his disability represents a pre-existing condition (Council for Responsible Genetics, Position Paper on Genetic Discrimination).

You suspect your other child may have the same disability. Would you decide to have your other child tested for this condition even though the child could lose his or her health care coverage?

• A private insurer in Colorado notified parents of a three-year-old child, who had been recently

diagnosed with a syndrome associated with mental retardation, that the child's policy was terminated even though the family had been on the policy for nine months before the diagnosis.*

What legal rights do you have in your state that can protect your child from this type of genetic discrimination? Can the ADA protect you from genetic discrimination?

• An HMO had covered the medical expenses of a child since birth but refused to pay for occupational therapy after she was diagnosed with a condition associated with mental retardation, claiming the condition was pre-existing. All bills relevant to the condition had been paid up to the time of diagnosis.*

If the child has not shown any outward signs of having the condition, is it fair for the insurance company to deny the child medical benefits based on his or her genes alone?

*Geller, L., Alper, J., Billings, P., Barash, C., Beckwith, J. & Natowicz, M. (1996). Individual, family and societal dimensions of genetic discrimination: A case study analysis. *Science and Engineering Ethics*, 2, 71-88.

Helpful Resources

Council for Responsible Genetics (CRG)
5 Upland Road, Suite 3, Cambridge, Mass. 02140
(617) 868-0870 <http://www.essential.org/crg>

The CRG is a national non-profit organization representing over 1,000 scientists, bioethicists and religious leaders who are concerned about the social and ethical implications of new genetic technologies. They document cases of genetic discrimination and civil liberties abuses that occur as a result of genetic testing and DNA profiling.

The Genome Action Coalition
317 Massachusetts Avenue, N.E., Suite 100
Washington, D.C. 20002 (202) 546-4732
Contact: Lyle Dennis

The purpose of this voluntary association of patient advocacy and professional groups, individuals in scientific research, and pharmaceutical and biotechnology companies is to create an environment within the government and the general public in which genome research is strongly supported. They provide The TGAC Hotline for members and friends of the Coalition which includes up-to-date information on legislation, up-coming conferences and pertinent resources relating to genetic research.

The HuGEM Project: Issues in Genetic Privacy and Discrimination, Georgetown University
3307 M Street NW, Suite 401
Washington, DC 20007 (202) 687-8635 Cost: \$15.00

A 45 minute video of four people affected by genetic disorders who discuss their experiences and concerns about discrimination in insurance and the workplace when privacy and confidentiality are not maintained.

Internet Resources

Center for Bioethics at the University of Pennsylvania
<http://www.med.upenn.edu/~bioethic/>

Maintains the "Ethics and Genetics - A Global Conversation" page which allows individuals to post comments instantly and engage in live conversation about articles on innovative genetic research. Also has a virtual library which contains recent articles on ethical issues regarding genetic technology.

Exploratorium's Ethical Scenarios Forum (ETHEX)
<http://www.exploratorium.edu/genepool.ETHEX.html>

ETHEX is designed to offer an opportunity for members of the general public to discuss ethical issues with each other and with professionals in the fields of ethics, genetics, law, theology, sociology and medicine. Individuals can respond to different case scenarios relating to decision-making and genetics, discuss how they would respond and read the responses of others.

For more information, contact:

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500 E. Border St., S-300
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[Http://TheArc.org/
welcome.html.](http://TheArc.org/welcome.html)

Produced by The Arc's Human Genome Education Project, Sharon Davis, Ph.D., Principal Investigator and Leigh Ann Reynolds, Project Associate. Funded by the U. S. Department of Energy ELSI Program under Grant No. DE-FG03-96ER62162. Support from DOE does not constitute an endorsement of the views expressed in this publication. October 1996.

The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 1, No. 3

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Genetic Testing, Screening and Counseling - An Overview

Genetic Testing - Harmful or Helpful?

The international Human Genome Project, an effort to map all the genes within our bodies, has greatly expanded our ability to test for the potential presence of certain diseases* that can result in various disorders and conditions, such as mental retardation. This rapid increase in genetic technology is outpacing our ability to develop treatments to correct these diseases and conditions. A growing list of disease-causing genes has been identified, enabling an otherwise healthy individual to know whether or not he or she will develop a disorder or possibly pass a disease gene on to his or her children. This is the first time in history that such specific, predictive genetic information has been available. How will having this information impact society? Do most of us want to know about future genetic information that could change our lives? As a society, we must make decisions we have never had to make before on issues such as the following:

- Who decides who should be screened or tested for genetic disorders?
- Which specific disorders should we screen or test for?
- Who should be providing genetic screening or testing?
- Should we screen or test for disorders even if there is no treatment or cure for the disorder?

A variety of issues have been raised under the areas of prenatal, newborn, carrier and occupational screening, and the testing of children. This report provides an overview of these issues by explaining what genetic

testing and screening is, the different types of genetic screening, advantages and disadvantages of genetic testing and other important topics, such as the testing of children and the use of informed consent. The brief

discussion on genetic counseling can help individuals decide in choosing whether or not to obtain genetic counseling and how to locate a genetic counselor.

Key Points on Genetic Testing

- Everyone may not need genetic testing, but those with a history of genetic disorders within the family should consider testing.
- Genetic screening and testing has both positive and negative consequences. It's important to weigh the advantages and disadvantages when considering genetic screening or testing.
- The value of genetic testing depends on several factors: the accuracy of the test, the reliability of the interpretation of the results, the ability to treat the condition and the quality of genetic counseling available.
- Genetic tests can provide medical information that affects the entire family. Testing has implications for future reproductive decisions, usually providing a *probability* of disease, rather than predicting future "diagnoses."
- Reliable genetic tests can predict the chance of having a disease gene with high accuracy. However, not everyone with a disease gene may go on to develop a disease or condition due to possible effects of other genes or environmental factors.
- Informed consent, the communication of information between a patient and health care provider about a genetic test, can be an important component of genetic testing, yet there are no national standards to guide health care providers on how this information should be given.
- Although physicians have not agreed on standards for the testing of children, some experts think that testing should be conducted only when there is clear benefit to the child. Others feel that testing should also be considered if it can benefit other family members.

Facts on Genetic Testing and Screening

What is genetic testing?

Genetic testing is "the use of specific laboratory tests to determine the genetic status of individuals already suspected to be at high risk for a particular genetic condition based on family history or a positive screening test" (Lapham, et.al., 1996). Genetic testing is typically recommended for those individuals who suspect they may have a disease-causing gene or who may be at an

increased risk of developing disease or a condition for reasons other than a family history.

Pre-symptomatic testing (also referred to as predictive gene testing) is an example of genetic testing. It refers to an individual who is at risk for a genetic disorder (usually because of a family history) but who does not have any symptoms at the time of testing. It is often used to identify single-gene disorders and to determine predisposition to a large number of genetically inherited disorders.

* Note: Disease is a comprehensive medical term which can include disorders, conditions and illnesses. For this reason, it is used throughout the document to describe the origin of the condition of mental retardation that is directly attributed to genetic inheritance.

What is the difference between genetic testing and genetic screening?

Genetic testing and screening are similar in that both involve the use of laboratory tests to reveal the presence of disease-causing genes. Although genetic screening and testing are essentially the same since they both involve the same medical procedures, the major difference between them can be explained in examining WHY an individual undergoes laboratory testing. If someone desires to be tested due to the possibility that he or she may have a disease gene because a large percentage of people in the same age group or ethnic group are at high risk for having the gene, this individual would need to undergo **genetic screening**. If, however, the individual suspects he or she may have a disease gene as a result of a family member having the gene, this person would need to undergo **genetic testing**.

Screening is often called "population-based" screening since it is used to test those individuals in the population who are at a higher risk for having a disease-gene. For example, people of African American descent are known to be at higher risk for having a gene causing sickle cell disease. On the other hand, genetic testing is used, not to screen a population already at risk, but to "test" individuals for the presence of a specific gene. For example, if a person has a family history of fragile X syndrome, the individual will be tested (as opposed to screened) for the specific gene (FMR1) that causes fragile X syndrome.

What are the different types of genetic screening?

Genetic screening is "the testing of apparently healthy people in the population to identify those at increased risk of genetic disease themselves or whose children (including future children) may be at increased risk of disease" (Lapham, et.al., 1996). Genetic screening can include carrier, prenatal and newborn screening.

Carrier screening is often considered by couples who want to have children, but who are concerned that they may "carry" a gene for a certain disorder that has the potential to affect their children.

Prenatal screening is available to those individuals who have a higher

risk for passing a disease gene on to the child. It is used to determine the genetic make-up of an unborn child.

Newborn screening identifies biochemical or other inherited conditions in newborns that may result in mental retardation or other complications. Newborn screening is an effective measure in preventing mental retardation. However, only a handful of disorders are screened for since screening all newborns is expensive (The Arc, 1994).

What is prenatal screening?

Prenatal screening examines the genetic makeup of a fetus. It is recommended when either parent's side of the family has a history of a genetic disorder or if the mother is over age 34 (since older mothers have a greater chance of having a baby with certain chromosomal disorders, such as Down syndrome) or if there are problems noted through ultrasound (March of Dimes, 1992). Prenatal screening is used to detect certain birth defects or genetic disorders before a baby is born. Examples of genetic disorders that can be detected with prenatal testing include:

- chromosomal abnormalities, such as Down syndrome, trisomy 13 and trisomy 18
- single-gene disorders, such as hemophilia, sickle cell anemia and cystic fibrosis
- neural tube defects, such as spina bifida and anencephaly

Prenatal screening cannot find all genetic abnormalities (since there are only 5,000 known abnormalities out of a total of 100,000 genes in our bodies), and there is some risk involved (as with any medical procedure) depending upon which test is used. Prenatal screening tests currently available include:

- *chorionic villus sampling (CVS)* - usually done at 10 to 12 weeks of pregnancy to obtain a sample of the placenta by passing a plastic tube through the vagina and into the uterus or by passing a needle through the abdomen and into the uterus. This allows doctors to diagnose many of the same conditions as amniocentesis, but earlier in the pregnancy.
- *blood test for alpha-fetoprotein (AFP)* - may be performed at 16 to 18 weeks of pregnancy and is used to indicate the level of AFP, a substance

produced by the fetus and passed to the mother's blood.

- *amniocentesis* - may be done at 13 to 18 weeks of pregnancy and is a widely-used procedure of obtaining amniotic fluid from the uterus by using a needle to pass through the abdomen.
- *ultrasound* - usually performed as early as possible in pregnancy, and is a non-invasive procedure that provides a visual image of the fetus (Bowe, 1995).

How do you know if you should be screened or tested for a genetic disorder?

Not everyone needs to undergo genetic testing. People who know of a genetic condition within the family are prime candidates since they are susceptible to inheriting a specific disease-causing gene.

Individuals who could benefit from genetic testing (or diagnostic testing) include:

- those who are concerned that they may have a genetic or chromosomal disorder because of a specific condition in their families
- couples who already have a child with a genetic disorder, unexplained mental retardation or a birth defect
- women who have had two or more miscarriages or whose baby dies in infancy
- people with unexplained short stature
- people with unusual physical features, especially poor growth or development

Individuals who could benefit from genetic screening include the following groups of people:

- women who deliver a child after age 35
 - couples who would like testing or information about genetic disorders that occur frequently in their ethnic group
- Others who could benefit from genetic services, such as genetic counseling:*
- pregnant women concerned about the effects of exposure to medication, chemicals or radiation
 - couples who are first cousins or other blood relatives (March of Dimes, 1992)

The decision to be tested should always be voluntary and thoughtfully

What Do You Think?

Once it becomes possible to test quickly and reliably for thousands of genetic conditions, should doctors be expected to perform such tests? Should the doctor be liable for failing to test or for failing to inform parents of every detail of the test result?

Who should counsel patients about what their genetic blueprints mean and how will people react to their particular genetic makeup?

Do health and life insurers who deny policies to people with disease genes have the right to do so?

Should laws be passed to protect people against genetic discrimination?

How can genetic information be kept confidential and how can the discriminatory use of test results be prevented? Since some tests will reveal information about other family members, can the privacy of these relatives be protected?

Do people have the right to choose not to know about their genes? Do mothers have the right to choose not to have their fetuses tested?

Taken from *Genetic Screening and Ethics: An Overview*. The Woodrow Wilson Biology Institute, 1992, David Devore.

Helpful Resources

Alliance of Genetic Support Groups
35 Wisconsin Circle, Suite 440
Chevy Chase, MD 20815
1-800-336-4363
<http://medhlp.netusa.net/www/agsg.html>

Created a helpful 30-minute video on genetic testing called "Genetic Testing Across the Lifespan," and also provides referrals for genetic counseling.

March of Dimes Birth Defects Foundation
1275 Mamaroneck Ave.
White Plains, NY 10526
1-914-428-7100
<http://www.noah.cuny.edu/providers/mod.html>

Provides referrals for genetic counseling and a variety of helpful educational materials related to genetic testing and counseling.

Understanding Genetic Testing
NCI Cancer Communications Office
Building 31, Room 10A28
Bethesda, MD 20892
1-800-422-6237
<http://www.gene.com/ae/AE/AEPC/NIH/index.html>

An easy-to-understand booklet providing an overview of genetics, genetic testing and genetic counseling (Single copies free).

For more information, contact:



The Arc of the United States
500 E. Border St., S-300
Arlington, Texas 76010
(817) 261-6003
TDD (817) 277-0553
[Http://TheArc.org/welcome.html](http://TheArc.org/welcome.html)

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examined. Individuals should not be forced to make decisions based on pressure from family members, health care providers or others. The possible outcomes (both advantages and disadvantages) of learning what diseases or conditions an individual is at risk of inheriting should be carefully analyzed before making a final decision to undergo genetic testing.

What are the advantages and disadvantages of genetic testing?

Genetic testing can cause either a feeling of relief or anxiety, depending on the outcome of the test results. Ultimately, testing provides individuals with an opportunity to seek genetic counseling so that the risk of inheriting a genetic disease may be reduced. Testing can lessen the anxiety of not knowing the possibility of developing a disease and provide a tremendous sense of relief once a definitive test result is given. An individual who chooses to undergo testing has the opportunity to seek medical help, prepare for, and possibly help prevent, a genetically-caused condition (Cho, 1995). Testing can help people to make more informed decisions about their future.

Unfortunately, several negative consequences may result from genetic testing as well. Once a person has tested positive for a disease or condition, he or she risks stigmatization, loss of health or life insurance, loss of employment or educational opportunities and possibly can lose the ability to adopt a child (Geller, et.al, 1996). Privacy of other family members is threatened since, if one family member is tested, this information implies that relatives also could have the disease gene or may have an increased risk for disease.

Another problem of genetic testing is the inability to predict the severity of future disease. The severity of a disorder can vary according to a number of unique factors. Even couples who choose prenatal testing cannot always know in advance the severity of the disability in their child. Also, undesired test results may produce depression and feelings of hopelessness. Relatives may even experience "survivor guilt" which is the feeling of guilt felt by individuals

What Genetic Professionals Do (Genetic Counselors, Clinical Geneticists, etc.)	How They Do It
A family history or pedigree including all medical problems is constructed.	33 % of people referred for genetic counseling have other genetic issues in their families that need to be addressed. These issues are identified by taking a detailed family history.
The family history of genetic disorders and birth defects is analyzed.	Separate the genetic from the non-genetic issues in the family history to avoid unnecessary testing.
Genetic counselors assess and interpret the risk for occurrence or recurrence of genetic conditions in the family.	The risk for a genetic condition to occur or recur must be explained with total accuracy.
The nature of the condition(s), including the process of inheritance, is carefully discussed.	People need to understand the meaning of a diagnosis (range of severity) and how it is inherited to be able to make a decision about whether they want to be tested and whether they want their unborn child tested.
Options available to reduce recurrence risk(s) and specific genetic testing currently available is discussed.	Many options are available to people at risk for a genetic disease, such as carrier screening, adoption, egg/sperm donation and prenatal testing.
The risks and benefits of each option is discussed with careful attention being given to the individual's level of understanding.	Each option has risks, benefits, and limitations that individuals need to understand in order to choose the option appropriate for them.
Assist in selecting the option appropriate for an individual or family.	Much of the information provided can be confusing. Assisting individuals with decision-making requires good counseling skills and a non-directive approach.
Supportive counseling and/or referrals to community resources are provided when appropriate.	Genetic counselors often refer individuals to other health care professionals or family support groups when necessary.
The genetic tests performed are coordinated, when indicated.	Genetic testing is sometimes complex and involves obtaining screening test results and documenting the correct diagnosis.
A summary letter documenting the counseling session and an outline of the plan of care is sent to the one tested and the referring physician.	Documenting the counseling session ensures an accurate record for the patient and physician. It becomes a medical-legal document for the patient chart.

Adapted from *Genetic Consultation/Counseling: The Process* by Beth Balkite, M.S., Certified Genetic Counselor, Genzyme Genetics, August 1996.

who have not tested positive for a disease while other family members have (Cho, 1995).

Obtaining a positive test result does not guarantee that a person will become ill and a negative test result cannot completely rule out the possibility of becoming ill. Genetic testing, therefore, often deals in probabilities rather than certainties (NIH, 1995). Physicians can misapply genetic tests now available. Some inexperienced doctors are using genetic testing without fully understanding its consequences (Cotton, 1995). Many genetic tests are being marketed by commercial enterprises without approval from the Food and Drug Administration (FDA), raising questions about the quality of genetic tests and testing procedures (Harvard Women's Health Watch, 1996).

What is informed consent?

Informed consent is the communication of information between a patient and health care provider about a testing procedure. The purpose of informed consent as it relates to genetic testing is to provide an individual with enough knowledge about the risks and benefits of a genetic test so that a truly informed and educated decision can be made about whether or not to be tested. Informed consent is also important since it limits the scope of testing performed by the health care provider and protects the health care industry in situations involving consumer liability issues.

Health care providers are responsible for providing this vital information in a clear and understandable manner. However, there are no universal standards within the medical field to oversee how this information is communicated and no legal entity which has the responsibility to ensure that enough information is being offered. Some health care providers give a great deal of information, including detailed explanations about testing procedures, while others may provide only minimal information.

Because such variability exists, people considering genetic testing must be aware of what they have a right to ask for and receive throughout the testing process. Some examples include having a right to obtain up-to-date information about each genetic test, to know the benefits and risks of

each genetic test, to request a referral for genetic counseling to help decide whether or not to have a genetic test and to receive privacy regarding the test results (Blatt, 1996).

Should parents be allowed to obtain genetic testing on a child?

Parents have their children undergo genetic testing for several reasons: 1) testing can offer immediate health benefits to the child, such as prevention or early treatment, 2) testing offers no immediate benefits, but can help the child in the future when he or she makes reproductive decisions, 3) testing offers no specific, visible benefits, but the parent or the child requests testing, or 4) testing is done for other family members (Wertz, et.al., 1994).

Often parents want to have their children tested to plan for the future or reduce the anxiety of not knowing. Yet, receiving test results showing that a child does have a disease gene may actually restrict the child's future in many ways. For example, after parents become aware of their child's disease gene, their expectations of the child's abilities and chance of a meaningful life may be substantially lowered. Children could be psychologically damaged by such low expectations, even though treatment may be found to lessen the effects, or eventually cure the disorder. Children, especially younger children, often blame themselves for having a genetic disorder. Such test results may create anxiety within the family, causing the child to suffer abuse or be treated as a scapegoat since the child is the one with the "problem." Other negative consequences of testing children are the possibilities of stigmatization, loss of self-esteem and discrimination by family, employers, insurance companies, educational institutions and others.

Experts feel that allowing children to make important life decisions is risky due to their inability to weigh the future adequately or to realize that their values may change over time. In order to make informed decisions, children need to be able to develop hypotheses and predict future possibilities. But at which age can a child make informed decisions and, therefore, undergo genetic testing? Most children

cannot fully comprehend all possible implications of being tested until they reach a certain developmental stage where formal operational thought can be used. They may reach this stage anywhere from age 11 to several years later (Wertz, et.al., 1994).

There are no universally agreed upon standards among physicians for the testing of children. Geneticists and ethicists from around the world recommend that testing be conducted only when there is clear benefit to the child, but others feel testing should be considered if it can benefit other family members.

What is genetic counseling and how can it help?

Genetic counseling provides important information about the results of a genetic test by translating genetic knowledge into easily understandable and practical information. The interpretation of genetic tests - whether positive, negative or ambiguous - needs to be accurately communicated. Individuals who are considering genetic testing may want to talk with genetic counselors or clinical geneticists who use their knowledge about the basic laws of heredity, family health history (called a pedigree) and results from the genetic testing to estimate the probability that a disorder may recur within the family. Genetic professionals attempt to emotionally and psychologically prepare the individual for receiving positive, negative or unclear test results. Genetic counselors and clinical geneticists provide individuals with relevant information in an unbiased manner about their options after receiving test results so that informed decisions can be made (NIH, 1995).

Genetic professionals typically work in large medical centers or hospitals affiliated with a medical school or university. There are about 300 comprehensive genetic services centers in the United States. Individuals can seek genetic counseling by calling a local hospital associated with a medical school, asking their physician for a referral to a genetic counselor, calling a local chapter of the March of Dimes or by contacting:

- The National Society of Genetic Counselors at 233 Canterbury Drive, Wallingford, PA 19086-6617 (<http://members.aol.com/nsgcweb/nsgchome.htm>)

- The Alliance for Genetic Support Groups at 1-800-336-4363
- The Council of Regional Networks (CORN) at 1-404-727-1475 (<http://www.cc.emory.edu/PEDIA/TRICS/corn/member/coorlist.htm>)

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Possible Negative Consequences of Genetic Screening

- 1) Genetic discrimination- People with genetic flaws, not all of which show up as dysfunctions, may be denied life insurance, health insurance, and access to schooling or to jobs.
- 2) Differential treatment- Employers could hire only those people whose genes indicate they are resistant to the health hazards of the work place, which is a less expensive alternative to making the work place safe for all.
- 3) Eugenics- Social or political pressure may be applied to people to make childbearing decisions on the basis of genetic information. Mating between those with valued

genes may be encouraged while mating between two people with recessive traits that are not valued may be prohibited. Women carrying fetuses with genetic abnormalities may be encouraged to abort.

- 4) Genetic determinism- Genetic determinism is the belief that behavioral and personality characteristics, such as intelligence or criminal behavior, are mostly a function of genes. Genetic determinism implies a fatalistic attitude toward health and disease. It can be used to justify bigotry and to perpetuate racial or ethnic inequalities. A genetic underclass could be created.

Adapted from *Genetic Testing - Health Care Issues: An Interview with Dr. Neil Holzman*, Symposium at University of California, San Francisco, 1992.

Common Myths about Genetic Testing and Genetic Counseling

Myth:

If a person has a genetic disorder or has an affected child, usually their chances are high that future children will be affected.

Truth:

The recurrence risk depends on the inheritance pattern for that particular disorder in that particular family, and usually ranges from less than 1% to 50%.

Myth:

Given that abortion is legal in the United States, many people believe that prenatal diagnosis inevitably means abortion.

Truth:

A couple undergoing prenatal diagnosis is never obligated to choose abortion if the result is abnormal. Most of the time, results are normal and parents are reassured and can relax for the remainder of the pregnancy. The availability of prenatal diagnosis has allowed many couples who would otherwise be too afraid to have children to have healthy families.

Myth:

A normal chromosome test means that there are no genetic problems in the individual.

Truth:

Chromosomes can be seen under the microscope; genes cannot. A normal chromosome test means that the packages of the genes appear to be normal, that is, there is no missing or extra packages of genes. Abnormalities at the level of a gene or a few genes cannot be seen with this test. Most individuals with dominant recessive or X-linked diseases would have normal chromosome tests.

Taken from *Common Myths About Genetics and Genetic Counseling*. The Genetics & Metabolism Department, Children's Medical Center of Dallas.

The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 2, No. 1

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Protecting Genetic Privacy

What is genetic privacy and why is it important?

Genetic privacy, in its simplest definition, could be described as the right to decide for yourself what genetic information others can know about you and the right to decide what genetic information you want to know about yourself (Baker, 1997). The growing ability of scientists and researchers to identify genes causing (or contributing to the cause of) certain diseases and conditions threatens the privacy of genetic information in a way that never before required attention.

Without genetic privacy, discrimination based on our genes alone may become commonplace in society. Members of The Arc should become aware of issues surrounding genetic privacy, since many conditions associated with mental retardation are caused by a person's genes. Genetic discrimination has already become pervasive enough to warrant legislation in many states, yet such legislation has fallen short in providing adequate or comprehensive protection of genetic privacy.

Why has genetic privacy become an issue for The Arc?

The study, definition and "banking" of human genes, heavily influenced by the research of the Human Genome Project (HGP), is quickly becoming a great concern to those who have any defective genes within their bodies (and that means all of us). The Human Genome Project is an effort among scientists worldwide to identify all 80,000 to 100,000 genes within the human body. This goal

is being reached faster than originally expected, which means genetic information is being discovered before society is ready to know what to do with the information. Some fear the advance in research made by the HGP will be used to deny health insurance to more and more people, such as individuals with mental retardation and their family members. Hundreds of DNA tests will become available early in the next century, so we must prepare ourselves by learning how to protect genetic information.

Why is genetic privacy a concern for individuals and families affected by mental retardation?

A person's genes can tell a lot about that person. Employers, insurance companies, educational

institutions, adoptive agencies and others can find out what conditions or diseases a person may have or be predisposed to getting. However, genetic test results can be misinterpreted by such organizations who are unfamiliar with genetics and the correct interpretation of the results of such tests. Having a gene for a certain condition does not necessarily mean the individual will ever show symptoms of the condition. This is a fact insurance companies and prospective employers may not know and thus incorrectly assume the presence of a condition.

Also, federal law does not require those who obtain genetic information to protect it. Although some states have banned genetic discrimination, the chance that a person will be discriminated against based solely on his or her genetic make-up remains a high possibility.

KEY POINTS ON GENETIC PRIVACY

- Many people do not know how to protect their genetic information, or realize that the privacy of their genetic information needs protection.
- A person's genes have the potential to tell a lot about that person, but genetic test results can be misinterpreted by insurance companies and prospective employers.
- Genetic information is significantly different from other medical information since genetic testing often involves other family members who may or may not want to know or do not want to provide genetic information.
- Genetic databanks (or DNA databanks) are computerized databases that store records obtained through genetic testing. Once genetic information is obtained, those receiving the information are under no obligation to protect it.
- Fourteen states have enacted laws that prohibit using genetic data in insurance underwriting, but such laws do not provide adequate protection of genetic privacy.
- Protecting the privacy of genetic information isn't easy, but there are steps one can take to obtain the most protection possible.

For example, some people may be discriminated against because they carry the gene that causes fragile X syndrome, the most common inherited cause of mental retardation. Twenty percent of people with this gene will never display any form of mental retardation. Yet, since they carry the fragile X gene, they could be treated as though they had mental retardation even though they do not (Boyle, 1995).

The importance of protecting privacy is not new, but protecting *genetic privacy* is raising concern and has its own unique set of issues. Although there is currently no DNA-based test for newborn screening in the United States, within the next ten years it may be possible for such testing to reveal disease genes (or genetic mutations). Individuals who may never be affected by a disease gene, but only be a carrier for the genetic condition, could face a future of discrimination due to the increased use of genetic testing in society. Without laws in place to protect genetic information, the possibility of being discriminated against based on genetic make-up alone is one of the major concerns related to privacy.

In addition to these problems, genetic testing provides highly sensitive health-related information that, while some individuals feel is important to know, others choose not to know. Genetic information is significantly different from other medical information since genetic testing often involves other family members who may or may not want to know or do not want to provide genetic information.

How is genetic information obtained?

Genetic information is obtained through the study of our body cells. Genes are the basic units of heredity that are passed down from one generation to the next. Genes are made up of a body chemical called DNA (deoxyribonucleic acid). Our DNA can be

obtained through several different ways, such as from saliva, hair, fingernails, blood, semen, skin and nail clippings. Virtually all clinical DNA testing uses blood as the method of obtaining a sample of DNA.

Why is our genetic information being stored?

Genetic information is routinely stored within hospital data banks. It's collected with the goal of improving patient care or to reduce the likelihood of disease (Council for Responsible Genetics, 1995). Our genetic information provides a way to easily identify who we are and certain information about us. Other reasons why our genetic information is being stored are to:

- Conduct research

In mapping our genes, scientists hope to prevent future disease and discover treatments and cures for diseases and conditions, such as mental retardation.

- Establish identity of suspects

DNA is being used by lawyers as strong evidence to establish the identity of individuals suspected of committing crimes. It has been used in thousands of cases in the U.S. and other countries.

- Prove fatherhood

In order to prove paternity (whether or not a man is the father of a child), a blood sample is often taken in order to extract DNA. In divorce proceedings, this is often used to determine who is responsible for child support payments and who will get custody of children.

- Identify bodies

DNA can be taken from bodies that may be difficult to identify due to severe damage of the body, such as from fire or military combat. In the latter application, there is hope that never again will there be an unknown soldier.

- Study human evolution

Scientists are collecting DNA samples from skeletons of humans who lived thousands of years ago in order to better understand the process of our evolution (Baker, 1997).

DNA-based tests are also used for:

- prenatal testing (for some conditions)
- identification of a carrier for a specific condition
- diagnostic testing
- pre-symptomatic testing
- risk-oriented or susceptibility testing, e.g., such as determining susceptibility to inheriting breast cancer (Kotval, 1994).

What are genetic databanks?

Genetic databanks (sometimes referred to as DNA databanks) are computerized databases that store records obtained through genetic testing. Gene databanks are used for several different purposes, but predominantly for forensic purposes. Genetic information may be obtained directly from a crime scene through blood (in the case of murder or other violent crimes) or semen (in the case of rape). Other genetic information stored includes actual biological samples from genetic tests and newborn blood samples taken to test for PKU and other genetic conditions.

Why is The Arc concerned about DNA Databanking?

There are many situations where people must provide personal information. Several include applying for a job, life or health insurance, credit or financial aid and benefits from the government. As the use of genetic testing grows, insurers and employers will want to obtain test results in order to determine the health status of the applicant or

employee. Such information can be highly sensitive and personal. Once this information is provided, the companies/institutions/individuals are under no obligation by law to protect it. In fact, "there is no law which says that a blood sample collected for one kind of DNA testing can't be used for another purpose" (Baker, 1997). The law also does not give individuals the right to check their DNA file to see if the information is correct.

Genetic information may be used by people other than medical professionals. For example, insurance companies or employers may want to "weed out" applicants or possible new hires whose genetic information is considered undesirable. Although the definition of desirable or undesirable genetic information remains somewhat ambiguous, genes causing mental retardation are susceptible to being labeled "undesirable" which can negatively impact the individual and family members of someone with this disability. Although some types of medical information, such as HIV status, may be kept in separate files so that fewer people can see them, if a "release of medical records" form is signed, insurers are entitled to see everything, including separate files (Wertz, 1997).

This lack of protection of genetic privacy raises a variety of ethical issues, especially in respect to genetic discrimination. Genetic discrimination in health insurance and employment is common since an individual's medical information is often requested by non-medical personnel, such as insurance companies and employers. A survey conducted by the University of Illinois found that 50% of companies use prospective employee's medical records when making employment-related decisions, and 19% of these individuals are not told that their medical records are being considered as a factor in the hiring process (Alpert, 1993).

Another concern is that as medical records become more centralized and computerized, they will more easily be made available to corporations, social service agencies and others, similar to the wide availability of credit histories (Alper and Natowicz, 1993).

Are there any laws to protect genetic privacy?

Genetic privacy legislation covers a wide array of issues, such as informed consent, privacy and confidentiality, as well as genetic discrimination in health insurance and employment. A few states have some legislative protection of genetic privacy, mostly in the form of genetic nondiscrimination laws. Fourteen states have enacted laws that prohibit using genetic data in insurance underwriting, but such laws fall short of providing adequate or comprehensive protection of genetic privacy (Council for Responsible Genetics, 1997). With support from the Department of Energy's ELSI (Ethical, Legal and Social Implications) program, Boston University School of Public Health developed a "Model Privacy Act" based on the premise that genetic information is different from other types of information in ways that require special protection (Annas, et.al., 1995).

Privacy legislation generally fails to address whether or not data obtained for one purpose can be used for another unrelated purpose (also referred to as secondary uses of information). Genetic information is especially vulnerable to this type of misuse. Genetic test results obtained to verify the risk of disease may have originally been obtained only for that purpose. However, such information may serve a number of secondary purposes for insurance companies and employers who can use the information to their advantage.

A national survey revealed state statutes are often silent about the degree of privacy protection provided, allow weaker protection to certain types of health information, or give health officials broad

discretion to disseminate personal health information (Gostin, et.al., 1996). Due to the wide variability that exists between state law regarding privacy, federal law has been proposed that, some suggest, should preempt state law. However, depending on the strength of yet to be enacted federal law, it could weaken existing state law (Marwick, 1996).

In 1996, several bills calling for uniform national standards in privacy law were introduced in Congress, but none were adopted. While it is expected that further activity will occur, most privacy legislation activity is taking place at the state level.

Aren't medical records private?

Anyone who has ever filled out an application for individual life, health or disability insurance should have filled out an "MIB Notice" within their application. Through the Medical Information Bureau (MIB), insurance companies have access to the medical records of people who have applied for insurance. The MIB, a private, non-profit corporation located in Massachusetts, manages a computerized data bank of information to provide insurance companies with medical and certain non-medical information about applicants for insurance. Originally created to prevent insurance fraud, the MIB holds medical information for 10 to 20 million Americans (Geller, et.al., 1996).

If an insurance applicant has a condition significant to health or longevity, such information must be provided by insurance companies to the MIB. Some of the information routinely reported include height and weight, blood pressure, EKG readings and x-rays if such information is considered significant to health and longevity. Non-medical information that could affect insurability can also be reported,

such as adverse driving record, participation in hazardous sports and aviation activity.

Consent from the individual must be given in order to establish an MIB file or to allow a data bank search. However, if the applicant decides not to give consent, insurance companies may automatically deny coverage (Council for Responsible Genetics, 1995).

How can I attempt to protect the privacy of my genetic information?

Protecting the privacy of genetic information is challenging and difficult. For example, if an applicant for health insurance responds honestly to the question of whether or not he or she has a genetic or hereditary illness, this could eliminate any chance of obtaining health insurance. If genetic information is withheld or concealed from the insurance company, does this mean that

coverage for associated problems would be denied? If one declines to answer truthfully does this mean that insurance will be denied? Either way, whether a person decides to respond truthfully or decides to not respond at all, coverage can be denied.

Until adequate legal protection is available, the following suggestions should be considered to protect your genetic information.

To attempt to keep genetic information as private as possible, physicians and other medical providers should be instructed in writing that they are not allowed to disclose your genetic information to anyone without prior verbal and/or written consent.

Whenever you apply for insurance, note if the application says, "if you have been advised of" any genetic or hereditary illnesses, conditions or diseases. If yes, and you sign a completed application, the insurance company can send a copy of your application to the MIB, which means all future

insurers will have access to your genetic information (Morelli, 1992).

If MIB has a file on you, you can obtain a copy of the report to determine if anything in the file is incorrect and change it if it's wrong. The information within the report is translated from code to reveal the specific conditions. Medical conditions are reported by using one or more of about 210 codes.

You can file a statement of dispute if you disagree with information in the file. If the information was accurate when reported, but has changed and is no longer accurate (for example, a medical condition that has improved), a "statement of additional information" can be submitted describing the improvement or correction. To determine if you have a file or to request a copy of your medical file, contact the MIB at 617-426-3660 (P.O. Box 105, Essex Station, Boston, MA 02112). Cost is \$8.00.

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The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 2, No. 2

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Fragile X Syndrome

Introduction

Many forms of mental retardation are assumed to result from a disrupted or abnormal gene, but only a small fraction have been identified. Some genetic conditions, such as Down syndrome, are spontaneous abnormalities, whereas others are inherited, transmitted by carriers or affected individuals from one generation to another. Of the known genetic causes of mental retardation, fragile X syndrome is currently considered the leading inherited cause, with an incidence between 1:2,500 and 1:4,000.

What is Fragile X Syndrome?

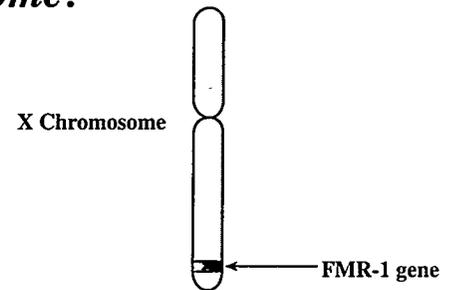
Fragile X syndrome is a single gene disorder located on the X chromosome. Understanding the basics of fragile X syndrome requires an understanding of how genes themselves are constructed and what they do.

Genes are made up of DNA, which provides the blueprint for life. This blueprint is a code containing four letters (C, G, A, T), abbreviations for four different nucleotides (cytosine, guanine, adenine, and thymine). Nucleotides are the essential building blocks which make DNA. The letters and the sequences in which they are arranged construct the messages which lead the body to produce key proteins.

Fragile X syndrome results from a *mutation* (a change in the typical DNA sequence) known as a trinucleotide repeat expansion. This means that a series of three particular nucleotides (CGG) in the DNA is greatly expanded beyond its normal size, disrupting the normal messages that need to be

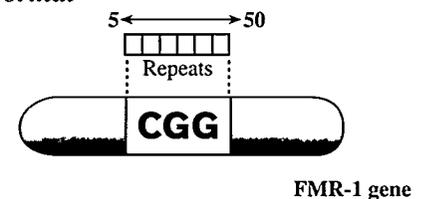
What is Fragile X Syndrome?

1 The FMR-1 gene is located on the X chromosome. This gene is responsible for instructing the cell to make FMRP, a protein assumed to be essential for normal brain functioning.



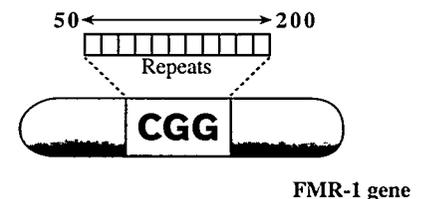
2 The genetic code for the FMR-1 gene usually contains a limited repetition of CGG sequences. The *normal* range is 5-50 repeats.

Normal



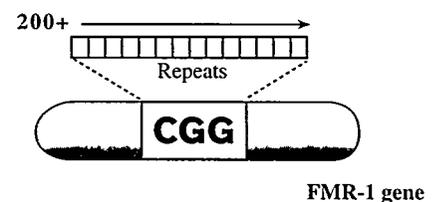
3 Some people have an expanded number of CGG repeats. When the number of CGG repeats is between 50 and 200, the individual is a *premutation carrier* of fragile X syndrome. Carriers are not usually affected by fragile X syndrome, but they are at risk of having affected children.

Premutation



4 If the number of repeats exceeds 200, usually this disrupts the code and prevents the production of the FMR protein. These individuals have the *full mutation* and usually are affected by fragile X syndrome.

Full Mutation



sent. This fact was discovered in 1991 by several teams of researchers studying the X chromosome.

In the FMR-1 gene located on the X chromosome, most individuals

have a CGG trinucleotide repeat that occurs between 5 and 50 times, the average being around 30. These individuals are *normal* with respect to fragile X syndrome, and usually carry no

risk of transmitting it, although the 40-60 repeat range is sometimes considered a "gray zone" which may or may not be unstable (have a risk of expanding). Some individuals have CGG sequences that are repeated in the range of about 50 to about 200. These individuals are generally referred to as *premutation carriers*. This means that they carry the syndrome and can transmit it to their children. Premutation carriers, however, are not usually affected by fragile X syndrome. When the number of CGG repeats expands beyond 200, the individual usually has the *full mutation*. This means that they have fragile X syndrome and will experience the impairments and delays associated with the syndrome.

How is Fragile X Syndrome Detected?

Fragile X syndrome is detected through a DNA analysis that almost always requires drawing blood. The technique for identifying fragile X syndrome is a specialized process and not all genetic labs have this capability. For those that do have this capability, the procedure is virtually 100 percent reliable. Prenatal identification is also possible. However, it is impossible to determine how severely affected the child might be based on this procedure.

How is Fragile X Syndrome Inherited?

Fragile X syndrome is carried on the X chromosome. Since both males (XY) and females (XX) each have at least one X chromosome, both can be carriers or have the syndrome. If a father is a carrier, he can only pass the gene defect to his daughters, since he transmits a Y chromosome to his sons. All of his daughters will inherit the gene, and as far as is known, transmission from father to daughter only occurs in a premutation state. In other words,

if a daughter inherits the gene from her father, she will have the premutation, not the full mutation. Interestingly, this happens even if the father has the full mutation, as the sperm of males with the full mutation has been shown to be in the premutation phase.

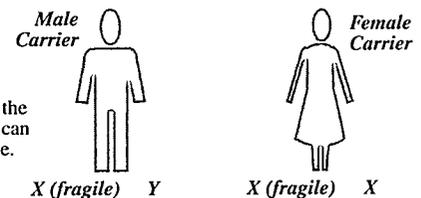
If a mother is the carrier, she can pass the gene defect to either sons or daughters, since she contributes an X chromosome to each. Children of carrier mothers have a 50 percent chance of inheriting the gene, since the mother has two Xs to give and only one is affected. It

is through mothers that the gene can expand from the premutation to the full mutation. So, a carrier mother can have normal children, children with the premutation, or children with the full mutation.

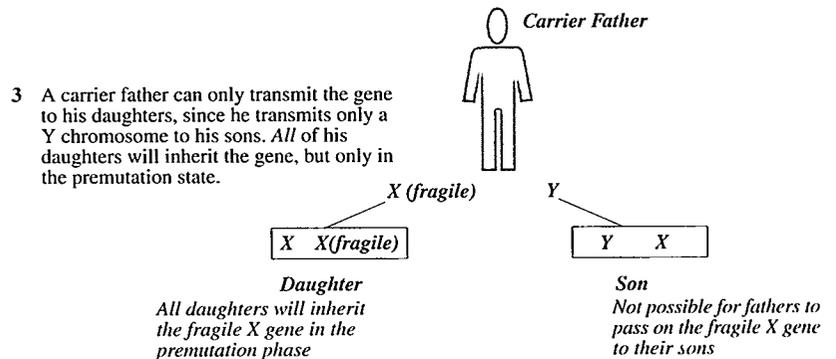
The chances of expansion into the full mutation increase with successive generations. Thus the gene could be passed down in the premutation phase for several generations without anyone suspecting that the family has a genetic disorder that ultimately will lead to mental retardation or other developmental disabilities.

How is Fragile X Syndrome Inherited?

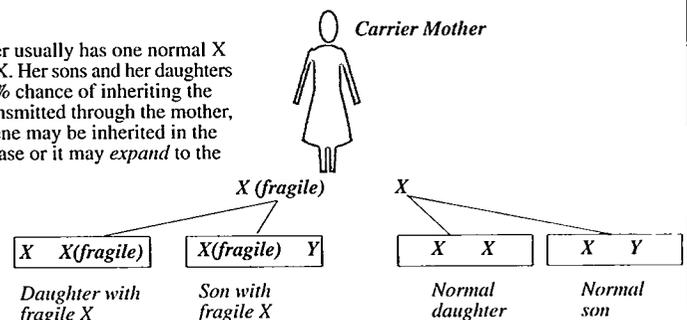
- 1 For a child to inherit fragile X syndrome, one parent must be a *carrier*.



- 2 Since fragile X syndrome is carried on the X chromosome, both males and females can be carriers and can inherit the syndrome.



- 4 A carrier mother usually has one normal X and one fragile X. Her sons and her daughters each have a 50% chance of inheriting the gene. When transmitted through the mother, the fragile X gene may be inherited in the premutation phase or it may *expand* to the full mutation.



What Are the Effects of Fragile X Syndrome?

The biological effect of this expansion of CGG repeats is to shut down the production of the FMR-1 protein. The function of this protein is currently the subject of intense study, but it is clear that it is essential for normal brain function. Loss of the protein affects overall development, patterns of behavior, and physical features. These effects are different for males and females.

Effects on males. Males with the full mutation are more severely affected than females. Most will have mental retardation, ranging from mild to severe. Delays are usually evident in all developmental domains, although cognitive and communication skills are likely to be most affected. They may seem shy and often have problems with social skills and attention. One common feature that has been described is hyperarousal, which means that they can easily become overstimulated and may appear to overreact to changes in environment, routines, or expectations. Lack of eye contact is frequently observed.

Males also have several distinguishing physical features. They often have large ears, loose joints and muscles, and an elongated face. After puberty males usually have testicles which are significantly larger than usual.

Effects on females. Females generally have more mild impairments. Females have two Xs, but in each cell only one becomes activated, a process that appears to be random. On average, therefore, about half of a female's cells will use the normal X (from the non-carrier parent) and half will use the fragile X. About one-third of females with the full mutation will have normal development, about one-third will exhibit learning disabilities, and about one-third will have mental retardation. They may also be shy and have mild social problems.

What Are Some Major Issues Facing Parents and Professionals Today?

Now that researchers know the genetic basis for fragile X syndrome, much work is being invested in understanding the function of the FMR-1 protein. Behavioral scientists are working to describe in more detail the specific kinds of learning challenges faced by persons with fragile X syndrome and to identify the kinds of educational and therapeutic strategies most likely to be successful. In the meantime, families and practitioners are trying to address a number of challenges:

Promoting early identification. Most cases of Down syndrome are identified at birth on the basis of physical features. However, fragile X syndrome is not at all obvious at birth. Usually parents begin to notice behavioral problems (inability to cuddle, lack of regular routines, fussiness) or delayed attainment of developmental milestones (walking, talking). Sometimes these signs are subtle, and it may take a long time for a physician or other professional to acknowledge that a problem exists. Even then the child may not be referred for genetic testing. As a result, many cases of fragile X syndrome remain undiagnosed or are diagnosed later than most parents would prefer. Physicians need to be better informed about fragile X syndrome, and more research is needed that will help identify early signs of fragile X syndrome.

Supporting extended families. Often fragile X syndrome is identified in families where there was no prior knowledge of its existence. Because it is an inherited disorder, other family members inevitably become involved and may be identified as carriers or as having the disorder. The process of informing other family members and helping extended family members cope with this unexpected information is challenging and one for which outside support can be especially helpful.

Determining medical treatments. There is no cure for fragile X syndrome. Many researchers are studying gene therapy in hopes of ultimately identifying ways to correct genetic disorders. However, this process has yet to be successful with any disease, and since brain disorders pose unique challenges, a cure is unlikely in the near future. Medical interventions are thus primarily limited to medications. A number of medications have been identified as being helpful in addressing problems related to anxiety, attention, and activity. However, there is not a standard prescription regimen and usually several drugs must be tried independently or in combination with each other before an effective treatment is identified.

Determining educational and therapeutic treatments. Most persons with fragile X syndrome need special education and therapeutic services. Unfortunately, little research has systematically examined the effectiveness of various treatments or interventions. General suggestions include designing a structured, predictable environment, eliminating distractions, allowing for periods of rest and escape from demands, and clear communication of expectations and feedback. Speech and language therapy as well as occupational therapy are recommended for most affected individuals.

Differentiating fragile X syndrome and autism. Males with fragile X syndrome may display autistic-like behaviors such as hand-flapping or social avoidance, and many are initially referred for an autism evaluation. Research shows that while fragile X syndrome is not a major cause of autism, about 15 percent of persons with fragile X syndrome may meet diagnostic criteria for autism at some point in their lives. However, the basis for autistic-like behavior may be different for the two populations and more research is needed on the implications for treatment.

Conclusion

Although fragile X syndrome is the most commonly occurring known inherited cause of mental retardation, it accounts for only a small portion of all the cases of mental retardation. However, it is an interesting disorder from a genetic perspective and knowledge of the mechanism by which it is caused may help our understanding of other genetic

causes as well. The syndrome has implications both for affected individuals and for their families. Research to date has focused primarily on the genetic aspects of fragile X syndrome. Effort now needs to be invested in educational, psychological, and therapeutic intervention studies to identify ways to maximize development, adaptive functioning, and quality of life.

This report was prepared by Don Bailey, Ph.D. Don is Director of the Frank Porter Graham Child Development Center of the University of North Carolina at Chapel Hill, where he and his colleagues are conducting several studies of fragile X syndrome during the early childhood years. Thanks to Dr. Deborah Hatton (UNC-CH) and Dr. David Nelson (Baylor College of Medicine) for their feedback on the report. The graphics were produced by Brady Fowler of the FPG Center.

Fragile X Syndrome Resources

Books and Pamphlets

The Fragile X Child. (1992). B. B. Schopmeyer & F. Lowe (\$39.95 plus \$5.25 shipping). Singular Publishing Group, 4284 41st St., San Diego, CA 92105-1197 (1-800-521-8545)

Educating Boys with Fragile X Syndrome. (1994). G. A. Spiridigliozzi, A. M. Lachiewicz, C. S., MacMurdo, A. D. Vizoso, S. M. O'Donnell, A. McConkie-Rosell, & D. J. Burgess (\$10, checks to DUMC) (919-684-5513). Gail Spiridigliozzi, Child Development Unit Box 3364, Duke University Medical Center, Durham, NC 27710

Behavior and Development in Fragile X Syndrome. (1994). E. M. Dykens, R. M. Hodapp, & J. F. Leckman. Sage Publications, 2455 Teller Road, Thousand Oaks, CA 91320

A Parent's Guide to Drug Treatment of Fragile X Syndrome. (1995). Michael R. Tranfaglia. (\$25). FRAXA Research Foundation, P.O. Box 935, West Newbury, MA 01985 (508-462-1990)

Fragile X Syndrome: Diagnosis, Treatment, and Research, Second Edition. (1996). R. J. Hagerman & A. Cronister (\$35). Johns Hopkins University Press, 2715 N. Charles St., Baltimore, MD 21218-4319 (410-516-6956)

Fragile: Handle with Care--Understanding Fragile X Syndrome. (1996). M. Braden (\$25). Avanta Publishing Company, 75 South Elliott St., P.O. Box 17023, Chapel Hill, NC 27514 (919-967-0322)

Newsletter

National Fragile X Advocate. Pam Brode, Editor-in-Chief. One year subscription for individuals/nonprofits (4 issues), \$36. Avanta Publishing Company, P.O. Box 17023, Chapel Hill, NC 27516-1702. (919-967-0322/800-434-0322)

Email address: pbrode@nando.net

Resource Centers, Agencies

National Fragile X Foundation, 1441 York St., Suite 215, Denver, CO 80206 (1-800-688-8765/303-333-6155) Fax: 303-333-4369,

Website: www.fragilex.org

Email address: natlfx@aol.com

FRAXA, P.O. Box 935, West Newbury, MA 01985-0935 (508-462-1990/Fax: 508-463-9985) Email address: fraxa@seacoast.com

Web site: <http://www.fraxa.org>

Listserve: Instructions to join found on FRAXA website.

Articles

Hagerman, R. J. (1997). Fragile X syndrome: Meeting the challenges of diagnosis and care. *Contemporary Pediatrics*, 14(3), pp. 31-59.

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The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

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Gene Therapy and Mental Retardation

What Is Gene Therapy?

Gene therapy is an experimental treatment in which normal genes are introduced into the body's cells in order to correct or modify the function of the cell which is not working. The initial purpose of gene therapy was to treat hereditary diseases by adding good genes to function for missing or defective genes. Researchers soon discovered that genes could also be introduced into cells to help patients fight disease.

There are two kinds of gene therapy. Somatic cell gene therapy is directed at treating the somatic cells (the non-sex cells) which are all the body cells, except the reproductive cells. Somatic cell gene therapy is generally viewed as a conventional medical therapy that is not a major departure from established medical practice (Morsy et al, 1993). It would result in correcting a genetic defect only in the non-sex cells of the person being treated.

In contrast, germ line gene therapy would treat cells of the reproductive tissues of a patient, the germ or sex cells, in such a way that the disorder would also be corrected in any offspring of the individual (Anderson, 1985). (The sex cells are called germ cells and include the egg and sperm.) Because future generations are affected, germ line gene therapy is the focus of concern and discussion regarding whether it is an ethical approach to treating genetic disorders. The federal government does not fund this type of gene therapy at this time.

Key Points

- Gene therapy is an experimental treatment in which normal genes are introduced into the body's cells in order to correct or modify the function of the cell.
- No one has yet been "cured" of a genetic condition by gene therapy, although it is considered a promising tool for treating single gene defects causing mental retardation.
- The potential availability of gene therapy raises a variety of ethical issues including acceptance of gene therapy as an appropriate means to treat mental retardation, eugenics, fair allocation of resources to gene therapy research, genetic enhancement of cognitive abilities and participation of infants and children in research.
- Families must be informed about gene therapy ethical issues in order to express their views and personal experiences to policy-makers.

Status of Gene Therapy

More than 250 research trials are under way using somatic cell gene therapy (Lyon, 1997). Many studies have involved treatment of cancer; others involve inherited disorders like cystic fibrosis. While researchers are learning a lot about how to conduct gene therapy, there has not yet been a cure for any of the conditions being treated. Most studies have only involved a small number of patients to test the possibilities of the transfer of genes into body cells and to evaluate the effects of this treatment.

Members of a National Institutes of Health panel that investigated the status of research on gene therapy believe gene therapy holds great promise. However, the panel noted the public's mistaken and widespread perception that gene therapy is further developed and more successful than it actually is. The panel expressed concern that patients, their families and health providers may

make unwise decisions regarding treatment alternatives, believing cures are "just around the corner" (Orkin and Motulsky, 1995.) Scientists disagree on how many years of development are needed before gene therapy becomes a proven treatment, but most of them in the field believe gene therapy is on track to be the "most powerful curative and diagnostic tool ever" (Lyon, 1997).

Basic Gene Therapy Techniques

In gene therapy, healthy copies of genes are given to someone whose own versions are faulty or missing. There are two basic methods for doing this. The *ex vivo* method removes selected cells from the patient's body, introduces the normal copy of the defective gene (therapeutic gene) into these cells and then returns the cells to the body. The *in vivo* method inserts the therapeutic genes directly into the targeted

body cells generally using a type of virus as a carrier (Batshaw, 1997).

There are many challenges to accomplishing gene therapy. One hurdle is to get the therapeutic genes into cells without causing harm to the body. Researchers also need to control the specific types of cells a therapeutic gene enters. For example, if the condition affects liver function, the therapeutic genes will be targeted to reach the liver cells. Once the genes are inside the cell, scientists would like to be able to control the level of activity needed to correct the problem. This means the new gene must function normally in the cell (Orkin and Motulsky, 1995).

Can Gene Therapy Be Used to Treat or Cure Mental Retardation?

At this time, the most promising use of gene therapy is to treat single gene defects causing significant disability that cannot be treated satisfactorily by other approaches (Moser, 1995). Gene therapy studies to test the safety and the effects of the treatment have begun in a number of genetic disorders causing mental retardation, including phenylketonuria (PKU), Gaucher Disease, Lesch-Nyhan syndrome, urea cycle disorders and Duchenne muscular dystrophy. (See box).

The current approaches to gene therapy cannot be used to treat the most common chromosomal abnormality that causes mental retardation, Down syndrome. Even though we know that an extra chromosome 21 causes Down syndrome, scientists have not yet identified the specific number and location of genes involved. The gene causing fragile X syndrome, another common genetic cause of mental retardation, has been identified. At some time in the future, it may become possible to apply gene therapy to fragile X. However, much more knowledge is needed about the function and control of the fragile X gene before gene therapy experiments are undertaken (Moser, 1995).

Conditions Undergoing Gene Therapy Research

Lesch-Nyhan Syndrome (LNS)

Lesch-Nyhan syndrome is an X-linked metabolic disorder caused by deficiency of hypoxanthine-guanine phosphoribosyltransferase (HPRT). It is characterized by excess uric acid in the blood which results in symptoms including, writhing movements, communication deficits, mental retardation and involuntary self-injurious behavior. Most males with the disorder have to be restrained to keep from inflicting severe damage to themselves.

LNS is considered suitable for gene transfer techniques because the genetic defect is well understood. There are also mice with HPRT deficiency suitable for testing gene transfer carriers. The major impediment to gene therapy for LNS is the gap in knowledge about causes of the various neurological defects, including communicative defects, mental retardation and self-injurious behavior (Friedmann, 1995).

Phenylketonuria (PKU)

PKU is an autosomal recessive disorder caused by a deficiency of hepatic phenylalanine hydroxylase which is usually diagnosed at birth through newborn screening programs. A diet low in phenylalanine will prevent the profound, irreversible mental retardation characteristic of the disease. However, individuals on the diet may still have some cognitive impairments or behavioral disturbances.

Animal models have been useful for evaluating the effectiveness of different gene therapy treatments. As yet, no effective mechanism for inserting the gene and for obtaining therapeutic results over time has been found. However, research continues, and scientists are optimistic that the challenges will be solved (Fang, Eisensmith and Savio, 1995).

Ornithine Carbamoyltransferase (OTC) Deficiency and Other Urea Cycle Disorders

Urea cycle disorders are inborn errors of metabolism caused by a deficiency of one of the enzymes needed for the synthesis of urea from ammonia. The deficiencies cause an excess of ammonia in the blood and body tissues. Many children with this condition do not survive the newborn period and those that do have a high incidence of mental retardation and other developmental disabilities.

Gene therapy studies have focused on OTC deficiency in part because there are mouse models of this disease and in part because this disease is particularly resistant to current therapies. Different approaches to gene therapy are being developed for treatment with the prospect of clinical trials beginning soon (Robinson, Batshaw, Ye, and Wilson, 1995).

Duchenne Muscular Dystrophy (DMD)

Duchenne muscular dystrophy is a wasting disease of muscle caused by mutations in a single gene on the X chromosome. Because no effective treatment is available, the disease is inevitably fatal by the third decade of life. About one third of all males with DMD have mental retardation.

Gene transfer technology focuses on correcting the biochemical defect (dystrophin-deficiency) in muscle fibers of DMD patients which somehow is likely related to the mental retardation as well. Experimental studies in mice have shown that dystrophin gene transfer to skeletal muscle is possible and that its efficiency in the mouse may be high. The next stage of inquiry will use dystrophic dogs in order to answer questions related to efficiency, dosage, route of administration and safety limits (Dunckley, Piper, and Dickson, 1995).

Gaucher Disease

Gaucher disease is an autosomal recessive disorder that is the result of inherited deficiency of the enzyme glucocerebrosidase. The enzyme deficiency can result in massive enlargement of the liver and spleen, decreased numbers of red blood cells and platelets and skeletal deterioration. There are three types; Type 1 is the mildest (and most common), while Types 2 and 3 are more serious and include mental retardation.

Gene therapy research has focused on Type 2 Gaucher disease which is rapidly progressive and usually leads to death by two years of age. Because no naturally occurring animal model is available, researchers first developed a Type 2 Gaucher mouse. These mice have provided new insights into the mechanisms that result in the most severe forms of Gaucher disease. They will be valuable for testing gene therapy strategies for Gaucher disease (McKinney et al., 1995).

increase the IQ of a child with mild mental retardation, so that the child would function in the normal range, should it be considered? Currently, it is not considered acceptable to use gene therapy to treat conditions that are not diseases. Is mild mental retardation a disease that needs to be treated or a condition that does not justify a need for treatment? Walters and Palmer (1997) suggest that intellectual genetic enhancement that allows people with mental retardation to achieve functioning within the normal range is acceptable ethically. Even though such a treatment for mild mental retardation does not yet exist and may never exist, members of The Arc need to be involved proactively in discussing genetic enhancement before any policy governing its use is enacted.

Allocation of Resources to Gene Therapy Research for Mental Retardation

At this time, gene therapy research is expensive. Assuming it remains so, there are concerns about how to allocate fairly the resources toward such research. Currently, much government and private research is focusing on conditions affecting many people (cancer, for example) where there is great potential for helping large numbers of individuals.

This raises questions about which conditions and diseases should be targeted in developing treatments for mental retardation and who decides. Clearly, most

genetically caused mental retardation is of low incidence, affecting few numbers of people, ranging from 1 in 1,000 to 1 in 100,000 or fewer (Moser, 1995). Given the tendency to select disorders for gene therapy in which cost effectiveness is a strong force, there is concern about access to funding for genetic disorders causing mental retardation (Fletcher, 1995). Within mental retardation gene therapy research, there is a further question of fairness. Should limited resources be allocated to those genetic conditions that cause mental retardation in the greatest number of people or to those that cause the most severe forms of mental retardation? These are questions for discussion within The Arc.

Participation of Children in Gene Therapy Research Studies

Infants and young children will be the subjects of most gene therapy research related to treating mental retardation, because the therapy must be applied before the child suffers irreversible brain damage. Research involving children requires heightened ethical sensitivity because of their vulnerability (Fletcher, 1995). First, there must be assurance that children will benefit from participation in the research. Their participation must be voluntary and informed (by them and their legal representatives). The selection of children for the research must be fair, and the research itself must be safe (Fletcher, 1995). To ensure safety,

the research procedures should be tested first on animals, followed by adults and older children, before using young children with disabilities (Batshaw, 1997). The issue of fair selection for gene therapy research relates to the issue of allocation of resources, that is, how diseases or conditions are selected and how research subjects are selected given resource limitations.

Before a gene therapy study involving human subjects begins, researchers must obtain participants' informed consent for participation in the research. Informed consent is an acknowledgment by an individual that he/she understands the risks and benefits of a procedure, the possible alternatives to having the procedure, and the means that will be used to minimize risks. Children under age 18 cannot legally give informed consent. Their parents or guardians must sign for them. However, federal regulations require that researchers seek "assent" verbally from children age 7 and older. Assent means that the child knows he/she is in a research project and has some knowledge about its risks and benefits (Wertz, 1997). If a child has mental retardation, parents will have to determine if their child can understand the nature of the research and what is involved. Children who are capable of giving an informed refusal to experimental gene therapy should not be coerced to participate (Fletcher, 1995).

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Role of Families in Helping Shape Views on Ethical Issues

Genetic research and diseases are changing the world in which we live. It is important for families potentially affected by the knowledge gained from research to become involved by becoming educated and by expressing their personal views/opinions. Human gene therapy research has been widely scrutinized since scientists began requesting funds for its support. The ethical issues have been widely debated by scientists, ethicists and others. However, few voices from families directly affected by a genetic condition have been heard.

As a family member, you may think you can have very little

impact on what scientists do. Not true! Your opinions are important. By keeping informed about the issues as they affect you and your family and by speaking out, you can help shape what happens. You can advocate for the passage of certain laws or elect leaders who believe as you do. This is what The Arc has done historically in areas such as education, employment, social security and Medicaid with significant success. It is also important for you to make informed personal choices regarding participation in gene therapy research for you and your family.

As families affected by mental retardation, all of us must continue to advocate for understanding and acceptance of the condition and fair treatment of citizens with mental retardation. We must ensure that genetic technology offering a treatment for these conditions does not create a less accepting attitude within society toward people who have mental retardation. We must continue advocating for their opportunity and right to live full and satisfying lives in communities across the nation, regardless of the possibility of cure.

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Additional reading:

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The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 3, No. 1

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Participating in Genetic Research: Considerations for People with Mental Retardation and Their Families

Introduction

This report presents information to help families make decisions about whether they should participate in genetic research. The types of genetic research and the benefits and risks of participation are described. Also discussed are issues related to informed consent of individuals with impaired decision-making skills, such as mental retardation. After reading this report, families will be informed of the protections mandated and desirable in any research and recognize the unique issues associated with genetic research.

of genetic defects. Newborn screening tests detect serious genetic disease. Carrier status tests determine if individuals are carriers of a gene or chromosome abnormality that might have serious health implications for their children or future generations. Prenatal tests detect the presence of genetic or chromosomal abnormalities in fetuses. Risk assessment tests determine the probability that a person will develop a genetically-linked disease some time in the future.

4) Gene therapy research to develop treatments for genetic

disease by altering an individual's cells. Properly functioning genes are introduced into the body's cells in order to correct or modify the function of the cell that is not working.

Who benefits from genetic research?

Individuals and families participate in genetic research for many reasons. Some people participate because they hope they will receive a treatment that will benefit them personally.

What is genetic research?

Human genetic research involves the study of inherited human traits. The U.S. Human Genome Project that is part of the worldwide effort to map the human genome is driving much of the research. The types of research may include (National Institutes of Health, 1993):

- 1) Studies to discover the pattern of inheritance of a disease and to catalog the range of symptoms involved (referred to as pedigree studies). Researchers study members of families who have the disease, condition or characteristic and obtain information about them and other family members.
- 2) Research to localize and identify specific genes. This research relies on DNA analysis of tissue samples taken from the members of families in which the condition appears.
- 3) Research aimed at developing genetic tests. Genetic tests are used to determine the presence

Key Points

- Genetic research involves the study of inherited human traits. It includes discovering the pattern of inheritance in families, identifying specific genes, developing genetic tests and conducting gene therapy. Genetic information about an individual may be information about other family members.
- People who participate in genetic research may benefit from receiving a new treatment, gaining access to specialized care or receiving satisfaction from advancing the understanding of a genetic disorder. However, research participation may also involve risks, including social and psychological harm and physical injury.
- Researchers must obtain informed consent from people considering participation in genetic research studies. There is concern about the use and effectiveness of informed consent among people with impaired decision-making, such as mental retardation.
- Federal law places responsibility on Institutional Review Boards (IRBs) to ensure protection of individuals with mental retardation and other mental disorders who are research subjects.
- The National Bioethics Advisory Committee's draft report on involving people with impaired decision-making in research advises a number of recommendations for IRBs to ensure the safety of those with mental disorders.
- The Alliance of Genetic Support Groups developed a list of questions to assist family members in deciding whether or not to participate in genetic research.

Sometimes, participating in a study can put the person in contact with specialists and specialized care that may be inaccessible otherwise (Alliance of Genetic Support Groups, undated). Families are often interested in working with scientists to advance the understanding of the cause, diagnosis and treatment of mental retardation knowing that they may not personally benefit. They receive satisfaction from knowing society may benefit from what is learned.

Research participants may also benefit by learning genetic information about themselves that can lead to early treatment, even when they have requested not to be informed about genetic findings. While research participants in general have a right not to know genetic findings about themselves, a possible exception exists if early treatment of a genetic disease could benefit the individual. In this situation, researchers may have an ethical obligation to inform the individual about the disease gene and the treatment available (National Institutes of Health, 1993).

The identification of a disease gene in a research subject may also have important implications for other family members. The subject should be asked to give consent to disclose such information. If the subject refuses to consent, the ethical obligation to protect the subject's confidentiality may be overridden in certain situations. Other family members could be informed about their risk of harm and the need for diagnosis and treatment under the following conditions: the risk of harm is serious; disclosed information will be used to avert harm; and only genetic information needed for diagnosis and/or treatment is disclosed (National Institutes of Health, 1993).

What are some of the risks regarding participation in genetic research?

Families must recognize that if they choose to participate in a research study, they are engaging in a form of public service that may involve risk. The research team should explain the purposes of a study and the benefits that might be gained from participating. Researchers should also inform participants about potential risks, as all risks rarely can be eliminated (National Bioethics Advisory Committee, 1998).

Genetic research that studies pedigrees, identifies genes, and develops genetic tests may involve risks of psychological and social harm. Research subjects may learn information about their own genetic status that can provoke anxiety and confusion in themselves and affected family members. Their insurance and employment status may be compromised if genetic information is disclosed to insurers or employers. Even though these studies may not involve physical risks of harm, researchers must be aware of and disclose the social and psychological risks. Gene therapy research, on the other hand, requires special safety precautions because it attempts to treat genetic conditions by inserting properly functioning genes into the individual's somatic (body) cells. At this time, researchers are still learning how to control the genes inserted for the treatment, and there may be risks of physical injury (National Institutes of Health, 1993).

Psychological risks from learning genetic information. Genetic studies typically involve families. One of the first steps in most genetic research studies is to draw a family tree (a pedigree) that also contains some medical information. Highly sensitive information may be revealed about a person's health and the health of family members.

Individuals may learn information about their own genetic status, such as a risk of

developing symptoms of a genetic disorder. This information is typically limited to probabilities. Many factors determine whether or not the person will develop the disorder. Participants are subjected to the stress of receiving such information and may experience emotional distress. Other participants may be grateful to learn they will not develop a disease that runs in the family, or, if they do have the gene, be glad they know their risk and can plan accordingly for the future.

Some family members do not want to participate in research or know about certain information that could be found during the research project. Special privacy and confidentiality protections should ensure that such individuals do not learn by chance about genetic information affecting them.

Social risks from unwarranted disclosure of genetic information to third parties. Persons other than the research team may learn information about a participant in genetic research. While researchers strive to protect confidential health information, there is no absolute guarantee that at some point other researchers, insurance companies, employers, or other people will not find out this information. Participants should ask for assurance that this information will not be put in their medical record. However, it is important for families to realize that insurance companies will learn about it if an individual files a claim for any costs associated with the research project.

People may be discriminated against because they have a disease gene or genes, even when they show no symptoms of disease. The denial of health insurance is one of the most common forms of discrimination. In addition, healthy people have been fired from jobs, treated differently in school or barred from adopting a child because they carried genes that could potentially result in disease or

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disability. Some states have laws against discrimination based on genetic information.

Risk of physical injury in gene therapy studies. Any genetic research involves social and psychological risks. Gene therapy involves the additional risk of possible physical injury. One hurdle is to get the therapeutic genes into cells without causing harm to the body. Researchers also need to control the specific types of cells a therapeutic gene enters. For example, if the condition affects liver function, the therapeutic genes will be targeted to reach the liver cells. Once the genes are inside the cell, scientists need to be able to control the level of activity needed to correct the problem. This means the new gene must function normally in the cell (Orkin and Motulsky, 1995).

Because of the risks that something can go wrong in each of these functions, gene therapy research proposals submitted to the National Institutes of Health undergo stringent review. Researchers must justify the gene therapy research techniques against alternative methodologies and state the risks and benefits of the research. They must also address how subjects will be selected for the research, how their informed consent will be obtained and how their privacy and confidentiality will be protected (National Institutes of Health, 1993).

What is informed consent?

Informed consent is a term explaining the process by which information given to a patient by a physician or other health care provider about a test, treatment or research study is adequately understood. Signing a consent form indicates a voluntary willingness on behalf of the participant or patient to submit to a procedure with an awareness of its inherent risks, benefits and alternatives. Informed consent is usually obtained through a written document that a person signs

before a procedure. Obtaining informed consent is required by law for research studies (Wert, 1997).

Why is informed consent needed when conducting genetic research?

Obtaining informed consent from research participants has not always been an area of concern in conducting research. It was common during the 1940s and 1950s for physicians to use patients as subjects of research without their consent or awareness. During World War II, the federal government sponsored several thousand human radiation experiments. This research included some people with mental retardation who lived in state institutions. They and their family members often were not informed that they were subjects of risky experiments.

A number of safeguards have been introduced since 1974 when regulations were enacted to protect human subjects involved in research experimentation. Today, federally funded researchers must abide by guidelines found in the Federal Policy for the Protection of Human Subjects (known as "the Common Rule") in research studies (Federal Register, 1991). Table 1 lists the information that must be provided to all potential research participants before they are asked to consent to be in the study.

Why is informed consent important to people with mental retardation and other cognitive disabilities?

Informed consent is a legal concept based on the premise that competent adults have the right to decide whether or not to participate in genetic research. Vulnerable populations, such as the elderly, prisoners, children and people with mental disabilities, are much more susceptible to involvement in genetic research without a full understanding of the risks involved (Loscialpo, 1997).

Table 1
Federal Requirements for Informed Consent

- 1. State and describe:**
 - a) Research nature of study
 - b) Purpose of study
 - c) Duration of participation
 - d) Procedures to be followed
 - e) Which procedures are experimental
- 2. Describe:**
 - f) Reasonably foreseeable risks, including physical, emotional and social/economic risks
 - g) Discomforts
- 3. Describe:**
 - h) Benefits to the individual
 - i) Benefits to others
- 4. Disclose:**
 - j) Alternative procedures or treatments
- 5. Describe:**
 - k) Confidentiality of record identifying individual
- 6. Explain if the project involves more than minimal risk:**
 - l) Policy on compensation for injuries due to research
 - m) Availability of medical treatment for such injuries
 - n) Sources of further information
- 7. Explain:**
 - o) Whom to contact for questions about the test results or about research, or
 - p) In the event of research-related injury
- 8. State:**
 - q) Participation is voluntary
 - r) No loss of benefits on withdrawal
 - s) May withdraw at any time

Those with mental retardation participating in genetic research must first be recognized as having a disability and, therefore, requiring greater attention when research studies or the consequences of genetic testing are being described and explained. Researchers must ensure that participants fully understand for what they are volunteering. Having a solid understanding of the research process can be challenging, and the informed consent forms used are often confusing (Marwick, 1997).

Can people with mental retardation give informed consent?

Yes, some are able to make competent and informed decisions about research participation. One should never automatically assume that having a disability disallows giving consent. Some may be able to make many choices for themselves while others lack such ability completely. People with cognitive disabilities vary considerably in their ability to make independent decisions.

Autonomous decision-making by participants can be enhanced when researchers use videotapes, graphics and other information disclosure methods to assist prospective participants with mild cognitive disabilities. The use of peers in this process and making consent forms understandable increases the likelihood of obtaining quality consent. Information should be easily understood and given in small segments rather than all at once. Additionally, to ensure consent is truly voluntary, researchers should talk in private to participants (away from family members, health professionals and others) about their reasons for desiring to participate in a research project (Dresser, 1996). Otherwise, some individuals may be more dependent on caregivers whom they want to please which can considerably affect the decision-making process. Those who live in

institutional settings are especially vulnerable to direct or indirect coercion.

How is a person's ability to give informed consent determined?

There is no single standard used to determine whether or not people with mental retardation can give competent, informed and voluntary consent in order to participate in genetic research. The person's ability to give informed consent should not be determined through general cognitive testing procedures alone. Experts agree that individuals should at least demonstrate the ability to understand and appreciate the significant information that relates directly to the genetic research study (Dresser, 1996).

Can surrogate decision-makers give informed consent?

If an individual with mental retardation is unable to give informed consent, it may be obtained through a surrogate decision-maker (usually a parent or guardian). Federal regulations allow a person's "legally authorized representative" to provide consent if he or she is unable to do so. This representative is "an individual, judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research" (Federal Register, 1991).

What are Institutional Review Boards?

An IRB (Institutional Review Board) is a committee made up of individuals from a broad spectrum of professions that attempts to ensure research participants are protected from harm in research. An IRB includes both scientists and nonscientists, such as clergy, community representatives, social workers, ethicists, lawyers and nurses. The federal regulations

suggest an IRB that regularly reviews research involving a vulnerable category of subjects, such as people with mental retardation, children, prisoners and pregnant women, should consider having a member knowledgeable about and experienced in working with these individuals.

IRBs are required to recognize special problems of research involving vulnerable populations. If the research participants are likely to be vulnerable to coercion or undue influence, the study should include additional safeguards to protect their rights and welfare. However, IRBs need guidance on developing protective measures when obtaining informed consent for participants with mental retardation.

The National Bioethics Advisory Commission's (1998) draft report, "Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity," advises the implementation of a number of recommendations for IRBs to ensure the safety of people with "mental disorders" in scientific research. Selected draft recommendations include:

IRB membership. All IRBs that regularly consider proposals involving persons with disorders affecting decision-making capacity should include at least two members who are familiar with the nature of these disorders and the concerns of the population being studied.

Necessary use. An IRB should not approve research that targets persons with mental disorders as subjects when such research can be done with other subjects.

Design. Investigators should provide IRBs with a thorough justification of the research design they will use.

Risk determination. Researchers should provide to IRBs a thorough assessment of the risks and potential benefits to the human subjects involved in the proposed research.

Informed consent. No person who is capable of making informed decisions may be enrolled in a study without his or her informed consent.

Dissent. Researchers must honor a person's choice not to participate in research or not to continue in a study in which he or she is enrolled.

Assessing decision-making capacity. For research studies that present greater than minimal risk, an IRB should presume that the study will employ an appropriate method, administered by an independent, qualified professional, to assess the potential subjects' capacity to decide whether to participate in the study.

Legally authorized representative. A legally authorized representative (LAR) may give permission to enroll a person who lacks the capacity to decide whether to participate in a research study. The LAR must base decisions about participation on a best estimate of what the subject would have done if capable of making a decision. The LAR must be available to monitor the subject's recruitment, participation and withdrawal from the study.

Greater than minimal risk research that is potentially beneficial to the subject. An IRB may approve this category of research if the subject has given informed consent, or the subject's legally authorized representative has given permission for the subject's participation in the research.

Greater than minimal risk research that is not potentially beneficial to the subject. An IRB may approve this category of research only if the potential subject has given informed consent, or gave informed consent in advance and has a legally authorized representative available to give permission.

What questions can families ask researchers to help in deciding whether or not to consent to genetic research?

The Alliance of Genetic Support Groups developed questions families can ask before making the

decision to participate in genetic research studies. These questions are displayed in Table 2.

Genetic counselors are also a good resource families can turn to when making such decisions. Contact the Alliance to locate a genetic counselor.

Table 2 - Questions for Families to Ask Researchers

General Information

What is the purpose of the study? What are the names of the investigators? Who would be your contact person (and what is his or her phone number)? What agency is funding the research?

Benefits of Participating in Genetic Research

What are the benefits of participating in this research? For myself or family members? For others?

Risks of Participating in Genetic Research

What are the general risks of participating in this research? What physical risks may exist (beyond a blood sample)? What are some of the personal issues that could cause harm to me or my family (e.g., anxiety, stigma, discrimination, unpredicted disclosure of information)?

Treatment Issues

Will treatment be provided if unexpected problems arise while I am participating in the study? Who will pay for this treatment?

Support & Special Services

May I bring a friend or family member to help me, either while deciding to participate or while participating? Will special services be available for me if I need them (e.g., interpreters, Braille, child care)?

Costs and Reimbursement

How will costs associated with participation in this research be handled? Is there compensation for the time involved? Will the costs associated with travel/child care/special services be reimbursed? What additional health care costs may be associated with participation (e.g., will anything such as imaging scans and blood tests be billed to me or my insurance)?

Storage of Genetic Information

What will happen to the stored DNA sample or any of my genetic information after this project is completed? What will happen if I decide to withdraw from this project? If this research plan changes in the future, if additional steps are added, or if new findings emerge, will I be notified and asked to sign another consent form? Will any of my genetic information be distributed (e.g., to pharmaceutical or biotechnology companies, genetic laboratories or government agencies)?

Involvement of Other Family Members

What happens if you need to have other family members involved in the study? How will they be contacted and by whom? What will happen to cells, DNA, or personal genetic information if they choose not to participate at all or withdraw from the study?

Study Results & Confidentiality Issues

What will happen to the results of my tests from the study? Will I receive them? If so, how? May I choose not to receive the results (can I change my mind)? Who will get them (will they be put anywhere except in the research records)? How will confidentiality of the records, including photographs, be maintained?

Communication and Follow-Up

How will the results of the research project be communicated to participants? If genetic services, tests, or treatments are developed from this research, how will I be told about their availability? How will I be informed if you publish information about me and my family? What happens if I do not participate in the research?

Source: Alliance of Genetic Support Groups

The Genetic Issues In Arc Mental Retardation

A Report on The Arc's Human Genome Education Project

Vol. 3, No. 2

The Arc's Human Genome Education Project is part of the U.S. Human Genome Project, which is an international effort to identify all the genes within the human body. The goal of The Arc's project is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. It is funded through the U.S. Department of Energy's ELSI (Ethical, Legal and Social Implications) program.

Mental Retardation & Developmental Disabilities Research Centers: An Overview of Current Genetic Research

About Mental Retardation/Developmental Disabilities Research Centers (MRDDR Centers)

Research is vital in building our knowledge about the prevention of mental retardation and the development of effective services for those with this disability. President John F. Kennedy realized this need when he authorized the creation of twelve Mental Retardation Research Centers, also called "centers of excellence for research in mental retardation," in 1963. For the first time in U.S. history, researchers united to begin an organized effort to conduct research related to mental retardation.

Today, a total of fourteen centers, now called Mental Retardation Developmental Disabilities Research Centers, conduct research related to the cause and treatment of mental retardation throughout the United States. The centers are combining both medical service programs and organized research efforts, representing the world's largest group of scientists and researchers devoted solely to the study of mental retardation.

These centers of excellence have a long history in conducting genetic research. Examples of past studies include: the application of genetic engineering techniques to correct defective enzymes, isolating the enzyme responsible for an inherited enzyme disorder called galactosemia and using animal models of inherited storage diseases to attempt to gain a better understanding of how mental retardation is caused in those with these types of diseases.

Current genetic research conducted by research centers covers a broad range of disorders, including Gaucher disease, Down syndrome, Williams syndrome, autism, fragile X syndrome and Prader-Willi syndrome. This report provides a glimpse into these centers by describing several MRDDR Centers' activities.

The Center on Human Development and Disability (CHDD)

University of Washington Seattle, Washington

The Center on Human Development and Disability (CHDD) at the University of Washington consists of two major programs: the University Affiliated Program (UAP) and the MRDDR Center. The CHDD's mission is to improve the lives of people with developmental disabilities and their families. Through research, training, clinical services and community outreach, the Center seeks to prevent or ameliorate developmental problems. The CHDD pursues new knowledge through scientific investigations directed toward uncovering the underlying causes of developmental disabilities and finding ways to prevent these disorders. Researchers study biomedical and behavioral processes that can cause mental retardation and other developmental disabilities. Once the causes of mental retardation are better understood, researchers hope to discover new ways to intervene and prevent mental retardation and developmental disabilities in the future. Genetic

research projects include studies seeking to identify genes associated with specific developmental disorders, investigations aimed at developing new methods to increase the success of gene therapy, and continued studies of the genetic mechanism underlying disorders such as fragile X syndrome, the most common known inherited cause of mental retardation. Other disabilities being studied include autism and learning disabilities.

Autism

Scientific evidence points to a genetic basis for autism, but scientists do not yet know the identity of the genes involved or the form they take that is related to autism. To uncover the genes associated with autism and ultimately learn how their function is related to the disorder, Gerard Schellenberg, Ph.D., Research Professor of Medicine and Neurology, and his colleagues are studying families with two or more members who have autism. Eligible families from across the country are being invited to participate in the study.

Learning disabilities

Genetic factors are a component of learning disabilities. Research has suggested that genes on three different chromosomes may play a role in learning disabilities, but how these and other as yet unidentified genes may be related to specific subtypes of learning disabilities is unclear. A group of researchers led by Wendy Raskind, M.D., Ph.D., Associate Professor of Medicine, Orthopedics and Psychiatry and Behavioral Sciences, is

investigating genetic factors associated with various subtypes of learning disabilities. The study aims to identify genes related to specific learning disabilities and provide the foundation for understanding how these genes interact with one another and with environmental factors.

Gene therapy

Another group of researchers, including William Osborne, Ph.D., Research Professor of Pediatrics and Hans Ochs, D.M., Professor of Pediatrics, is focusing on developing improved methods for delivering gene therapy (the process of inserting a functional gene in cells of the body to compensate for a gene that is not functioning). Because the "new" genes do not function permanently, they need to be replenished periodically. CHDD researchers are working to develop more effective methods for replenishment and new carriers for transporting the genetic material into cells.

Fragile X syndrome

Charles Laird, Ph.D., Professor of Zoology and his colleagues are continuing investigation of the molecular events that lead to the alteration of the gene responsible for fragile X syndrome. Understanding how repression of a critical gene relates to fragile X syndrome could lead to better clinical assessment of disorders involving similar genetic processes, such as Prader-Willi and Angelman syndromes.

Children's Seashore House University of Pennsylvania School of Medicine Philadelphia, Pennsylvania

Founded in 1990 by Mark L. Batshaw, M.D., this MRDDR Center has been involved in many research initiatives to attempt to discover the causes and treatment of mental retardation and other developmental disabilities. The Children's Seashore House, the University of Pennsylvania and the

Stokes Research Institute have joined together to operate the Center's research activities. This is done through six different "cores." They are: 1) administration, 2) study design and statistical analysis, 3) molecular genetics, 4) analytical neurochemistry and spectroscopy, 5) cellular neuroscience and 6) functional neuroimaging. Specific disorders now under study include holoprosencephaly, velocardiofacial syndrome, ornithine transcarbamylase deficiency (OTC) and Williams syndrome.

Holoprosencephaly

In the category of gene identification, one disorder being studied is holoprosencephaly syndrome. Holoprosencephaly is a birth defect caused by the failure of the forebrain to divide into halves during embryonic development. It can also be caused by an extra chromosome. This developmental brain malformation is usually associated with severe mental retardation and may be sufficiently severe to prevent long-term survival. Recently, Max Muenke, M.D., a pediatric geneticist at this center, has identified a gene called sonic hedgehog that appears to be capable of causing holoprosencephaly. This gene is important as it has already been shown in fruit flies to be essential for midline development of the brain early in the formation of the embryo. Once the function of this gene is understood, more will be known about the early development of the brain in humans.

Velocardiofacial syndrome

Children with velocardiofacial syndrome have congenital heart disease, cleft palate and speech deficits, in addition to mild cognitive impairment. Beverly Emanuel, Ph.D., a geneticist with the center, has discovered that this genetic disorder resides in a small region of chromosome 22 and represents a contiguous gene disorder, where two or more genes are responsible for the clinical findings in a particular syndrome.

Extensive neuropsychological testing by her group has demonstrated that affected children have a nonverbal learning disability which is quite rare and may permit a clearer understanding of how people learn.

Ornithine transcarbamylase deficiency

In correcting genetic disorders, the center has focused on an inborn error of metabolism, ornithine transcarbamylase (OTC) deficiency, to develop gene therapy. In this disorder, an enzyme deficiency leads to the accumulation of ammonia which is highly toxic to the brain and leads to mental retardation in affected children. Mark Batshaw, M.D., a developmental pediatrician and James M. Wilson, M.D., Ph.D., a pioneer in gene therapy, are working to develop a virus containing the OTC gene to correct this disorder. Their work has already been successful in correcting, for a short period of time, the defect in a mouse model of this disorder, and human safety trials have just started. If this research is successful, the transfer virus, an adenovirus, could be used to treat other inborn errors of metabolism that cause mental retardation.

Williams syndrome

The center is using neuropsychology and functional neuroimaging to better define the specific cognitive deficits in Williams syndrome. Children with Williams syndrome are small and have been shown to have similar IQ scores to children with Down syndrome, but a much different cognitive profile. Paul Wang, M.D., a developmental pediatrician, is studying how these differences in cognitive abilities translate into differences in brain regions and functions. This research may help to identify specific regions of the brain as origins for different aspects of thought process. They may also lead to innovative approaches to educational programming that

Other Mental Retardation Developmental Disability Research Centers

Civitan International Research Center

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University of California at
Los Angeles
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Los Angeles, CA 90024
310-825-5542

Mental Retardation Research Center

University of California, Irvine
Medical Center
101 City Drive,
Building 2, 3rd floor
Orange, CA 92868
714-456-5333

B.F. Stolinsky Research Laboratories

University of Colorado Health
Science Center
4200 E. 9th Ave., Box C233
Denver, CO 80262
303-315-7301

Mental Retardation Research Center

University of North Carolina at
Chapel Hill
Chapel Hill, NC 27599
919-966-4250

Kansas Mental Retardation Research Center

Schiefelbusch Institute
1052 Dole Human Development
Center
University of Kansas
Lawrence, KS 66045
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The Center for Research on Mental Retardation and Related Aspects of Human Development

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Mental Retardation and Developmental Disabilities Research Center

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Additional Resources

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Through funding from the U.S. Dept. of Energy, The Arc produced a series of reports (including this one) on the ethical, legal and social implications of genetic research on people with mental retardation and their families. Completed reports may be downloaded at the web site address shown above.

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AAUAP provides the most up-to-date listing of all MRDDR Centers in the country. The MRDDR Centers are often housed at the same academic settings as the UAPs.

Reference

The National Institute of Child Health and Human Development (November 1986) *Centers of excellence: The mental retardation research centers.* NIH Publication No. 86-2882.

Acknowledgement

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could be specified to certain cognitive deficits. The results from the research could be assessed using functional imaging techniques.

**John F. Kennedy Center for Research on Education and Human Development
Vanderbilt University
Nashville, Tennessee**

As one of the original twelve national mental retardation research centers, The Kennedy Center strives to discover why child development goes awry and attempts to find out how to prevent developmental disabilities. The mission of the Center is to conduct and support collaborative research, training, and information dissemination on behavioral, intellectual, and brain development. Today, the Kennedy Center has 94 researchers from 16 departments in Peabody College, the Schools of Medicine and Nursing, and the College of Arts and Science at Vanderbilt University. Together they work to solve problems of development. Over the past few years, the Kennedy Center has developed a core working group of investigators with an interest in genetic abnormalities associated with developmental disabilities, focusing initially on Prader-Willi syndrome. More recently, efforts have expanded to include fragile X syndrome, Down syndrome and autism. Through their research efforts, the Kennedy Center is hoping to make major contributions toward understanding the underlying mechanisms of genetic disabilities, developing new treatments and possibly even preventing some conditions.

Prader-Willi syndrome

At Vanderbilt University, the research project, "Prader-Willi Syndrome: Genetics and Behavior" is being co-directed by Travis Thompson, Ph.D., Director of the John F. Kennedy Center and Merlin G. Butler, M.D., Ph.D.,

Associate Professor of Pediatrics in the Department of Pediatrics, Pathology and Orthopedics. Both researchers have a long-standing history of research in individuals with Prader-Willi syndrome and developmental disabilities. Their project includes over twenty research investigators representing nine departments and the John F. Kennedy Center for Research on Human Development at Vanderbilt University in Nashville, Tennessee.

Prader-Willi syndrome (PWS) is a complex genetic disorder associated with a severe, life-threatening eating disorder and other unusual behavior problems, as well as mental retardation. PWS is characterized by short stature, hypotonia (marked floppiness at birth), feeding difficulties during infancy, early childhood obesity and rapid weight gain after two years of age, small hands and feet, minor facial anomalies and mental retardation. It has an incidence of about 1/15,000 individuals. PWS is caused by an abnormality of chromosome 15 and is generally considered not to be an inherited condition, but rather a spontaneous genetic birth defect that occurs at or near the time of conception.

To prevent PWS, researchers must understand more precisely what each gene in chromosome 15 does. For example, what is the level of DNA making up the gene, how does the gene regulate body chemistry or metabolism and how does all of this affect the person's behavior. The research program consists of five separate research projects and four research cores and includes a large comprehensive study of Prader-Willi syndrome. The goal of the project is to discover the steps along the pathway from the gene to behavior and to gain a better understanding of Prader-Willi syndrome. Researchers plan to recruit fifty people with PWS from ten years of age and older along with comparison subjects with similar age, weight and intelligence level. A better understanding of the syndrome should lead to medication treatments, behavioral interventions and, possibly, gene therapies.

Shriver Mental Retardation Research Center

**E.K. Shriver Center
Waltham, Massachusetts**

The Shriver Center seeks to understand neurological and behavioral development, focusing specifically on assisting people with mental retardation and other developmental disabilities. The Center was founded in 1969 and was one of the first MRDDR Centers in the United States. The Center was named after Eunice Kennedy Shriver, a woman with a deep and lifelong commitment to improving the lives of people with mental retardation. The Center's primary functions consist of conducting research and providing training and services to people with mental retardation and their families. Currently, the Center is conducting a number of interesting research projects that affect people with Gaucher disease, lysosomal disorders, Down syndrome and Alzheimer's disease.

Gaucher disease

Gaucher disease, a disease of variable severity that may involve brain damage, is caused by a deficiency in the lysosomal enzyme acid beta-glucosidase (betaGlc). The lysosome is an essential cell component that processes metabolic products. Dr. Frances Smith with the Shriver Center has characterized mutations that result in the severe, neurological form of Gaucher disease. She has also identified elements of the betaGlc gene that are essential for its expression in various cell types. These findings are critical in order to create gene therapy strategies that can prevent central nervous system damage. Currently, there is no therapy available. The success of such therapies will depend on the ability of the cells which contain the corrective gene to deliver the enzyme to their neighboring

cells. Dr. Smith is optimizing parameters for correctly expressing betaGlc in brain cells.

Results from this research will have important therapeutic implications for Gaucher disease as well as increase our understanding of the mechanisms involved in uptake and targeting of enzymes by brain cells. Another aspect of Dr. Smith's research is the ability of adeno-associated virus and adenovirus vectors to deliver engineered genes to the brain. High level, long-term expression of genes introduced by such vectors in different brain regions is a critical requirement for effective treatment of central nervous system diseases.

Lysosomal disorders

Dr. Marvin Natowicz with the Shriver Center studies the intracellular transport and regulation of lysosomal enzymes. He is interested in the transport of newly synthesized lysosomal enzymes to lysosomes and the genetic and nongenetic factors important in lysosomal enzyme regulation. He recently discovered a new lysosomal disorder, hyaluronidase deficiency, and is focusing now on this particular enzyme.

Down syndrome & Alzheimer's Disease

Research in Dr. Athena Andreadis's laboratory at the Shriver Center examines alternative splicing, a gene regulatory mechanism vital for the proper functioning of the entire organism, and the nervous system in particular. Her chosen model is the human tau gene, whose product is instrumental in the function of the axon. The axon is a cylinderlike extension of a nerve cell that conducts electric impulses away from the neuron. Disturbances in tau splicing result in disruption of the axon and formation of pathological tau structures called neurofibrillary tangles, which are prominent in the neuropathology (any abnormal condition with inflammation and wasting of the nerves) of aging

individuals with Down syndrome and Alzheimer's Disease. Dissection of the tau system by molecular biology is beginning to clarify the identity and role of molecules that interact with tau. These may control nervous system function and either prevent or promote tangle formation.

Waisman Center on Mental Retardation and Human Development

University of Wisconsin Madison, Wisconsin

The Waisman Center at the University of Wisconsin was created soon after the establishment of research and training centers in 1961. In 1973, the Center officially opened and was chosen as a research site because of its outstanding research in the neurosciences and clinical capabilities related to developmental disabilities. The Center was named after Harry A. Waisman, a pediatrician and biochemist who was a pioneer in mental retardation research. Four missions tie all programs together at the Waisman Center: 1) research on the nervous system, 2) services and support programs, 3) training of more than 400 students each year and 4) outreach programs that ensure the sharing of resources and knowledge.

Within the molecular and genetic sciences, Waisman scientists research the biochemical aspects of normal and atypical development of the nervous system with a focus on the development of new methods for diagnosing and treating genetic diseases. Researchers use modern molecular techniques to search for anomalies in the underlying genome and continue to pursue biomedical intervention strategies including gene therapy. Waisman's research on gene therapy is focused on neuromuscular and metabolic disorders, with an interest in developing a biomedical research program for neurodegenerative disorders.

Duchenne muscular dystrophy

One example of a neuromuscular disorder for which Waisman has a very strong research program in gene therapy is Duchenne muscular dystrophy (DMD). DMD, one of about 40 different types of neuromuscular disorders, affects approximately 35,000 male children in this country. If the disease follows its typical course, the child endures a long and profound deterioration of the body's muscular and motor system, and dies in his mid-twenties. The Waisman Center's research program to develop a clinically viable gene therapy treatment for DMD is directed by Jon Wolff, M.D. His laboratory specializes in molecular genetic technology with an emphasis on developing treatment approaches for genetic muscle and liver disease.

DMD is caused by a defective gene which fails to produce a protein called "dystrophin." Gene therapy attempts to deliver healthy dystrophin genes to muscle tissue cells where it will remain active, or "express," long enough to result in therapeutic value. Of the many challenges associated with gene therapy, the most significant are delivering the gene into enough of the target cells and achieving sufficient therapeutic value from the gene expression. Dr. Wolff's laboratory has successfully delivered the dystrophin gene to small animal models of DMD, and has shown that the gene remains active, leading to muscle improvement. This approach is effective because it delivers the therapeutic gene to the muscle cells through the blood vessels that supply the muscles, thereby infecting a large number of cells. Dr. Wolff continues this research to develop the technique and to demonstrate its successful application in larger animal models.

The Critical and On-going Need for Research

As seen in this report, MRDDR Centers' research efforts have far-reaching implications for people with mental retardation and their families. Although the focus of this report is genetic research, the centers also conduct research in other important areas such as sensory and motor, communication, and social and affective processes. The Arc strongly supports all research that impacts the lives of people with mental retardation and their families, which is demonstrated by the organization's position statement. (See box at right.) By supporting research in the area of mental retardation, we can help create a better understanding of the condition and a brighter future for those with this disability and their families. For additional information about research on a specific disorder listed in this report, or to contact other MRDDR Centers, a list of all fourteen centers are provided below.

RESEARCH RELATED TO MENTAL RETARDATION

Abbreviated position statement of The Arc of the U.S.

The Arc believes:

- An aggressive effort must be made by members and chapters of The Arc to ensure funding of research in mental retardation, both in public and private sectors and to include people with mental retardation in research of general importance to their lives (such as aging, health and fitness, medication effectiveness studies, mental health, etc.).
- Research must follow generally accepted professional standards in research to protect confidentiality, privacy and rights and do no harm to human subjects.
- Researchers must provide their findings to families, people with mental retardation, and other research users in formats that are understandable to them.
- National, state and local chapters of The Arc should keep abreast of current research, provide research findings in understandable terms to parents, families and people with mental retardation and participate in and support research when appropriate.

Adopted by Delegate Body, Nov. 1996.

Mental Retardation Developmental Disability Research Centers highlighted in this report

Child Development and Mental Retardation Center

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Shriver Mental Retardation Research Center

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Genetic Causes of Mental Retardation

What is genetics?

Genetics is "the science that studies the principles and mechanics of heredity, or the means by which traits are passed from parents to offspring" (Glanze, 1996). Through genetics a number of specific disorders have been identified as being genetically caused. One example is fragile X syndrome, a common genetic cause of mental retardation, which is caused by the presence of a single non-working gene (called the FMR-1 gene) on a child's X chromosome.

Genetics originated in the mid-19th century when Gregor Mendel discovered over a ten year period of experimenting with pea plants that certain traits are inherited. His discoveries provided the foundation for the science of genetics. Mendel's findings continue to spur the work and hopes of scientists to uncover the mystery behind how our genes work and what they can reveal to us about the possibility of having certain diseases and conditions. The scientific field of genetics can help families affected by genetic disorders to have a better understanding about heredity, what causes various genetic disorders to occur, and what possible prevention strategies can be used to decrease the incidence of genetic disorders.

Can a person's genes cause mental retardation?

Some genetic disorders are associated with mental retardation, chronic health problems and developmental delay. Because of the complexity of the human body, there are no easy answers to the question of what causes mental retardation. Mental retardation is attributable to any condition that impairs development of the brain before birth, during birth or in the childhood years (The Arc, 1993). As many as 50 percent of people with mental retardation have been found to possess more than one causal factor (AAMR, 1992). Some research has determined that in 75 percent of children with mild mental retardation the cause is unknown (Kozma & Stock, 1993).

The field of genetics has important implications for people with mental retardation. Over 350 inborn errors of metabolism have been identified, most of which lead to mental retardation (Scriver, 1995). Yet, the possibility of being born with mental retardation or developing the condition later in life can be caused by multiple factors unrelated to our genetic make-up. It is caused not only by the genotype (or genetic make-up) of the individual, but also by the possible influences of environmental factors. Those factors can range from drug use or nutritional deficiencies to poverty and cultural deprivation.

How often is mental retardation inherited?

Since the brain is such a complex organ, there are a number of genes involved in its development. Consequently, there are a number of genetic causes of mental retardation.

Most identifiable causes of severe mental retardation (defined as an IQ of 50 or less) originate from genetic disorders. Up to 60 percent of severe mental retardation can be attributed to genetic causes making it the most common cause in cases of severe mental retardation (Moser, 1995). People with mild mental retardation (defined as an IQ between 50 and 70-75) are not as likely to inherit mental retardation due to their genetic make-up as are people with severe mental retardation. People with mild mental retardation are more likely to have the condition due to environmental factors, such as nutritional state, personal health habits, socioeconomic level, access to health care and exposure to pollutants and chemicals, rather than acquiring the condition genetically (Nelson-Anderson & Waters, 1995). Two of the most common genetically transmitted forms of mental retardation include Down syndrome (a chromosomal disorder) and fragile X syndrome (a single-gene disorder).

What causes genetic disorders?

Over 7,000 genetic disorders have been identified and catalogued, with up to five new disorders being discovered every year (McKusick, 1994). Genetic disorders are typically broken down into three types: Chromosomal, single-gene and multifactorial.

Chromosomal disorders affect approximately 7 out of every 1,000 infants. The disorder results when a person has too many or too few chromosomes, or when there is a change in the structure of a chromosome. Half of all first-trimester miscarriages or spontaneous abortions occur as a result of a chromosome abnormality. If the child is born, he or she usually has multiple birth defects and mental retardation.

Most chromosomal disorders happen sporadically. They are not necessarily inherited (even though they are considered to be genetic disorders). In order for a genetic condition to be inherited, the disease-causing gene must be present within one of the parent's genetic code. In most chromosomal disorders, each of the parent's genes are normal. However, during cell division an error in separation, recombination or distribution of chromosomes occurs. Examples of chromosomal disorders include Down syndrome, Trisomy 13, Trisomy 18 and Cri du chat.

Single-gene disorders (sometimes called inborn errors of metabolism or Mendelian disorders) are caused by non-working genes. Disorders of metabolism occur when cells are unable to produce proteins or enzymes needed to change certain chemicals into others, or to carry substances from one place to another. The cell's inability to carry out these vital internal functions often results in mental retardation. Approximately 1 in 5,000 children are born with defective enzymes resulting in inborn errors of metabolism (Batshaw, 1992). Although many conditions are generally referred to as "genetic disorders," single-gene disorders are the most easy to identify as true genetic disorders since they are caused by a mutation (or a change) within a single gene or gene pair.

Combinations of multiple gene and environmental factors leading to mental retardation are called **multifactorial disorders**. They are inherited but do not share the same inheritance patterns typically found in single-gene disorders. It is unclear exactly why they occur. Their

inheritance patterns are usually much more complex than those of single gene disorders because their existence depends on the simultaneous presence of heredity and environmental factors. For example, weight and intelligence are traits inherited in this way (Batshaw, 1992). Other common disorders, including cancer and hypertension, are examples of health problems caused by the environment and heredity. Multifactorial disorders are very common and cause a majority of birth defects. Examples of multifactorial disorders include heart disease, diabetes, spina bifida, anencephaly, cleft lip and cleft palate, clubfoot and congenital heart defects.

How are genetic disorders inherited?

Genetic disorders can be inherited in much the same way a person can inherit other characteristics such as eye and hair color, height and intelligence. Children inherit genetic or hereditary information by obtaining genes from each parent. There are three common types or modes of inheritance: dominant, recessive and X-linked (or sex-linked).

Dominant inheritance occurs when one parent has a dominant, disease-causing gene which causes abnormalities even if coupled with a healthy gene from the other parent. Dominant inheritance means that each child has a 50 percent chance of inheriting the disease-causing gene. An example of dominant inheritance associated with mental retardation is tuberous sclerosis.

Recessive inheritance occurs when both parents carry a disease-causing gene but outwardly show no signs of disease. Parents of children with recessive conditions are called "carriers" since each parent carries one copy of a disease gene. They show no symptoms of having a disease gene and remain unaware of having the gene until having an affected child. When parents who are carriers give birth, each child has a 25 percent chance of inheriting both disease genes and being affected. Each child also has a 25 percent chance of inheriting two healthy genes and not being affected, and a 50 percent chance of being a carrier of the disorder, like their parents. Examples of disorders which are inherited recessively and are also associated with mental retardation include phenylketonuria (PKU) and galactosemia.

X-linked or sex-linked inheritance affects those genes located on the X chromosome and can be either X-linked recessive or X-linked dominant. The X-linked recessive disorder, which is much more common compared to X-linked dominant inheritance, is referred to as a sex-linked disorder since it involves genes located on the X chromosome. It occurs when an unaffected mother carries a disease-causing gene on at least one of her X chromosomes. Since females have two X chromosomes, they are usually unaffected carriers because the X chromosome that does not have the disease-causing gene compensates for the X chromosome that does. Therefore, they are less likely than males to show any symptoms of the disorder unless both X chromosomes have the disease-causing gene.

If a mother has a female child, the child has a 50 percent chance to inherit the disease gene and be a carrier and pass the disease gene on to her sons (March of Dimes, 1995). On the other hand, if a mother has a male child, he has a 50 percent chance of inheriting the disease-causing gene since he has only one X chromosome. Consequently, males cannot be carriers of X-linked recessive disorders. If a male inherits an X-linked recessive disorder, he is affected. Some examples of X-linked inheritance associated with mental retardation include fragile X syndrome, Hunter syndrome, Lesch Nyhan syndrome and Duchenne muscular dystrophy.

Can genetic disorders which cause mental retardation be fixed?

In the past, only a few genetic disorders could be detected and treated early enough to prevent disease. However, the Human Genome Project, an international project among scientists to identify all the 60,000 to 100,000 genes within the human body, is significantly increasing our ability to discover more effective therapies and prevent inherited disease (National Center for Human Genome Research, 1995). As more disease-causing genes are identified, scientists can begin developing genetic therapies to alter or replace a defective gene. However, the development of gene therapies is still in the infancy stage.

Gene therapy (also called somatic-cell gene therapy) is a procedure in which "healthy genes" are inserted into individuals to cure or treat an inherited disease or illness. Although there is a role for gene therapy in the prevention of mental retardation, it will most likely benefit only those people who have single-gene disorders, such as Lesch-Nyhan disease, Gaucher disease and phenylketonuria (PKU) that cause severe mental retardation (Moser, 1995). Gene therapy is far less likely to provide treatment of mild mental retardation which accounts for 87 percent of all cases of mental retardation (The Arc, 1993).

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Facts About Genetic Discrimination

What is genetic discrimination?

Genetic discrimination describes the differential treatment of individuals or their relatives based on their actual or presumed genetic differences as distinguished from discrimination based on having symptoms of a genetic-based disease (Geller, et al, 1996). Genetic discrimination is aimed at people who appear healthy or whose symptoms are so mild that their functioning and health are not affected. Such individuals may include people who carry the gene for fragile X, the most common inherited cause of mental retardation. Twenty percent of people with this gene will never display any form of mental retardation. Yet, because they carry the gene for fragile X, they could be treated as though they had mental retardation even though they do not (Boyle, 1995).

Why is concern about genetic discrimination increasing?

The Human Genome Project, a collaboration of scientists worldwide, is conducting research to find the location of the 100,000 or so human genes by the year 2005. Understanding the complete set of genes, known as the human genome, will lead to precise new approaches to the diagnosis, treatment and prevention of disease. Errors in our genes are responsible for an estimated 3000 to 4000 clearly hereditary diseases and conditions. They play a part in cancer, heart disease, diabetes and many other common conditions, such as mental retardation. Within the next five to ten years we may be able to discover almost all of the diseases we are at risk of inheriting.

Genetic testing can be harmful if the information is used to deny jobs or insurance or if it leads to other forms of discrimination. According to Francis S. Collins, Director, National Center for Human Genome Research (1995), "all of us carry probably four or five really fouled-up genes and another couple of dozen that are not so great and place us at risk for something" (p. 16). However, although everyone has a few defective genes, not everyone will be affected. Multiple factors within the environment have a significant impact on a person's health. These factors, either alone or combined with a disease-causing gene, can increase or decrease an individual's risk of developing a disease (Nelson-Anderson & Waters, 1995).

Where is genetic discrimination happening?

A recent study which questioned people with defective genes that could lead to a disease, but who had no symptoms, found that genetic discrimination occurred in many settings (Geller, et al, 1996). As a result, people who fear potential genetic discrimination may be discouraged from obtaining genetic information that could bring health benefits to them and their families.

One of the most common forms of discrimination is denial of health insurance based on a person's genes. Insurance companies gather and use medical information to predict a person's risk of illness and death. They use this "risk" information to determine which individuals and groups they will insure and at what price. That information plays a critical role for people in determining access to health care.

Employment is another area with reported cases of discrimination. Many individuals believe they were not hired or were fired because they were at-risk for genetic conditions. In other cases, individuals who were employed were reluctant to change jobs because they feared losing health insurance coverage (Geller, et al, 1996). Having a defective gene could be considered a pre-existing condition by insurance companies who, on that basis, may deny coverage. Recently passed federal legislation places limitations on the exclusion period for pre-existing conditions when people change jobs (The Health Insurance Portability and Accountability Act of 1996).

Discrimination has also occurred when medical professionals counseled individuals about child bearing by urging prenatal diagnostic testing or telling them they should not have children. Similarly, some adoption agencies have unfairly treated prospective parents with a genetic condition by refusing adoption or assuming they should adopt only children at risk of inheriting a disability (Geller, et al, 1996).

Doesn't the ADA protect people against genetic discrimination?

The Americans with Disabilities Act (ADA) offers protection from discrimination to individuals currently affected by a genetic condition or disease. It also applies to individuals who are regarded as having a disability. The Equal Employment Opportunities Commission, which oversees enforcement of nondiscrimination in employment, has ruled that ADA applies specifically to individuals who are subjected to discrimination on the basis of genetic information relating to illness, disease, condition or other disorders (EEOC, 1995). This interpretation extends coverage to

people who have genes making them predisposed to a disease-causing disability or who have genes for a late-onset disorder. However, it may not protect carriers of genetic disorders who do not yet manifest symptoms of a disease (the "unaffected carrier"). They may be discriminated against based on concerns about health costs of future affected dependents.

The Americans with Disabilities Act does not cover the insurance industry. Insurance companies may deny health, life, disability and other forms of insurance to people with defective genes if there is a sound basis for determining risks consistent with state law. Health maintenance organizations can also refuse to cover an individual with a genetic diagnosis even if the individual has no symptoms of the genetic disorder, provided there is a sound basis for the decision based on actual risk experience (Alper and Natowicz, 1993).

What are the implications of genetic information for family members?

When people learn that they have a gene that places them at increased risk for certain diseases, they face the dilemma of whether or not to tell other family members about their potential susceptibility to disease. This information is directly relevant to their biological relatives, for other family members may also have the gene and be at increased risk. It also has implications for family members being at risk of genetic discrimination, since genetic information about an individual is also information about that person's family.

Genetic information may profoundly affect people's decisions about having children. There is also evidence that some individuals who have defective genes are stigmatized, suffering a loss of social and economic opportunities (NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research, 1993).

What steps are being taken to eliminate genetic discrimination?

In addition to federal law and regulations, several states have developed and adopted legislation banning discrimination in health insurance and employment. Currently eleven states have laws prohibiting health insurers from denying health care coverage because of a genetic condition. Seven states prohibit employers from requiring genetic tests or using genetic health predictions in employment decisions. Seven other states have bills pending to protect individuals from discriminatory use of genetic information in employment practices or for insurance purposes (Council for Responsible Genetics, 1996).

As noted earlier, the Federal Health Insurance Portability and Accountability Act of 1996 offers protections against discrimination in health insurance by limiting pre-existing condition exclusions. It also prohibits discrimination against individuals based on health status, including their genetic information.

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Prader-Willi Syndrome

by Prader-Willi Syndrome Association (USA)

What is Prader-Willi syndrome (PWS)?

PWS is a complex genetic disorder that includes short stature, mental retardation or learning disabilities, incomplete sexual development, characteristic behavior problems, low muscle tone, and an involuntary urge to eat constantly, which, coupled with a reduced need for calories, leads to obesity.

Does PWS run in families?

Although PWS is associated with an abnormality of chromosome 15, it is generally considered not to be an inherited condition, but rather a spontaneous genetic birth defect that occurs at or near the time of conception. PWS is found in people of both sexes and all races.

How common is this problem?

About 1 in 14,000 people in the U.S. are estimated to have PWS, and the birth rate may be even higher. Prader-Willi syndrome is one of the 10 most common conditions seen in genetics clinics and is the most common genetic cause of obesity that has been identified.

Does the eating problem associated with PWS begin at birth?

No, newborns with PWS are typically described as "floppy" and are unable to suck well enough to get sufficient nutrients -- due to the low muscle tone (hypotonia). Often they must be fed through a tube for several months after birth, until muscle control improves. Sometime in the following years, usually by preschool age, children with PWS develop an increased interest in food and quickly gain excessive weight if calories are not restricted.

Why do people who have PWS eat so much?

People with PWS have a flaw in the part of their brain (the hypothalamus) that determines hunger and satiety (fullness). These people never feel full enough, so they have a continuous urge to eat. To compound this problem, people with PWS need considerably fewer calories than normal to maintain an appropriate weight. The obesity that results is the major cause of illness and death in this disorder. As in the general population, obesity in PWS can cause high blood pressure, respiratory difficulties, diabetes and other problems.

Can anything be done to control the eating?

Unfortunately, no appetite suppressant has worked consistently for people with PWS. Most must be on an extremely low-calorie diet all their lives and must have their environment designed so that they have very limited access to food. For example, many families have to lock the kitchen or the cabinets and refrigerator.

I know many people who eat a lot and have obesity. How do I know they don't have PWS?

There's more to PWS than the obesity. People with PWS have a characteristic appearance and speech quality, significant learning disabilities or mental retardation, and various other problems. A number of these features must be present for a clinical diagnosis of PWS, and specific genetic tests are available to confirm the diagnosis.

What is known about the genetic abnormality?

Basically, the occurrence of PWS is due to the absence of a few genes on one of the chromosomes that must affect functioning of the hypothalamus, among other things. This is an area of very active research in a number of laboratories around the world, since understanding this defect may be very helpful not only to people with PWS but also to understanding obesity, mental retardation, and behavior in otherwise normal people.

What kinds of behavior problems do people with PWS have?

In addition to sometimes extreme attempts to obtain food, people with PWS are prone to temper outbursts, stubbornness, rigidity, argumentativeness, and repetitive thoughts and behaviors. Strategies to deal with these problems usually include structuring the person's environment, implementing behavioral management techniques, and occasionally drug therapy.

Is it possible for people with PWS to lead normal lives?

People with PWS can accomplish many of the things their "normal" peers do -- attend school, enjoy community activities, get jobs, and even move away from home. However, they need a lot of help. School children with PWS are likely to need special education and related services, such as speech and occupational therapy. In community, work and residential settings, adolescents and adults often need special assistance to learn and carry out responsibilities and to get along with others. In all settings, people with PWS need around-the-clock food supervision. As adults, most affected individuals do best in a special group home for people with PWS, where food access can be restricted without interfering with those who do not need such restriction. Although in the past many died in adolescence or young adulthood, it is thought that prevention of obesity will allow a person with PWS to live a normal lifespan.

Does early diagnosis help?

Early diagnosis of Prader-Willi syndrome gives parents an opportunity to manage their child's diet and avoid obesity and its related problems from the start. Since infants and young children with PWS typically have developmental delays in all areas, diagnosis may facilitate a family's access to critical early intervention services and help identify areas of need or risk. Diagnosis also makes it possible for families to get information and support from professionals and other families who are dealing with the syndrome.

If someone believes that they or their child may have PWS, how do they find out?

The best way would be to contact their health care provider and ask to be evaluated

for Prader-Willi syndrome. Formal diagnostic criteria for the clinical recognition of PWS have been published (Holm et al, 1993). Many doctors will choose to refer to a medical geneticist who specializes in diagnosing and testing for genetic conditions such as PWS. After taking a history and doing a physical examination, the diagnostician will arrange for specialized genetic testing to be done on a blood sample to evaluate for the genetic abnormality found in people with PWS.

How can a person get more information about PWS?

There is a strong national organization of families and professionals dealing with PWS called the Prader-Willi Syndrome Association (USA). It has a toll-free number (1-800-926-4797) and is organized to answer questions and help individuals deal with the problems associated with PWS. PWSA (USA) provides a newsletter and other publications, an annual national conference, and chapters throughout the country to provide family support and advocacy. One also could call a local genetics unit to ask for information on PWS.

Reference

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FAX (314) 962-7869

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Phenylketonuria (PKU)

What is PKU?

PKU, which stands for Phenylketonuria, is an inherited metabolic disease (also called an inborn error of metabolism) that leads to mental retardation and other developmental disabilities if untreated in infancy. With an inborn error of metabolism, the body is unable to produce proteins or enzymes needed to convert certain toxic chemicals into nontoxic products, or to transport substances from one place to another (Glanze, 1996).

The body's inability to carry out these vital internal functions may result in neurological damage. In the case of PKU, the amino acid called phenylalanine accumulates. As phenylalanine builds up in the bloodstream, it causes brain damage. Infants with untreated PKU appear to develop typically for the first few months of life, but by twelve months of age most babies will have a significant developmental delay and will be diagnosed with mental retardation before school entry.

How is PKU inherited?

PKU is inherited as a single-gene disorder. Single-gene disorders are caused by a mutant or abnormal gene. They can be inherited in one of three patterns: autosomal dominant, autosomal recessive and X-linked. PKU is an autosomal recessive disorder. Each parent of a child with PKU carries one defective gene for the disorder and one normal gene. In a recessive condition, an individual must have two defective genes in order to have the disorder. Individuals with only one copy of a defective gene are called "carriers," show no symptoms of having the disease, and usually remain unaware of their status until they have an affected child. In order for a child to inherit PKU, both parents must be PKU carriers. When this occurs, there is a one in four chance of their producing an affected child with each pregnancy. Boys and girls are equally at risk of inheriting this disorder.

How is PKU diagnosed?

Before the 1960s, most infants born with PKU developed mental retardation and cerebral palsy. Although treatment for PKU using a low phenylalanine diet was first described in the 1950s, the inability to detect PKU early in the child's life limited effective treatment.

The first newborn screening test was developed by Dr. Robert Guthrie in 1959 specifically to test for PKU. This simple, yet very effective and economical test was developed to screen newborn infants for PKU before leaving the hospital. Today, all states routinely screen newborns for PKU. To test for PKU, the infant's

QUICK FACTS

Condition: Phenylketonuria (PKU)

Link to mental retardation: Brain damage leading to mental retardation that occurs in children with PKU due to high blood levels of phenylalanine that is not properly metabolized (broken down).

Primarily affects: Newborns; more common among North European descent, less common among Jewish, Asian and African-American families.

Symptoms: Typical appearance during first few months after birth, but at three - five months will lose interest in surroundings and have mental retardation by twelve months old. Often irritable, restless, destructive. May have dry skin or rashes, a strong, musty body odor and convulsions.

Incidence: One in every 12,000 to 15,000 babies is born with PKU in the U.S.

Cause: An inherited disorder caused by a build up of an amino acid called phenylalanine that, if left untreated, causes mental retardation. The higher the level of phenylalanine within the body, generally the more severe the disability.

Treatment: A low-protein diet consisting of foods that have little or no phenylalanine can decrease the high levels of phenylalanine and prevent the occurrence of mental retardation. All babies in the U.S. are routinely screened for PKU.

Contact for more information: National PKU News at 206-525-8140 (e-mail: pkunews@workmail.com) or Children's PKU Network at (619) 233-3202

heel is pricked and a few drops of blood are taken. This blood sample is then tested in a state laboratory for abnormal amounts of phenylalanine.

The normal phenylalanine level is less than 2 mg/dl. Those with phenylalanine levels of 20.0 milligrams per deciliter (mg/dl) or higher are considered likely to have "classical" PKU (Yanicelli, Davidson & vanDoornick, 1986). Infants with these high levels are further tested to confirm the diagnosis before treatment is started. Some infants will have more modest elevations of blood phenylalanine and are said to have "mild hyperphenylalanemia." Today many clinicians believe that any child with a phenylalanine level greater than 6 or 8 mg/dl should be treated with a modified phenylalanine restricted diet.

Is testing for PKU 100 percent accurate?

Experts recommend that testing for PKU should be done when the infant is at least twenty-four hours of age but less than seven days old. If an infant is tested too soon after birth, there is a chance that some cases of PKU will be missed as the phenylalanine level will not

have risen yet. Now that many hospitals are discharging mothers and infants twenty-four hours after birth, there is a greater likelihood of this happening. The American Academy of Pediatrics recommends that infants receiving the test during the first twenty-four hours of life be re-tested at two to three weeks of age during their first postnatal pediatric visit (March of Dimes, 1994).

How is PKU treated?

Although PKU is not preventable, its symptoms can often be treated successfully through the use of a carefully regimented diet. The diet consists of foods that have a restricted phenylalanine content. Babies are given a special formula that contains very low phenylalanine levels; then they gradually progress to eating certain vegetables and other foods that are low in phenylalanine. Affected children must have their blood tested regularly to ensure the presence of the correct level of phenylalanine.

Foods recommended for those affected by PKU contain small amounts of protein, such as fruits and vegetables, limited amounts of cereal and grain products and special low protein products available through mail-order. High protein foods such as meat, fish, eggs, poultry, dairy products, nuts, peanut butter, legumes, soy products and products containing Nutrasweet should be avoided (Yannicelli, Davidson & vanDoornick, 1986).

The food program used to treat those with PKU is quite expensive, typically costing up to \$10,000 a year or more. Although health departments may pay for the formula in some states and mandated insurance coverage may cover the cost in other states, most insurance companies do not cover the cost of treatment for children/adults with PKU because it is considered nutritional rather than medical therapy.

While phenylalanine restricted diets have proven to be highly effective in preventing mental retardation, it is now recognized that there may still be subtle cognitive deficits. Usually the individual has a normal IQ, but the incidence of attention deficit hyperactivity disorder (ADHD) and learning disabilities is higher compared to those children who do not have PKU (Yanicelli, Davidson & vanDoornick, 1986).

Do those affected by PKU have to stay on a regimented diet all their lives?

It was believed in the past that children could discontinue the diet when they turned five to six years old. Recent studies have found that children with PKU who did stop the diet in early childhood did not develop as rapidly as children who remained on the diet, and had more learning disabilities, behavioral problems, and other neurological problems. Thus, until research provides alternative treatments, all persons with PKU should remain on a restricted diet indefinitely in order to maintain a safe level of phenylalanine (believed to be in the range of 2-6 mg/dl) (Schuett, 1996).

What happens when women with PKU have children?

When women with PKU who are not receiving dietary therapy become pregnant, their high levels of phenylalanine can damage their unborn child, causing mental retardation and other congenital defects. High

levels of phenylalanine are extremely toxic to the brain of a fetus. Thus, although the child does not have PKU, he or she will have sustained brain damage from the toxic effects of phenylalanine in utero (in the womb). This is known as MATERNAL PKU.

More than 90 percent of infants born to women with PKU who are not on a specialized diet will have mental retardation, and may also have small head size (microcephaly), heart defects and low birth weight. These infants cannot be treated with a special diet since they do not have PKU. Therefore, women who have PKU should be on a phenylalanine restricted diet at least one year before pregnancy and should stay on the diet while breast-feeding to increase the chance of having a healthy child (Levy, 1988).

Are other rare metabolic disorders associated with mental retardation being screened for as well as PKU?

Dr. Guthrie's newborn screening test for PKU sparked the testing for other rare metabolic disorders associated with mental retardation: congenital hypothyroidism, galactosemia, homocystinuria, biotinidase deficiency and maple syrup urine disease. While all states and the District of Columbia screen for PKU, only some states screen for the other metabolic conditions (The Arc, 1994).

The development of a screening test for PKU was a significant step toward preventing mental retardation caused by metabolic disorders. Unfortunately, there remain more than 100 rare metabolic disorders that lead to mental retardation for which newborn screening is currently unavailable (McKusick, 1994).

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Appendix B

The Human Genome Project and Mental Retardation: An Educational Program

Advisory Panel

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Appendix C

The Arc undertakes human genome project

Professional staff at The Arc have joined a massive expedition that promises mystery, adventure, controversy and break-through discoveries.

It's not a journey of foreign hands or lost continents. The terrain is that of building blocks.

The Arc has undertaken a role in The Human Genome Project, a global, 15-year effort to define the sequence of all 3 billion DNA "letters," which are the specific instructions for how a human being is built and operates. The project's mission is to develop ways to predict, prevent, detect, treat and cure diseases and conditions.

"This undertaking is critically important to The Arc," said Sharon Davis, Ph.D., director of the Department of Research and Program Services at The Arc's National Headquarters. "As the mapping and sequencing of the human genome progresses, we will understand more about genetic disorders related to mental retardation. The knowledge offers hope for future treatments and cures for some forms of mental retardation."

The National Institutes of Health and the Department of Energy are directing human genome efforts in the United States. The DOE has granted \$200,000 to The Arc to conduct a two-year effort to educate the

Continued on page 4

The Arc undertakes human genome project

Spring 1996

organization's leaders and members about the ethical, legal and social implications of genetic knowledge and use. The amassed information will be used in discussions and evaluation of issues, leading to the development of position statements.

Specific genes have already been discovered for a number of single gene conditions, including fragile X syndrome, for which a treatment may be a possibility in the future."

The Arc also sees an opportunity to often basing their decisions on their beliefs about quality of life of a person with mental retardation," she added, "we must participate in the discussions on the ethical, legal and social issues regarding use of genetic knowledge."

Leigh Ann Reynolds has been named project associate for The Arc's Human Genome Project. Reynolds was the coordinator for The Arc's anencephaly but not declared brain dead.

"Many mental retardation disorders have a genetic cause, with Down syndrome and fragile X syndrome

being the most common," Davis said in explaining why The Arc became involved in human genome errors of discussions. "About 70 inborn errors of metabolism have been identified, most of which lead to mental retardation. Specific genes have already been discovered for a number of single gene conditions, including fragile X syndrome, for which a treatment may be a possibility in the future."

The Arc also sees an opportunity to often basing their decisions on their beliefs about quality of life of a person with mental retardation," she added, "we must participate in the discussions on the ethical, legal and social issues regarding use of genetic knowledge."

Leigh Ann Reynolds has been named project associate for The Arc's Human Genome Project. Reynolds was the coordinator for The Arc's anencephaly but not declared brain dead.

"With this history of

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discrimination," Davis said, "it is imperative that the scientific and medical communities hear the views of consumers and families regarding issues dealing with genetic testing, screening and counseling; discrimination in insurance and employment based on a genetic condition; and genetic therapies to 'cure' mental retardation.

"With the scientific community often basing their decisions on their beliefs about quality of life of a person with mental retardation," she added, "we must participate in the discussions on the ethical, legal and social issues regarding use of genetic knowledge."

Leigh Ann Reynolds has been named project associate for The Arc's Human Genome Project. Reynolds was the coordinator for The Arc's anencephaly but not declared brain dead.

Continued from page 1.

Sheep cloning: Good or baaad for humans?

States Human Genome Project's research, it recognized the importance of funding research and education related to the ethical, legal and social implications of the new genetic knowledge."

The Arc's Human Genome Education Project began in 1996 with a \$200,000 grant from the Department of Energy. The DOE and the National Institutes of Health are directing human genome efforts in the U.S.

In recent months, Davis conducted workshops for The Arc's national board of directors and for the statewide chapters of Oregon, Maryland, New Mexico and Indiana.

It is unsettling to many, for example, to imagine genetic engineering of "superior" people. On the other hand, the same knowledge could lead to cures for serious diseases and conditions. All of this leads to considerations for many communities, including medical, law and policy making.

The Arc is half-way through a two-year effort to develop materials and educate the organization's leaders and members about the ethical, legal and social implications of genetic knowledge and use.

It is unsettling to many, for example, to imagine genetic engineering of "superior" people. On the other hand, the same knowledge could lead to cures for serious diseases and conditions. All of this leads to considerations for many communities, including medical, law and policy making.

"The knowledge can lead to new ways to identify and treat genetic conditions," Davis said. "It could also be used in ways that are harmful." That is why science must be matched with attention paid to a huge range of human issues. She praised the United States' approach to the ongoing gene mapping project.

"When Congress funded the United

adult ewe to produce a genetically identical ewe, now known as "Dolly." "This achievement surprised most scientists who thought it would be an impossible task to bypass sexual reproduction," Davis said. "Public Project. The Arc's project is a piece of an overall Human Genome Project, a global, 15-year effort to define and obtain a precise picture of the genetic code that determines how a human being is built and operates.

"The cloning of a sheep in Scotland underscores the need for people to understand resulting issues that stand to have a huge impact on human beings, The Arc's director of a human genome education project says. Sharon Davis, Ph.D., is studying the emerging issues in the wake of the startling announcement that Scottish researchers used a single cell from an

A series of reports on The Arc's Human Genome Education Project has been distributed through editions of The Arc Now mailed to all chapters. Titles produced so far have been "Protecting Genetic Privacy," "Facts About Genetic Discrimination," "Genetic Causes of Mental Retardation," "Genetic Testing - An Overview," and "An Introduction to Genetics and Mental Retardation."###

Clinton recognizes need for anti-discrimination laws regarding genetics

President Clinton recently announced that he endorses the concept of legislation that would make it illegal for health insurance companies to discriminate against healthy people on the basis of their genetic inheritance.

This is good news to The Arc, which cast a wary eye on the issue more than a year ago through its Human Genome Education Project.

With the rising use of genetic tests to reveal the presence of any defective genes, it is now possible to discriminate against people who are carriers of genes for a disease or condition even when they show no symptoms. An example of genetic discrimination reported in the media was the problem of an entire family of six whose health insurance was canceled because of the presence of fragile X syndrome in a 6-year-old family member.

"As the number of genetic tests increase," said Sharon Davis, Ph.D., director of The Arc's Department of Research and Program Services, which houses the HGEIP, "That's why legislation

is so important."

The Arc's Board of Directors in 1996 passed a resolution calling for such legislation.

Clinton's announcement that he would support legislation designed to ban discrimination in health insurance and help assure privacy of genetic information came in response to a federal task force report. Health and Human Services Secretary Donna E. Shalala presented the report, which warned that the benefits of genetic testing may never be realized if people reject the tests out of fear that the findings could be used against them.

The goal of The Arc's HGEIP, which is part of the massive U.S. Human Genome Project, is to promote education and discussion of the ethical, legal and social concerns resulting from innovative genetic research. A workshop developed to guide groups through discussion of pertinent human genome issues is now being presented across the country by Davis and by several members of The Arc's board of directors.

Clinton 1997

Appendix D



**The Arc's Human Genome Education Project:
*Examining Genetic Ethical, Legal and Social Issues***

A two-year project funded through the
U.S. Dept. of Energy to create awareness of the
ethical, legal and social concerns arising from
The Human Genome Project (HGP).

An Interactive Workshop

Developed by:

Staff of The Arc of the U.S.

Sharon Davis, Ph.D., Principal Investigator
Leigh Ann Reynolds, Project Associate

The Arc's Health Promotion and Disability Prevention Committee

Deborah Cohen, Ph.D., Co-Chair; Maxine O'Kelley, Co-Chair
Peter Leibert; Joan Arnold

with assistance from
The Arc's Board of Directors

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Revised Jan. 1999



DISCUSS THE ETHICAL ISSUES INVOLVING GENETICS AND MENTAL RETARDATION

A WORKSHOP CREATED BY
THE ARC'S HUMAN GENOME EDUCATION PROJECT

PURPOSE OF WORKSHOP

- ✓ Find out what The Human Genome Project is all about and why The Arc is involved
 - ✓ Learn about ethical, legal and social issues involved:
 - genetic discrimination
 - deciding to be tested for a genetic condition
 - the use of genetic therapy
 - ✓ Give your input to The Arc's national Board of Directors about issues involving genetics
-

This interactive and thought-provoking workshop includes a video and case scenarios to help participants have a better understanding of The Human Genome Project, and to get a feel for the issues involved that have a significant impact on people with mental retardation and their families. Similar workshops are taking place across the country in order to educate members of The Arc about ethical and other issues involved in mapping our human genome. This is your chance to be an active participant in an area of growing concern in the lives of all people.

Where: _____ When: _____

For more information, contact:

The Arc's Human Genome Education Project: *Examining Genetic Ethical, Legal and Social Issues (ELSI)* An Interactive Workshop

INFORMATION FOR WORKSHOP LEADER

The following script is designed to aid workshop leaders in educating others about genetic issues and to encourage the discussion of the ethical, legal and social implications (ELSI) of the Human Genome Project. The workshop is intended to facilitate open discussion among workshop participants. By following the script, the leader does not need special expertise to conduct this workshop.

The workshop includes background information for the presenter, a pre/post-questionnaire, handouts, a short video, overheads and case scenarios to enhance the group's understanding and active involvement. The workshop is structured to last anywhere from one to two hours, depending on how many participants there are, how many case scenarios are discussed and whether they are discussed briefly or in great detail. All hand-outs (except the case scenarios) need to be given at the beginning of the workshop and referred to throughout the presentation. Case scenarios can be handed out at the time of discussion.

During the discussion of case scenarios, designate one individual in each group to take detailed notes during the discussion of the **ELSI** issues. These notes and the pre/post-questionnaires should be collected and returned to The Arc's national project staff who will analyze responses to document consensus (or non-consensus) on these issues. This information will be provided to The Arc's Board of Directors.

The workshop has two purposes:

1. To educate The Arc's membership about the international Human Genome Project.
2. To solicit input from members regarding their beliefs and opinions about the impact of new genetic research.

Note: If at anytime during the workshop questions are asked which you are unable to answer, you may want to ask participants to contact project staff at The Arc's National Headquarters for further information. If you would like clarification or assistance in presenting this material, contact project staff, Sharon Davis, Ph.D. or Leigh Ann Reynolds, at 1-800-433-5255 who can provide direction as needed.

WORKSHOP MATERIALS

Materials Needed

Pens/pencils (for pre/post-questionnaire and case scenarios)

VCR

Overhead projector

Flip chart and markers (optional)

Materials Included

Background information for presenter:

1. The Arc's *Resolution on Genetic Discrimination*
2. Article from Newsweek, "Flunk the Gene Test and Lose Your Insurance"
3. Excerpt from Dept. of Energy's (DOE) web site, "Genome Frequently Asked Questions"
4. Articles from USA Today, "Genetic Test Threat Grows," and "Insurers Need Information"

Handouts:

1. Pre/post-questionnaire - 30 copies
2. *Genetic Issues in Mental Retardation* (Vol. 1, Nos. 1-3; Vol. 2, Nos 1 & 3; Vol. 3, No. 1) - 30 copies of each report
3. Case scenarios - 12 of each of three different cases
4. Project description/request to be on mailing list - 30 copies

20 Overheads

1 Video (15 minutes)

NOTE: *Please contact The Arc if additional handouts are needed.*

**The Arc's Human Genome Education Project:
Examining Genetic Ethical, Legal and Social Issues
(ELSI)
An Interactive Workshop**

Getting Started (5 minutes)

- Pass out questionnaire – participant pre-test

Present The Arc's Human Genome Project: Examining The Arc's Concerns Regarding the Ethical, Legal and Social Implications. Lecture with video and overheads (45 minutes)

- Show video
- Use overheads

Case Scenarios – Small Group Exercise (35 minutes)

- Pass out handouts of case scenarios
- Small group discussion followed by group reporting

Concluding Remarks (5 minutes)

- Participant's post-questionnaire (Opinions on Issues)

GETTING STARTED - 5 MINUTES

Handout: Pre/post Opinion Questionnaire

To Facilitator: *If you suspect there are people in the group who may need help with reading, you may read the questionnaire to the whole group.*

Say: Before we get started, I would like for you to fill out a short questionnaire that asks your opinion on issues that involve the Human Genome Project. Fill out the side labeled "pre-questionnaire." Each question will ask how much you agree or disagree and you will be given a range of options, from "strongly disagree" to "no opinion." Circle the number that best corresponds to your answer.

As you answer these questions, keep your original opinion in mind as you go through the training because at the end of the session you will be asked to turn over the questionnaire and respond to the post-questionnaire (which is exactly the same as the pre-questionnaire). In doing so, we are able to see if you would change any of your opinions after learning more about the project and the issues involved.

Say After Questionnaire is Filled Out: In trying to answer these thought-provoking questions, you can see how difficult it will be to come up with any real answers to the dilemmas created by the Human Genome Project... and that is because, for the most part, there are none. But, that is why we are here today. Not to find solutions, but to begin to develop a framework of knowledge in order to have a more informed and educated discussion about these issues.

The Arc's Human Genome Education Project

Pre-Questionnaire (Please answer before the presentation.)

Please indicate how much you agree or disagree with each of the following statements.

	Strongly Agree	Agree	Disagree	Strongly Disagree	Don't Know
1. Newborns should be tested for genetic conditions even if no treatment exists.	1	2	3	4	5
2. People who have a genetic condition in the family should be tested before having children.	1	2	3	4	5
3. People should tell their husbands/wives the results of their own genetic tests.	1	2	3	4	5
4. People should tell their blood relatives about the results of their own genetic tests.	1	2	3	4	5
5. Children should be tested for genetic conditions even if there is no clear benefit to the child.	1	2	3	4	5
6. It is fair for insurance companies to deny medical benefits based on an individual's genes alone, including those who show no outward signs of having a disability.	1	2	3	4	5
7. Health insurers should be able to get genetic information if they pay for the tests.	1	2	3	4	5
8. Employers should be allowed to deny employment to people based on having genes with the potential to cause future disease or disability.	1	2	3	4	5
9. The Arc should support legislation banning genetic discrimination in health insurance and employment.	1	2	3	4	5
10. Gene therapy is a proven form of treatment for some conditions causing mental retardation.	1	2	3	4	5
11. Advocating for a cure for mental retardation does not devalue those who have the condition.	1	2	3	4	5
12. Based on my current knowledge, I believe The Arc should advocate for more funding for research to cure genetic conditions.	1	2	3	4	5

...over

The Arc's Human Genome Education Project

Post-Questionnaire (Please answer after the presentation.)

Please indicate how much you agree or disagree with each of the following statements.

	Strongly Agree	Agree	Disagree	Strongly Disagree	Don't Know
1. Newborns should be tested for genetic conditions even if no treatment exists.	1	2	3	4	5
2. People who have a genetic condition in the family should be tested before having children.	1	2	3	4	5
3. People should tell their husbands/wives the results of their own genetic tests.	1	2	3	4	5
4. People should tell their blood relatives about the results of their own genetic tests.	1	2	3	4	5
5. Children should be tested for genetic conditions even if there is no clear benefit to the child.	1	2	3	4	5
6. It is fair for insurance companies to deny medical benefits based on an individual's genes alone, including those who show no outward signs of having a disability.	1	2	3	4	5
7. Health insurers should be able to get genetic information if they pay for the tests.	1	2	3	4	5
8. Employers should be allowed to deny employment to people based on having genes with the potential to cause future disease or disability.	1	2	3	4	5
9. The Arc should support legislation banning genetic discrimination in health insurance and employment.	1	2	3	4	5
10. Gene therapy is a proven form of treatment for some conditions causing mental retardation.	1	2	3	4	5
11. Advocating for a cure for mental retardation does not devalue those who have the condition.	1	2	3	4	5
12. Based on my current knowledge, I believe The Arc should advocate for more funding for research to cure genetic conditions.	1	2	3	4	5

THE HUMAN GENOME PROJECT: EXAMINING THE ARC'S CONCERNS REGARDING THE ETHICAL, LEGAL AND SOCIAL IMPLICATIONS

Overhead 1

The Human Genome Project is an effort involving hundreds of scientists throughout the world who are attempting to map all 80,000 to 100,000 genes within our bodies by the year 2005. In the United States, Human Genome research is being conducted by both the National Institutes of Health and the Department of Energy.

Our complete set of genes is known as the "human genome." Errors in our genes are responsible for an estimated 7000 clearly hereditary diseases and play a part in cancer, heart disease, diabetes and many other common diseases. New genetic disorders are being discovered every year. Within the next five to ten years, we may be able to find out most all of the genetic conditions we are at risk of inheriting. The assumption is that knowing our genes will lead to diagnoses, treatments and prevention of genetic diseases and conditions.

The discovery of information that holds such promise and hope for the future is exciting. However, many people question whether or not society as a whole, or each of us individually, is ready to discover what genes are within us that predispose us to having certain diseases and conditions. The ELSI program was created to examine the ethical, legal and social issues arising from genetic knowledge.

ELSI is an acronym that stands for ethical, legal and social implications. Three to five percent of the United States' Human Genome Project's budget is devoted to funding research on the impact of new genetic findings within society.

Overhead 2

The Arc was funded through the Department of Energy's Ethical, Legal and Social Implications Program in February 1996 to conduct an educational program with two major purposes. The first is to make our members aware of this scientific undertaking, the Human Genome Project. The second is to examine the critical issues related to new genetic discoveries affecting people with mental retardation and their families. We want as many people as possible to begin to understand that this research affects all of us.

Video

Some of the issues we face are addressed in the 15 minute video we will watch next. It provides a broad overview of what the Human Genome Project is and some of the things it hopes to accomplish.

Overhead 3

We tell members of The Arc that the Human Genome Project deserves our attention because it has a direct impact on individuals and families affected by mental retardation. Most identifiable causes (up to 60 %) of severe mental retardation originate from genetic disorders. Researchers are rapidly discovering new genes which cause disease and disability, but research on treatments is lagging behind.

The lack of current treatments and emerging gene therapy research raise ethical dilemmas regarding such areas as privacy, fairness and discrimination. Remember, too, we are ALL affected. Dr. Francis Collins, head of the National Human Genome Research Institute, whom we saw in the video, says we each have four or five really fouled up genes and another couple of dozen that are not so great and place us at risk for something. We

need to actively educate ourselves and speak out on the issues that will eventually, either directly or indirectly, affect us all.

Overhead 4

Even though there are a wide range of issues important to families, we decided to focus on these three topics:

- Discrimination based on a person's genes in insurance and employment
- Decisions involving genetic testing, screening and counseling (including prenatal and newborn testing)
- Ethical issues involving genetic therapies that may eventually "cure" mental retardation

Overhead 5

The first issue we address is genetic discrimination. Discrimination based on the presence of a disability has always been an issue of great concern to The Arc. People with mental retardation have long been discriminated against in both insurance and employment. Now a new, less well-known type of discrimination is emerging due to the increasing use of genetic tests which can reveal the presence of defective genes. This new phenomenon is called genetic discrimination.

Genetic discrimination occurs when people are treated differently because they have a disease gene or genes, even when they show no symptoms of disease. Men and women who are carriers for a genetic condition may also be discriminated against because of their potential to have a child with a genetic condition.

An example of genetic discrimination was reported in *Newsweek* more than a year ago. A pediatrician who suspected a two-year-old boy (David) had

fragile X syndrome ordered lab tests that confirmed his suspicion. The family spent several years learning to deal with his condition. At age 6, David visited a neurologist who scribbled "fragile X" on a health insurance company claim form. The company responded promptly--by canceling coverage for the entire family of six. There is no medical treatment for fragile X, and none of David's siblings had been diagnosed with the condition.

The *Washington Post* newspaper cited a case in which a pregnant women whose fetus tested positive for cystic fibrosis was told that her health maintenance organization (HMO) would be willing to cover the cost of an abortion, but would not cover the infant under the family's medical policy if she elected to carry the pregnancy to term.

Overhead 6

The denial of health insurance based on a person's genes is one of the most common forms of discrimination. Insurance companies gather and use medical information to predict the risk of illness and death. They then determine which individuals and groups to insure and at what price.

Genetic discrimination has been documented in other settings as well. A recent study identified cases where healthy people were fired from jobs, treated differently in school or barred from adopting a child because they carried genes that could potentially result in disease or disability.

Overhead 7

The Americans with Disabilities Act offers some protection to those currently affected or predisposed to having a genetic disorder. The ADA does not, however, cover the insurance industry as long as its decisions on coverage are based on experience that demonstrates people's risk of illness, disability or death.

As the number of genetic tests increase, discrimination will increase. That's why legislation banning discrimination has been proposed. The Arc's Board of Directors passed a resolution two years ago calling for such legislation. The US Congress made a beginning step to deter genetic discrimination when it passed the Federal Health Insurance and Accountability Act of 1996. This law limits the use of preexisting condition exclusions by health insurers and specifically mentions "genetic information." Other legislation is currently being considered by the US Congress.

A number of states also have laws banning genetic discrimination in health insurance. Some states are also examining discrimination in employment and passing laws banning employment discrimination based on genetic information. Much of this legislation, however, has serious deficiencies.

Overhead 8

Legislation is also beginning to address issues of genetic privacy. Medical records are not private. If you have ever applied for individual life, health or disability insurance, information about you may be in the Medical Information Bureau, a computerized data base of medical and some non-medical information. Originally created to prevent consumer fraud, the Medical Information Bureau holds information on 10-20 million Americans. If an insurance applicant has a condition significant to health or longevity, such information must be provided by insurance companies to the MIB. Non-medical information that could affect insurability, such as adverse driving record or participation in hazardous sports, can also be reported.

You must give consent MIB to establish your record or for an insurance company to search your MIB record. If you don't give consent, the insurance company may automatically deny coverage. Next time you fill out an

insurance application, examine it carefully. I recently received a letter urging me to apply for mortgage insurance, and sure enough, if I signed the application, I was giving permission for the company to access my MIB file. An individual in one of our recent workshops informed the group he was denied mortgage insurance because of diabetes, a condition listed in his MIB file. As this data base grows, some people are concerned that corporations, agencies and others will have access to our medical records and genetic information just as they do to our credit histories.

Overhead 9

Issues related to genetic testing, screening and counseling are another area of concern to The Arc. Thanks to the Human Genome Project and the identification of new genes, specific laboratory tests are being developed that can determine whether or not an individual is at high risk for a particular genetic condition.

More and more people will be able to know whether or not they will develop a disorder or possibly pass a disease gene on to their children. How will having this information impact society? Do most of us want to know about future genetic information that could change our lives? For example if you could find out today that you have an 80 to 90 percent chance of developing a rare and untreatable form of colon cancer in the future, would you want to know?

Other issues of concern include: Must a physician offer prenatal genetic screening to all pregnant women or risk medical malpractice liability if she doesn't? Should a woman have a right to refuse prenatal screening? What if she's already had a child with a serious genetic condition? One of our workshop participants reported that her three year old son's serious genetic condition had already cost more than \$1 million, paid for by the state. She

expressed her intent to have another child and her strong belief that she would refuse prenatal testing. What about testing infants and children for genetic conditions when there is no treatment available?

Overhead 10

Genetic testing can have both positive and negative consequences. On the positive side, testing can help people make more informed decisions about their future when they can know what conditions they or their children may be predisposed to getting. Another advantage of testing is that it provides an opportunity to seek genetic counseling so that the risk of passing a disease-gene on to offspring is reduced.

Overhead 11

On the other hand, anxiety runs high when individuals are confronted with a positive test result confirming the existence of a genetic condition. Are people prepared to deal with such news? Also, testing does not provide clear cut answers. A positive result does not guarantee and a negative result cannot completely rule out the possibility that a person will become ill or show signs of being affected by the condition. Environment and other factors play a role. Another problem is that physicians may misinterpret the results of genetic tests.

If positive test results are not kept private, the individual risks the possibility of losing health insurance and employment for herself, the children and other family members.

This concern was expressed to me at a year ago by a woman who was president of a local chapter of The Arc in Massachusetts. She had just learned that her two older brothers, now in their 60s, have fragile X syndrome, a genetic condition that causes mental retardation. Her two grown sons are

unaffected. She could be a carrier, however, and so might they. There's now a simple test for fragile X, but she's read The Arc's educational materials and is concerned about genetic discrimination. She doesn't want any positive test results on her record or her sons', so she has decided to take the fragile X test and pay for it herself. If she is not a carrier, her sons won't have to make a decision regarding testing. Furthermore, her insurance company won't know the results.

Overhead 12

One major area of concern regarding genetic testing is the testing of children. Often parents want to have their children tested to plan for the future or reduce the anxiety of not knowing. Yet, receiving positive test results may actually restrict the child's future in many ways. Children suffer the possibilities of being stigmatized for their condition with a resulting loss of self-esteem. They may also face discrimination by family, employers, insurance companies, educational institutions and others. What rights does a child have to agree to or refuse testing?

There are currently no universal standards among physicians for the testing of children. Health professionals usually recommend that testing be conducted only when there is a clear benefit to the child. Family members, on the other hand, may feel testing should be considered if it can benefit others. For example, a member of our project's advisory committee had a daughter with severe disabilities but no diagnosis. He had his daughter tested because his sister, who wanted to have a child, wished to rule out a genetic condition in the family.

Overhead 13

The third issue area we're discussing as an organization is the use of gene therapy which potentially could cure some genetically-caused mental retardation. Gene therapy is an experimental treatment in which normal genes are introduced into the body's cells in order to correct or modify the cell's function.

Although gene therapy holds great promise for treating some genetic diseases and conditions that have not previously been treatable, no one has ever been "cured" of their condition by gene therapy. Much more scientific research is needed in order for gene therapy to have a significant impact on the treatment of genetic conditions.

At this time, the most promising use of gene therapy for mental retardation is to treat single gene conditions involving enzyme defects. Most of these defects cause significant disability that cannot be treated satisfactorily by such other approaches as modifying the diet or supplying the enzyme. Some examples include adrenoleukodystrophy, galactosemia and the urea cycle disorders.

At some time in the future, it may also become possible to apply gene therapy to fragile X syndrome. Scientists, however, say that more knowledge is needed about the function and control of the fragile X gene before such studies are undertaken.

Overhead 14

Gene therapy also raises some ethical questions related to the quality of life of people with diseases and conditions. We asked our members if The Arc should be advocating for the development of gene therapies that can "cure" people with mental retardation? Some people say that disabilities are not diseases and, therefore, do not need to be cured or repaired. They feel people

with conditions, such as mental retardation, can cope with their condition and lead meaningful lives, not in spite of their disability but with it. Yet, The Arc has always supported efforts to prevent mental retardation. Should we, as an organization, support gene therapy that could one day cure mental retardation?

We ask this question because in some groups, people with disabilities say they don't want to be cured. A segment of deaf people refers to itself as the deaf culture and prefers to have children who are deaf. Some people with physical disabilities say calls for cures demean them as individuals. These people are very critical of Christopher Reeve, who advocates for funding to cure spinal cord injuries. They say he hasn't accepted his disability. Others have difficulty with the idea of no longer being disabled.

This is what Ted Kennedy, Jr., said in a recent interview: "I think of myself as a person with a disability. In fact, going through the two years of chemotherapy and the cancer, losing my leg--it was probably the defining event of my life. It shaped who I am. And you know, if someone offered me a pill today that would somehow magically grow my leg back, I would say no."

Overhead 15

We asked members of The Arc what they believe about curing mental retardation if it were possible. Close to 90 percent participating in our workshops across the country said advocating for a cure did not devalue those with the condition. About 87 percent agree that The Arc should advocate for more funding for research to cure genetic conditions. This information will help guide our Board of Directors in its decision-making regarding these issues.

The major argument in favor of gene therapy is based on its potential for treating individuals severely affected by their condition. A perfect example is

Lesch-Nyhan disease, which is characterized by communication deficits, writhing movements and involuntary self-injurious behavior. Males who have this disorder have to be restrained constantly to prevent them from inflicting severe damage on themselves. Most have their teeth removed to keep from biting their lips off. If we have a new medical technology that will cure this condition, don't we have an obligation to use it?

Overhead 16

There are a number of arguments offered against gene therapy, including the concern that there is potential for harmful abuse if we don't distinguish between good and bad uses of gene therapy. The eugenics movement of the 1920s to the 1940s found people with mental retardation being involuntarily sterilized, along with others considered less desirable. Another concern is that in mental retardation gene therapy research, many candidates are likely to be children who are too young or too disabled to understand the ramifications of the treatment. Finally, gene therapy is very expensive and may never be sufficiently cost effective to merit high social priority. Opponents say if those who can afford gene therapy are the only ones to receive it, the distribution of desirable biological traits will widen the differences among various socioeconomic groups.

Another issue that's relevant here is that of genetic enhancement, using gene therapy to supply a characteristic that a parent might want in a child but which does not involve the treatment or prevention of disease. Such physical characteristics such as height and weight and enhanced cognitive abilities are common areas mentioned.

What about cognitive enhancement for children with mild mental retardation? If cognitive enhancement could increase the IQ of a child with mild mental retardation to allow functioning in the normal range, should it be

considered? Currently, it is not considered acceptable to use gene therapy to treat conditions that are not diseases. Is mild mental retardation a disease that needs to be cured or a condition or trait that does not justify a need for cure? This is a topic we haven't addressed as an organization yet. We have raised it as an issue in our report on ethical issues related to gene therapy. Even though such a cure does not yet exist and may never exist, we believe we should be proactively involved in discussing genetic enhancement before any policy is enacted governing use.

Overhead 17

The Arc's goal is to create an adequate level of awareness among its members on the issues I've outlined, so that our voices can be heard before harmful policy is created. There are differences of opinion on many of the issues we address and general agreement on others.

As families potentially affected by the knowledge gained from research, it is important that we become involved by being educated and expressing our views when appropriate. Even though ethical, legal and social issues have been widely debated by scientists, ethicists and others, few voices have been heard from families directly affected by a genetic condition. We urge our members to keep informed about the issues, so that they can also make informed personal choices regarding testing, participation in research and gene therapy should it become available in the future.

Finally, The Arc will continue to advocate for understanding and acceptance of the condition of mental retardation and fair treatment of citizens with mental retardation. The potential for cure for some must not make us less accepting of those living with the condition.

CASE SCENARIOS – 35 MINUTES

Handout: Case Scenario Exercises

To Facilitator: *You may want to go over only one or all three case scenarios depending on how much time is available and how many people are participating. If there is a very large group, more than one small group may be discussing the same scenario (genetic discrimination, genetic testing or genetic therapy). If the group is not large enough to form three groups of 4-6 people, select one or two scenario(s) to be discussed. The “General Questions for Discussion” should be addressed if time allows.*

Say: You will now have the opportunity to discuss some of the ethical, legal and social issues involved in the Human Genome Project as it relates to mental retardation by reading and discussing the case scenarios on this handout.

We will divide into small groups in order to allow ample time for each person to fully express his or her views. There are three scenarios for discussion. Each group will be given one scenario. You will be given approximately 20 minutes to discuss the questions provided.

If you have any questions, please feel free to ask me at anytime during the discussion. Keep in mind, most of these questions have no right or wrong answers. After you read through the scenarios and answer each question on the hand-out, we will reconvene and discuss each group’s answers.

Case scenario #1: Genetic Discrimination

A health insurance company had covered the medical expenses of a child since birth but refused to pay for an eye astigmatism operation after she was diagnosed with a condition associated with mental retardation, claiming the condition was pre-existing. All bills relevant to the condition had been paid up to the time of diagnosis.

Questions for discussion on above case:

1. What would you do in this predicament? What do you think would be the most effective way to convince the insurance company to pay for the operation?
2. Should third-party health insurers be able to get genetic information if they pay for the genetic testing? Should an HMO be able to get it? Why or why not?
3. Who should have a legal right to obtain your child's genetic information? How might you protect your child from such discrimination in the future?
4. Is the insurance company justified in denying coverage to the child based on concern over cost of her future health care?

General questions for discussion:

1. Should employers be allowed to deny employment to people based on having genes with the potential to cause future diseases or conditions?
2. Should states have legislation that can protect people from discrimination on the basis of their genes in areas such as employment, health and life insurance coverage? Or, should the federal government pass such legislation?
3. Many members of The Arc are carriers for genetic conditions associated with mental retardation. As a parent or relative of someone with a genetic condition, what concerns would you have related to genetic discrimination in insurance and employment?

NOTE: The Arc's Board of Directors passed a resolution in 1996 that supports the enactment of laws banning genetic discrimination.

Case scenario #2: Issues in Genetic Testing

Suppose your son has fragile X syndrome, and you suspect your older daughter may also be affected or at least could be a carrier for fragile X. You are considering whether or not to have your daughter tested.

Questions for discussion on above case:

1. Would you decide to have your daughter tested for fragile X syndrome?
How would you reach this decision?
2. At what age should a child be allowed to decide whether or not to be tested for a genetic disorder?
3. Is there a difference between an 8 year old and a 16 year old in participating in the decision process?
4. How might she be affected psychologically?
5. In your mind, would the benefits of genetic testing outweigh the disadvantages? Why or why not?

General questions for discussion:

1. What rights does a child have to agree to or refuse testing?
2. Do other family members have the right to the positive test results?
3. Who should be given the primary responsibility to decide whether or not a child needs genetic testing? Family members, family physicians or medical specialists, genetic counselors?
4. If you decide not to have your daughter tested during her childhood years, does she have an obligation to be tested prior to marriage?

Case scenario #3: Issues in Genetic Therapy

Suppose that scientists were merely six months away from developing a type of genetic therapy that could “cure” your child’s condition which includes mental retardation by replacing the gene that is causing mental retardation with a healthy one. You are considering whether or not this therapy would be safe for your son, or if the benefits of undergoing therapy are worth the risks.

Questions for discussion on above case:

1. Do people with mental retardation need to be “cured” of their disability?
2. Who decides which conditions/diseases should be targeted in developing treatments? How should this be decided?
3. Should diseases be targeted which cause the greatest number of mental retardation cases? Or should diseases be targeted which cause the most severe forms of mental retardation?
4. Who should decide whether or not to undergo treatment? The individual or his/her family or doctor?

General Questions for Discussion:

1. What are the possible consequences of finally having access to genetic therapies that have the power to “cure” mental retardation to the individual? To the family? To society?
2. If a “cure” could be accomplished at different ages, how would a 2 year old be affected as compared to someone 16 or 45?

Show: Overheads #18-#20 which depict case scenarios, depending on which case scenario is currently being discussed.

To Facilitator: *During discussion, participants' comments can be written on a flip chart to promote group understanding and enhance discussion.*

Say: Let's take about 10 minutes to discuss our answers. Each group should be able to give their response uninterrupted until their presentation is completed. Upon completion, participants in other groups can then ask questions or comment if time allows.

Say After Discussion: This exercise should demonstrate the complexity of the issues resulting from the Human Genome Project and why it is so important that we, as members of The Arc, begin to discuss possible consequences of genetic research and what to do with such powerful information.

CONCLUDING REMARKS - 5 MINUTES

Say: As you now recognize, the Human Genome Project is providing information that we may not be prepared to handle. Members of The Arc need to understand the major concerns involving genetic research in an attempt to be as prepared as possible for the new future dilemmas of the Human Genome Project. We will then be prepared to develop carefully thought out positions related to the use of genetic research.

Please take a few minutes to fill out the post-questionnaire that was handed out at the beginning of the workshop. *(Allow participants time to respond.)*

Would anyone like to share with the group an item on which you have changed your mind after our discussions? Please make sure you turn in any notes you took about your case scenarios and your questionnaire before you leave.

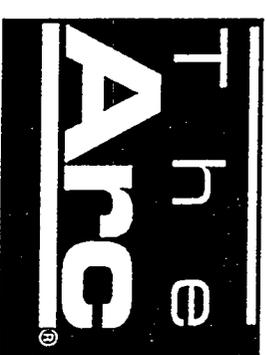
Thank you for your participation in this workshop. Your comments and ideas will be used to guide The Arc in developing comprehensive positions on important issues involving genetics and mental retardation.

T h e
Arc[®]

The Human Genome Project

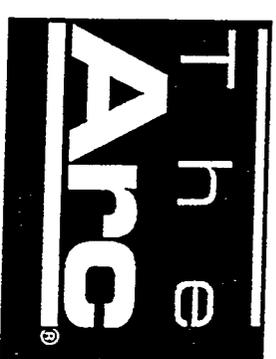
- Identifying the 80,000 to 100,000 genes in the human body
- Human genome = complete set of genes
- ELSI = **E**thical, **L**egal, **S**ocial **I**mplications

The Arc's ELSI Project:



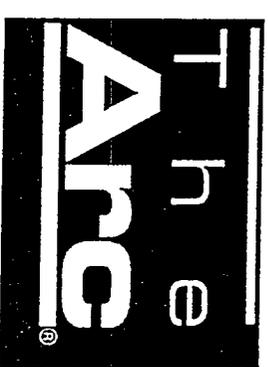
- Make members aware of HGP research
- Begin to examine ethical, legal and social implications as related to mental retardation

Why the HGP is important to members of The Arc



- Direct impact on people with mental retardation and their families
- Rapid discovery of new genes with treatment lagging behind
- Ethical dilemmas - privacy, fairness, discrimination

The Arc's issues:



- Discrimination based on a person's genes
- Decisions involving genetic testing, screening, counseling
- Ethical issues involving gene therapy

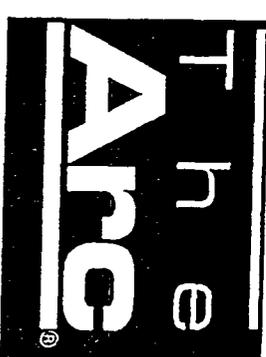
Genetic discrimination:

- People are treated differently because they have a disease gene or genes, even when they show no symptoms of disease.



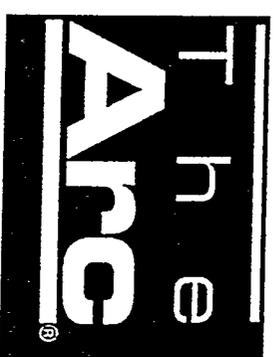
Genetic discrimination occurs in:

- Health insurance
- Employment
- Adoption
- Educational settings

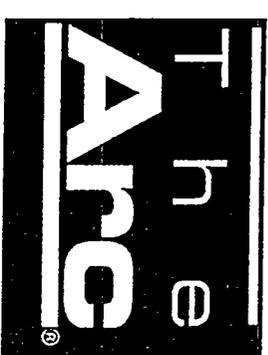


Legislation banning discrimination

- Federal Health Insurance and
Accountability Act of 1996
- State legislation



Genetic privacy



- Medical Information Bureau (MIB)
- Computerized data base of medical and some non-medical information
- 10-20 million Americans included

Genetic testing, screening, counseling:



- Rapid development of new tests
- Whether or not to get tested
- Prenatal genetic screening - an option or not?
- Testing when no treatment is available

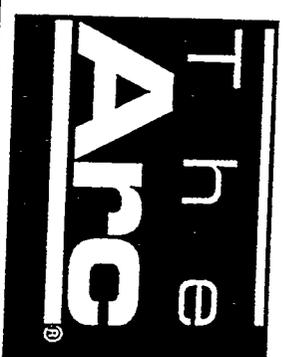
Positive consequences of testing:

- Informed decision-making
- Genetic counseling regarding child-bearing



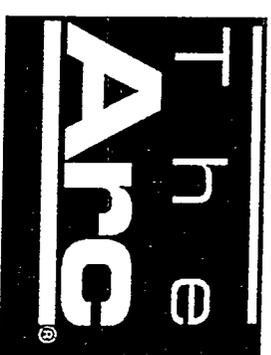
Negative consequences of testing:

- Anxiety regarding test results
- Information may not remain private



Testing children:

- Parents often want to know
- May restrict child's future
- Children's rights in decision-making
- No agreed on standards for testing children



Gene therapy:

- Normal genes introduced into the body's cells to correct or modify function of the cell
- No cure yet discovered
- Single gene most promising



Gene therapy and ethical issues:

- Does advocating for cure devalue people living with condition?
- Should The Arc advocate for funding for gene therapy research?

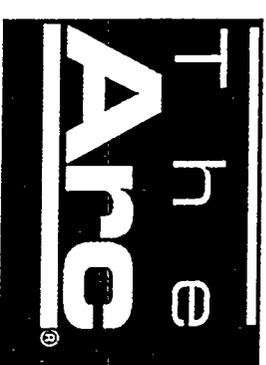


Table 2
Selected Members' Views
on Gene Therapy

Advocating for cure does not devalue person

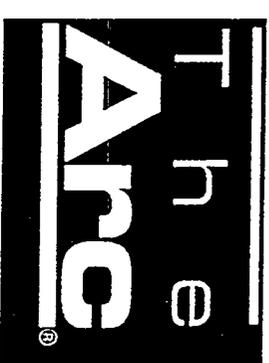
	#	%
Strongly agree or agree.....	229	89
Disagree or strongly disagree.....	12	5
Don't know.....	16	6
Total	257	100

The Arc should advocate for research funds to cure genetic conditions

	#	%
Strongly agree or agree.....	200	87
Disagree or strongly disagree.....	13	6
Don't know.....	18	8
Total	231	101

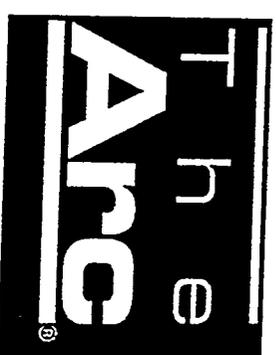
Arguments against gene therapy:

- Potential for harmful abuse - eugenics
- Children unlikely to understand ramifications
- Expensive - widen socioeconomic gap
- Genetic enhancement



Conclusions:

- Families need to understand implications of genetic research
- Families' views are important and need to be heard
- Professionals need to know families' concerns
- The Arc will continue to advocate for acceptance of people with mental retardation



Case Scenarios: Genetic Discrimination in Health Insurance

A health insurance company had covered the medical expenses of a child since birth but refused to pay for an eye astigmatism operation after she was diagnosed with a condition associated with mental retardation, claiming the condition was pre-existing. All bills relevant to the condition had been paid up to the time of diagnosis.

Case Scenarios: Genetic Testing

Suppose your son has fragile X syndrome, and you suspect your older daughter may also be affected or at least be a carrier of the gene for fragile X. You are considering whether or not to have your daughter tested.

Case Scenarios: Genetic Therapy

Suppose that scientists were merely six months away from developing a type of genetic therapy that could “cure” your child’s condition which includes mental retardation by replacing the disease gene with a healthy one. You are considering whether or not this therapy would be safe for your child, or if the benefits of undergoing therapy are worth the risks.

Appendix H

The Arc's Human Genome Education Project

Responses to Participant Opinion Survey

Number & percent of Agreement or Disagreement with the following statements.

	Strongly Agree	Agree	Disagree	Strongly Disagree	Don't Know	Total
Newborns should be tested for genetic conditions even if no treatment exists.	53 21%	92 36%	56 22%	32 12%	22 9%	255 100%
People who have a genetic condition in the family should be tested before having children.	56 22%	129 51%	39 15%	11 4%	18 7%	253 99% *
People should tell their husbands/wives the results of their own genetic tests.	107 42%	120 48%	11 4%	3 1%	11 4%	252 99% *
People should tell their blood relatives about the results of their own genetic tests.	47 18%	126 50%	47 18%	14 6%	20 8%	254 100%
Children should be tested for genetic conditions even if there is no clear benefit to the child.	26 11%	66 28%	66 28%	44 19%	33 14%	235 100%
It is fair for insurance companies to deny medical benefits based on an individual's genes alone, including those who show no outward signs of having a disability.	4 2%	6 2%	50 19%	196 76%	3 1%	259 100%
Health insurers should be able to get genetic information if they pay for the tests.	6 2%	23 9%	50 20%	169 67%	6 2%	254 100%
Employers should be allowed to deny employment to people based on having genes with the potential to cause future disease or disability.	3 1%	4 2%	32 13%	210 83%	4 2%	253 101% *
The Arc should support legislation banning genetic discrimination in health insurance and employment.	187 74%	42 17%	6 2%	10 4%	7 3%	252 100%
Gene therapy is a proven form of treatment for some conditions causing mental retardation.	26 11%	69 30%	44 19%	30 13%	58 26%	227 99% *
Advocating for a cure for mental retardation does not devalue those who have the condition.	140 54%	90 35%	10 4%	4 2%	13 5%	257 100%
Based on my current knowledge, I believe The Arc should advocate for more funding for research to cure genetic conditions.	131 56%	70 30%	8 3%	5 2%	18 8%	232 99% *

* Not all % totals = 100% because of rounding.

Appendix E

Arlington Week in Review

Today-day look at the top local stories as they appeared in the Star-Telegram.



Fort Worth Star-Telegram/DARRYL BYRNS

Former Texas Gov. Ann Richards looks at the selection at the J.C. Penney store in The Parks at Arlington mall. Richards was there for a shareholders meeting.

Main was driving west in the 100 block of East Randol Mill Road when he collapsed and the car rolled into a ditch, according to police reports. Edwina Main said she struggled to gain control of the car, which was accelerating and veering into oncoming traffic.

TUESDAY

WEDNESDAY

Officials at odds on track taxes

GRAND PRAIRIE — Recent suggestions by the Dallas Central Appraisal District that property taxes might be due on the \$110 million horse track are misquided and could have statewide

The main post office, 300 E. South St.; the Tate Springs Post Office, 4108 S.W. Green Oaks Blvd.; and the Watson Community Station, 1975 Ballpark Way, will stay open until midnight Monday to accept returns, Sprouse-Hudson said.

The Arc to look at ethics issues

ARLINGTON — If an obstetrician knew that a pregnant patient had an 85 percent likelihood of giving birth to a child with mental retardation, should the doctor tell her?
What if a scientist could, before the child was born, "fix" the gene that would cause the mental retardation?

Those are the sort of ethical, legal and social questions The Arc, an Arlington-based national advocacy group for the mentally retarded, will examine for the next two years.
The Arc, formerly the Association for Retarded Citizens, has been chosen for a \$200,000 grant from the Department of Energy, which, with the National Institutes of Health, is directing the U.S. human genome efforts.

UT-Arlington plans budget cuts

ARLINGTON — Falling enrollment will likely force the University of Texas at Arlington's athletic department — once touted as vital to the university's future — to make significant budget cuts for the second consecutive year.
President Robert Witt said \$30,000 in cuts recommended by a student advisory committee may be doubled, putting further pressure on a department that reduced expenditures by \$150,000 to \$250,000 this fiscal year under the direction of interim Athletic Director Dudley Wetsel.

Wetsel, a former vice president for business affairs who last year took the reins of a department with a \$2.4 million deficit, will retire in May. His successor will be announced Monday, Witt said.

Advocacy group for the retarded to study ethics of genetic research

196

BY CHRIS DOYLE

Special to the Star-Telegram

person's physical makeup. The ethical study will address questions such as:

- If an obstetrician knew that a pregnant patient had an 85 percent likelihood of giving birth to a child with mental retardation, should the doctor tell her?
- What if a scientist could, before the child was born, "fix" the gene that would cause the mental

(More on ARC on Page 17)

in appearance on CNN's *Inside* lists. ramm, too, is hoping for a race-ting on federal policy issues, spokesman Larry Neal. But ans will have to wait a few uths to see the donnybrook be- e (Tramm has no intention of ling with Morales until Labor going, 15-year global project study- Arc's work will be part of an on- ing the human genome, the genes that determine everything about a

More on MORALIS on Page 17)

At World Star Telegram

Five percent of the Human Genome Project's funding is devoted to study of the ethical, legal and social implications, commonly referred to as ELSI, which is the facet Arc will be exploring. "From the onset, they [the project's leaders] knew it would change the face of medicine and raise ethical, legal and social questions," said Skip Garner, associate director of the Human Genome Center at the University of Texas Southwestern Medical Center. The center in Dallas is among the 10 largest genome project sites in the world.

The Arc, which has a staff of 35 at its Arlington headquarters, will use the federal funds to educate the general public on ethical issues raised by the project and to develop some policy positions, said Davis. The education could take the form of newsletters, conferences and surveys, Davis said. The money for the two-year study also

heved to lie at the root of conditions ranging from heart attacks and cancers to forms of mental retardation. But unlocking that data raises fears that the information could be used to deprive people of jobs, insurance and privacy, as well as raising the possibility of selective abortion and discrimination. Scientists are beyond theory when it comes to genetics. Already, women in their late 30s or 40s considering pregnancy are being tested for the genetic error that causes Down syndrome. But deciding whether to cure disabilities and diseases through genetic changes is not as clean-cut a proposition as it might seem. Many people, particularly those with disabilities, find the idea of- "A lot of people think you shouldn't try to fix the condition if you could," said Sharon Davis, director of The Arc's Department of Research and Program Service.

tion for the two-year study also and a more centrally located national headquarters. Errors in these instructions, or miscoding of the genes, are be-

ARC

From Page 1

retardation?

The Arc, formerly the Association for Retarded Citizens, was chosen for the study by the Department of Energy, which, with the National Institutes of Health, is directing the U.S. human genome efforts.

The Human Genome Project, to which the U.S. Congress has pledged \$3 billion, is expected to be completed in 2005. It is expected to identify the genes that provide the map for development of the human body. Within the genes are an estimated 3 billion chemically coded instructions that determine everything about a person's physical makeup, from hair color to heart size.

Errors in these instructions, or miscoding of the genes, are be-

NOVEMBER 1997

\$4.00

EXCEPTIONAL PARENT

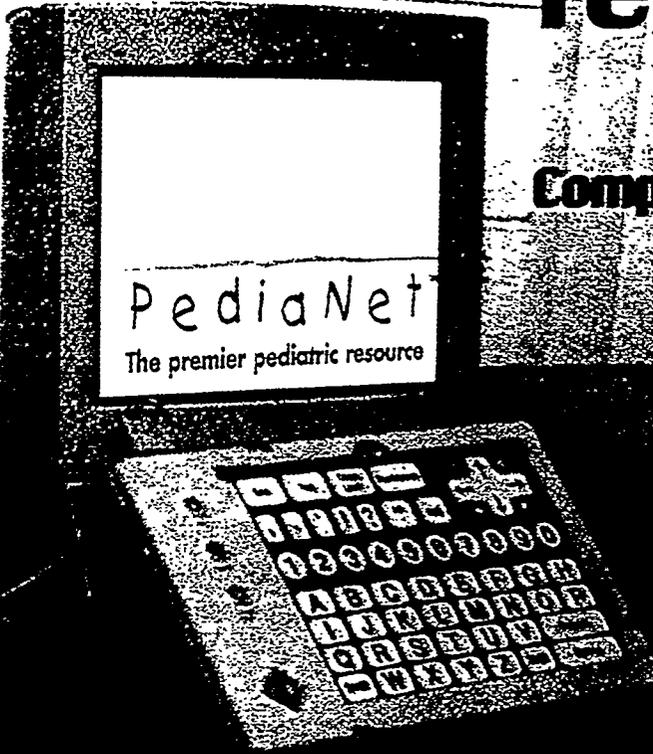
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YOUR
CHILD OR
YOUNG
ADULT
WITH A
DISABILITY

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Families and Professionals

Annual Technology Issue

Computers • Virtual Reality
• The Internet

*Over a
Quarter Century
of Caring*
1971-1997



**TECHNOLOGY'S ROLE
IN GENETICS**

PLAYGROUND ADVOCACY

Technology in Genetics

The Danger of Knowing Too Much

by Leigh Ann Reynolds

Sherry's Story

Sherry's brother has a rare genetic disorder that has only recently been identified by doctors. Due to the disorder, her brother will more than likely become fully disabled over the next year. Sherry recently changed jobs and was asked to reveal any new medical information for the employer's insurance company. She provided information about her brother's rare disorder upon being hired. Within one month of employment she was fired. The reason? "Unsatisfactory skill level." However, Sherry never showed any signs of inadequacy. She was fired due to the fact that her brother has the disorder, yet she has never exhibited any signs of her brother's disorder and has never even been tested herself.

**The name and content of this scenario are fictitious. This scenario is provided to demonstrate the real possibility of genetic discrimination within families of individuals with yet to be identified disabilities.*

The Human Genome Project

This is only one example of how technology in genetics can bring unforeseen consequences to families of individuals with disabilities. Spurring the advent of such rapid advancement in genetic understanding is the Human Genome (pronounced gee-no-mm) Project. This is an international effort involving hundreds of scientists who are attempting to find all 60,000 to 100,000 genes within the human body. In doing so, they hope to discover which genes cause, or are in some way associated with, certain diseases and conditions. Errors in our genes are responsible for an estimated 3000 to 4000 clearly hereditary diseases and conditions. They play a part in cancer, heart disease, diabetes and many other common conditions. Within the next five to ten years we may be able to discover almost all of the diseases we are at risk of inheriting.

The project began in 1990 and is being directed by the National Institutes of

Health and the U.S. Department of Energy (DOE). Aside from identifying disease-causing genes, it is also attempting to identify and answer specific ethical questions related to the consequences of new genetic findings in society.

The hope is to begin developing policy options which can address the ethical questions sparked by the project.

Three percent of DOE's overall Human Genome budget is devoted specifically to funding research that looks at the Ethical, Legal and Social Implications, called ELSI (pronounced el-see), of genetic findings in society. The danger of knowing too much about our

genes is that we may not be ready for the information. After all, we have never before had access to such specific information regarding our future health and that of our children.

The Arc of the United States, the country's largest volunteer-based organization on mental retardation, has spent the past two years developing reports and training on these issues through an ELSI grant. One concern we have found to be of paramount importance to families of individuals with disabilities is genetic discrimination and the issues surrounding it. Some of the concerns are deciding whether or not to be tested for a genetic disorder and how to protect genetic privacy.

Becoming familiar with the genetic causes of disabilities paves the way for more discussions of ethical issues involving genetic research.

Who should consider genetic testing and is it worth the risk?

In the above scenario, Sherry decided not to be tested for the same gene her brother has due to fear of more discrimination. Such discrimination brings understandable fear, since once a person is tested for a genetic disease or disorder, he or she runs the risk of losing health insurance and, possibly, employment.

Genetic testing can be harmful if the information is used to deny jobs or insurance, or if it leads to other forms of discrimination. Not everyone needs genetic testing. Although everyone has a few defective genes, they may never be the cause of a disability. Many factors within the environment have a significant impact

continued on page 34



Sharon Davis, Ph.D. is Director of the Department of Research and Program Services with the Arc of the U.S. and is the Principal Investigator of the Arc's Human Genome Education Project.

continued from page 33

on a person's health. Such factors either alone, or combined with a disease-causing gene, can increase or decrease an individual's risk of developing a disease which could lead to a disability. People who know of a genetic condition within the family are prime candidates since they are susceptible to inheriting a specific disease-causing gene. Others who could benefit from genetic testing include:

- Pregnant women concerned about the effects of exposure to medication, chemicals or radiation.
- Couples who already have a child with a genetic disorder, unexplained mental retardation or a birth defect and couples who are first cousins or blood relatives.
- Women who have had two or more miscarriages or whose baby died in infancy.
- People with unexplained short stature.
- People with unusual physical features, especially poor growth or development.
- Women who give birth after the age of 35.
- Couples who would like testing or information about genetic disorders that occur frequently in their ethnic group.

What is genetic counseling?

Genetic counseling provides important information about the results of a genetic test by translating genetic knowledge into easily understandable and practical information. Individuals who are considering genetic testing may want to talk with genetic counselors or clinical geneticists who use their knowledge about the basic laws of heredity, family health history (called pedigree) and results from the genetic testing to estimate the probability that a

disorder may recur within the family. Genetic professionals attempt to emotionally and psychologically prepare the individual for receiving test results so that informed decisions can be made.

Genetic professionals typically work in large medical centers or hospitals affiliated with a medical school or university. There are about 300 comprehensive genetic service centers in the United States. Individuals can seek genetic counseling by calling a local hospital associated with a medical school, asking their physician for a referral to a genetic counselor or calling a local chapter of the March of Dimes (see end of article for additional resources).

What are the pros and cons of being tested?

Testing can lessen the anxiety of not knowing the possibility of developing a disease and provide a tremendous

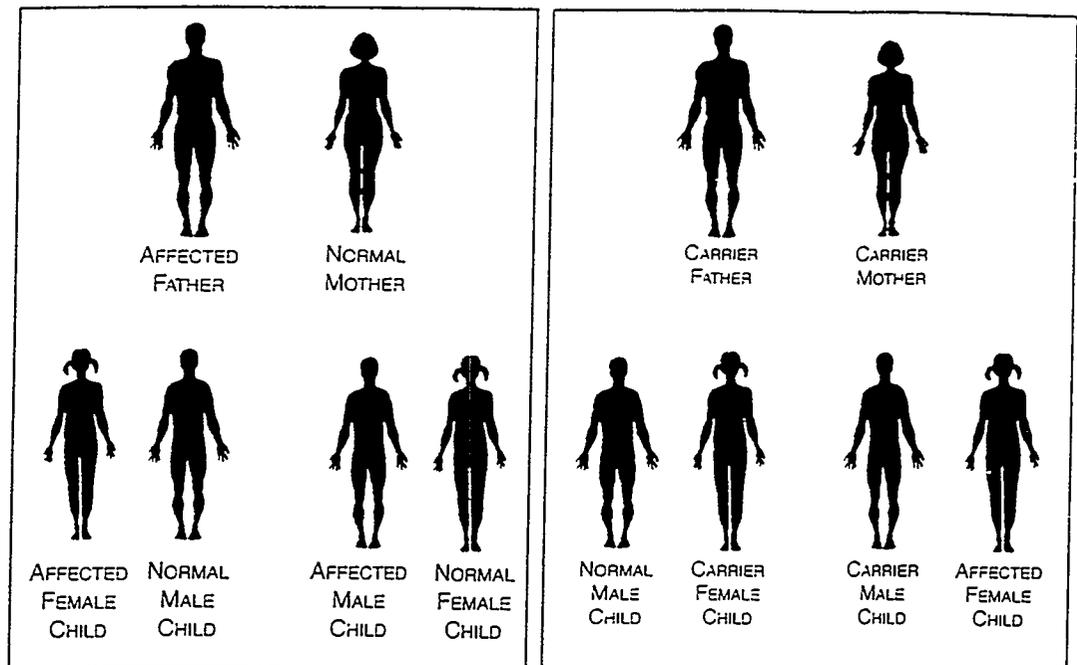
sense of relief once a definitive test result is given. An individual who chooses to undergo testing has the opportunity to seek medical help, prepare for, and possibly help prevent, a genetically-caused condition. Testing can help people to make more informed decisions about their future.

Unfortunately, several negative consequences may result from genetic testing as well. Once a person has tested positive for a disease or condition, he or she risks stigmatization, loss of health or life insurance, loss of employment or educational opportunities and possibly can lose the ability to adopt a child. Privacy of other family members is threatened since, if one family member is tested, this information implies that relatives could also have the disease gene or may have an increased risk for disease.

As more and more genetic tests are

continued on page 38

Dominant and Recessive Genes



In dominant genetic disorders, if one affected parent has a disease-causing gene that dominates its normal counterpart, each child in the family has a 50 percent chance of inheriting the disease-causing gene and the disorder.

In diseases associated with altered recessive genes, both parents—although disease-free themselves—carry one normal gene and one altered gene. Each child has one chance in four of inheriting two altered genes and developing the disorder, one chance in four of inheriting two normal genes, and two chances in four of inheriting one normal and one altered gene and being a carrier like both of the parents.

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38 • EXCEPTIONAL PARENT / NOVEMBER 1997

continued from page 36

created, individuals with disabilities and their family members will face the dilemma of whether or not to be tested for certain conditions. Understanding the basics of genetic testing and genetic counseling BEFORE being tested can assist individuals in making informed decisions about whether or not testing is the best decision for them and their family.

What is genetic discrimination and who does it impact?

Unfortunately, most of us already know what discrimination is, because people with disabilities have experienced different treatment purely based on having a disability. But genetic discrimination is a relatively new concept for many. This occurs when someone is treated differently, not based on having a disability, but based on having a gene that may or may not cause the person to show symptoms of a disability sometime in the future. This means everyone could potentially experience genetic discrimination, regardless of the presence of a disability. This is a real possibility since a recent study noted more than 200 instances of genetic discrimination in areas such as health insurance, employment and adoption. There is also evidence that some who have defective genes are stigmatized, suffering a loss of social and economic opportunities.

Francis Collins, Director of the National Center for Human Genome Research, often reminds people that all of us probably carry about four or five "really fouled-up" genes that place us at risk for something.

Genetic discrimination is aimed at people who appear healthy or whose symptoms are so mild that their functioning and health are not affected. However, people with

disabilities could experience genetic discrimination as well, depending on the level or severity of symptoms.

Protecting personal genetic information

With the threat of genetic discrimination, more people have become concerned with the need to protect themselves. But this is no simple feat. There are many situations where people must provide personal information. Several include applying for a job, life or health insurance, credit or financial aid and benefits from the government. As the use of genetic testing grows, insurers and employers will want to obtain test results in order to determine the health status of the applicant or employee. Such information can be highly sensitive and personal. Once this information is provided, the companies/institutions/individuals are under no obligation by law to protect it. In fact, there is no law which says that a blood sample collected for one type of DNA testing cannot be used for another purpose. The law also does not give individuals the right to check their DNA file to see if the information is correct.

How can my genetic information be used against me?

Genetic information may be used by people other than medical professionals. For example, insurance companies or

employers may want to "weed out" applicants or possible new hires whose genetic information is considered undesirable. Although some types of medical information, such as HIV status, may be kept in separate files so that fewer people can see them, if a "release of medical records" form is signed, insurers are entitled to see everything, including separate files.

A person's genes can tell a lot about that person. Employers, insurance companies,

For more information about legislation on genetic discrimination and to see if there are laws in your state, contact:

The Council for Responsible Genetics
5 Upland Road, Ste. 3
Cambridge, MA 02140
(617) 868-0870
<http://www.essential.org/crg>

The National Society of Genetic Counselors
233 Canterbury Dr.,
Wallingford, PA 19086-6617
<http://members.aol.com/nsgchome.htm>

The Alliance for Genetic Support Groups
Telephone: (800)336-4363

The Council of Regional Networks (CORN)
Telephone: (404)727-1475
<http://www.cc.emory.edu/PEDIATRICS/corn/member/coorlist.htm>

educational institutions, adoptive agencies and others can find out what conditions or diseases a person may have or be predisposed to getting. Genetic test results can be misinterpreted by organizations who are unfamiliar with genetic tests. Having a gene for a certain condition does not necessarily mean the individual will ever show symptoms of the condition.

Also, federal law does not require those who obtain genetic information to protect it. Although some states have banned genetic discrimination, the chance that a person will be discriminated against based solely on his or her genetic make-up remains a high possibility.

How can I attempt to protect my genetic privacy?

Anyone who has ever filled out an application for individual life, health or disability insurance should have filled out an "MIB Notice" within their application. Through the Medical Information Bureau (MIB), insurance companies have access to the medical records of people who have applied for insurance. The MIB, a private, non-profit corporation located in Massachusetts, manages a computerized data bank of information to provide insurance companies with medical and certain non-medical information about applicants for insurance. Originally created to prevent insurance fraud, the MIB holds medical information for 10 to 20 million Americans.

If an insurance applicant has a condition significant to health or longevity, such information must be provided by insurance companies to the MIB. Non-medical information that could affect insurability can also be reported. Consent from the individual must be given in order to establish an MIB file or to allow a data bank search. However, if the applicant decides not to give consent, insurance companies may automatically deny coverage.

Protecting the privacy of genetic information is challenging and difficult. For example, if an applicant for health insurance responds honestly to the question of whether or not he or

she has a genetic or hereditary illness, this could eliminate any chance of obtaining health insurance. If genetic information is withheld or concealed from the insurance company, does it mean that coverage for associated problems would be denied? If one declines to answer does this mean that insurance will be denied? Either way, coverage can be denied.

To attempt to keep genetic information as private as possible, physicians and other medical providers should be instructed in writing that they are not allowed to disclose genetic information to anyone without prior verbal and/or written consent. Whenever applying for insurance, note if the application asks "Have you been advised of any genetic

continued on page 34



“WHO WILL CARE
WHEN I’M NOT THERE?”

DIGNITY BY DESIGN

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continued from page 29

or hereditary illnesses, conditions or disease." If it does, and a completed application is signed, the insurance company can send a copy of your application to the MIB, which means all future insurers will have access to your genetic information.

If the MIB has a file on you, you can obtain a copy of the report to determine if anything in the file is incorrect and change it if it is wrong. Medical conditions are reported by using one or more of about 210 codes. The information within the report is translated from code to reveal the specific conditions. You can file a statement of dispute if you disagree with information in the file. If the information was accurate when reported, but has changed and is no longer accurate (for example, a medical condition that has improved), a "statement of additional information" can be submitted describing the improvement or correction.

To determine if you have a medical file or to request a copy of your file, contact the MIB at (617)426-3660 (P.O. Box 105 Essex Station, Boston, Massachusetts, 02112). For more information contact:

Leigh Ann Reynolds,
Project Associate of the Human Genome Project,
The Arc of the United States,
500 E. Border St.,
Ste. 300
Arlington, TX 76010
Telephone: (817) 261-6003,
Fax: (817) 277-3491
E-mail: lreynold@metronet.com

What steps are being taken to eliminate genetic discrimination?"

In addition to federal law and regulations, several states have developed and adopted legislation banning discrimination in health insurance and employment. Currently eleven states have laws prohibiting health insurers from

denying health care coverage because of a genetic condition. Seven states prohibit employers from requiring genetic tests or using genetic health predictions in employment decisions. Seven other states have bills pending to protect individuals from discriminatory use of genetic information in employment practices or for insurance purposes. The Federal Health Insurance Portability and Accountability Act of 1996 offers protections against discrimination in health insurance by limiting pre-existing condition exclusions. It also prohibits discrimination against individuals based on health status, including their genetic information. **EP**

Leigh Ann Reynolds, M.S.S.W., M.P.A. is Project Associate with the Arc's Human Genome Education Project and conducts a number of health promotion & disability prevention activities at the Arc's national headquarters in Arlington, Texas.

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LETTERS

(continued from page 8)

now more verbal and does not rely on augmentative communication devices. Since he has been in a regular class, he has started to say words and says more new words every day.

I urge all parents to rethink the placement of their children. Any accommodations for equipment, extra services, or modifications can still be available and put on the child's IEP.

D.T. Meggett, South Carolina

No ventilators allowed

My son has congenital hypoventilation syndrome (reduced rate and depth of breathing, causing an increase in carbon dioxide in the the blood stream), which requires mechanical ventilation (sometimes 24 hours a day). He had diaphragmatic pacers that were breathing for him during the day, but they began to fail at the end of the school year. As a result, he has had to use his home ventilation system, even while at school.

My son was very concerned about his classmate's reaction to this noisy, complicated piece of equipment, so I spoke with his teacher and the principal. Thankfully, their only concern was that he come back to school, ASAP! In fact, he was encouraged by his classmates to come back, and he finished the year on his ventilator.

There is a girl in Illinois with the same condition as my son who has not been so fortunate. Her ability to sustain adequate respiratory control has also declined, and it is necessary for her to be on her ventilator device at school. Her parents contacted the school to let them know, and they were told that she could not return to school with a ventilator because of the noise. In addition, the school does not want to be held liable if any damage is done to the equipment. She would not be allowed to return until a meeting with her IEP team took place, and this would take about a month to set up!

As I thought about this girl and her parents, I cried long and hard from frustration. It seems that the very people who are in the professions designed around our children's needs fight the hardest against us.

I thank your magazine for giving me resources and the strength in knowing I am not alone.

J.H., Tucson, Arizona

EDITOR'S NOTE: We encourage parents to send us more of their success stories.

ADDITION

The November, 1997 article (pp 34-44) entitled: "Technology in Genetics—The Danger of Knowing Too Much" was written through a project funded by the U.S. Dept. of Energy ELSI Program under Grant No. DE-FG03-96ER62162. Support from DOE does not constitute an endorsement of the views expressed in this article.

We encourage letters from readers on any subject. Letters should be sent to: Letters, EXCEPTIONAL PARENT, 555 Kinderkamack Road, Oradell, NJ 07649-1517, (201) 634-6570 (fax). Published letters may be edited for space and clarity. Unless otherwise requested, writers will be identified only by initials and state. Please indicate if you would prefer to be identified by name and state or by name, city, and state. Please include your full name, address, and daytime phone number with every letter. This information is not for publication but enables us to contact letter writers directly if necessary.

insurance.
"There's a real movement," Fuller said.

The issue promises to be a hot button in Michigan in 1998.

Gov. John Engler has formed a Commission on Genetic Privacy to study its implications.

The 11 members — doctors, ethicists, insurance industry representatives and individuals dealing with genetic conditions — began meeting in November.

Their aim is to recommend policy to gain the most from genetic discoveries in medicine, forensic science and other fields, while guarding the privacy of individuals and protecting against potential abuses.

In addition, 20 bills have been sponsored by lawmakers in both the House and Senate, generating bipartisan interest. The bills largely follow laws in other states.

So far, Michigan residents may be experiencing fewer discrimination problems than other states.

Blue Cross/Blue Shield of Michigan — the state's dominant insurer, covering 50 percent of the private

anne Udow, the Blues' senior vice president of Health Care Products and Provider Services. "I would hope that insurers compete on the basis of ability to manage care and the ability to provide service."

The insurance industry's promise to self-police has drawn skepticism from those who say abuses already exist:

■ Job applicants turned down out of employer fear that hefty insurance premiums may follow.

■ Families excluded from medical coverage because an illness has touched relatives.

"With our computer system the way it is today ... who is to say there is such a thing as confidentiality?" said Mott.

Her own medical history is documented in dozens of billing records generated by surgeries and annual scans of her brain, spine, kidneys and eyes. Surgeries in 1991 and last year have been successful in removing two brain tumors. Still, four lesions remain. And over the years, others have been detected in her left eye, pancreas and elsewhere. Some

other person is more qualified." She hopes her children — now 22 and 23, and entering the job market — will never face the closed doors discrimination brings.

Though American Civil Liberties Union officials aren't aware of any pending lawsuits involving genetic discrimination, the potential keeps many people from speaking publicly about their medical conditions or those of family members.

It keeps Julie Rhem's younger brother from pursuing his own tests. A younger sister also has chosen not to know.

The fear exists despite the fact that the eldest brother, who is self-employed, has had no problems with his insurance.

Rhem has her own concerns about whether her family would be able to gain new coverage should her husband ever change jobs or if she went back to work. Could any potential health problem be viewed as a pre-existing condition and, therefore, be uncovered?

Nearly one-fifth of people who have a family member with a he-

Company President Howard Cash likens Sequencher's ability to matching up and piecing together each line of a shredded version of the novel "War and Peace." Typographical errors in the text would represent genetic mutations.

Among Gene Codes' most noteworthy finds: The identification of the genetic mutation tied to colon cancer in 1993.

Each discovery offers the promise of a life-saving cure or treatment.

And raises yet more questions — those that go outside the workplace and political arena and into Michigan's homes.

"Where is the line between a physician's obligation to respect the privacy of a patient and the obligation to inform family members who may also be genetically affected?" Cash said.

Questions like those are the focus of the three-year project in which Mawhorter and hundreds of others statewide have taken part. It is conducted by the University of Michigan and Michigan State University

Lindau sufferers about the basics of the disease and how its effects differ among patients. Some patients show no symptoms of the condition. Mott reassures all their diagnosis isn't a death warrant.

"If everybody has their head in the ground, no one is going to get up there and help things," Mott said.

Her choice.
Rhem isn't so sure. She wrestles daily with the choice of knowing ... or not.

"There are no treatments and no cure," Rhem said. "I don't see what advantage I would have right now by knowing."

Her choice.
Her most immediate concern: her children, ages 7 and 12, who know about the disease and how it can be passed from parents to kids. It doesn't skip generations.

If Rhem is a carrier, her children have a 50-50 chance of a similar fate. On the other hand:

"There's, of course, the chance it could be negative and I could quit worrying about my life."

New discoveries bring new forms of discrimination

Lansing State Journal

Who's at risk and why has it captured the attention of lawmakers and others?

■ What is genetic discrimination? It describes the different treatment of individuals or families based on actual or presumed genetic differences. It is aimed at people who appear healthy or whose symptoms are so mild they don't have any effects on health.

■ Why is concern about such discrimination increasing? The Human Genome Project, a multinational effort, is identifying the 70,000 to 100,000 human genes. Understanding the complete set of genes, known as the human ge-

nome, will lead to new approaches to diagnose, treat and prevent disease.

■ What kinds of discrimination are happening? One of the most common is denial of health insurance. Insurance companies use medical information to predict a person's risk of illness and death. Risk determines price. Discrimination also can take place in employment — people who believe they were fired or not hired because they are at risk for genetic disease. Other evidence of discrimination comes from medical workers' attempts to influence individuals in their reproductive decisions or adoption agencies prohibiting adoptions based on such information.

■ Do protections exist? The

Americans with Disabilities Act offers employment protections to people affected by genetic conditions. It also extends to people who have genes making them predisposed to disability-causing diseases. But it may not protect carriers of genetic disorders, who may be discriminated against based on concerns about health costs of future dependents.

■ Can steps be taken to eliminate such practices? In addition to federal law and regulation, several states have developed and adopted legislation banning discrimination in health insurance and employment. Already, 24 states have laws prohibiting health insurers from denying health care coverage based on genetic conditions. A number of other states, including Michigan,

have various bills pending.

■ To learn more? There are a number of groups:

National Center for Human Genome Research, Office of Communications, Bldg. 31, Room B1C35, 9000 Rockville Pike, Bethesda MD 20892. (301) 402-0911. <http://www.nchgr.nih.gov>

Council for Responsible Genetics, 5 Upland Road, Suite 3, Cambridge MS 02140. (617) 868-0870. <http://www.essential.org/crg>

The Genome Action Coalition, 317 Massachusetts Ave. N.E., Suite 100, Washington DC 20002. (202) 546-4732.

The HuGEM Project: Issues in Genetic Privacy and Discrimination, Georgetown University, 3307 M St. N.W., Suite 401, Washington

What do you think?

If you have comments regarding this special report or suggestions for continuing coverage of this issue:

Call writer A.J. Evenson at 377-1015.

Fax her at 377-1298 or write her at Lansing State Journal, 120 E. Lenawee St., Lansing MI 48919.

DC 20007. (202) 687-8635.

Source: *The Arc's Human Genome Education Project, Sharon Davis and Leigh Ann Reynolds*

Santa Fe Workshop

ELSI Grantees Address Accelerated Societal Impact of Genome Data

Rapid worldwide progress in human genome sequencing has heightened the urgency of addressing the many complex ethical, legal, and social issues (ELSI) surrounding genetic data. Some topics presented at the Santa Fe workshop are summarized below.

Testing, Managed Care, and Confidentiality

Jeroo Kotval (University of Albany) spoke about the threat to patient welfare and confidentiality created by the confluence of three elements: DNA-based testing, the rise of market-driven managed-care organizations (MCOs), and the availability of the medical record on networked computers. Confidentiality of DNA-based tests provides new and heightened concerns because some of these tests can predict future healthcare costs and also implicate relatives. Such information handlers as secretaries and data-entry clerks are not licensed professionals and, therefore, not bound by medical confidentiality laws in most states, she pointed out.

Central to confidentiality concerns in the MCO setting, Kotval suggested, is

Informatics (from p. 13)

WIT/WIT2 reconstructions are based on the metabolic pathway (MPW) collection, which includes over 2800 diagrams covering primary and secondary metabolism, membrane transport, signal-transduction pathways, intracellular traffic, transcription, and translation. Selkov observed that identifying universal metabolic aspects and gene families will lead to integrated understanding of metabolic evolution and to technologies for developing higher-level functional models. In the current public release of MPW (wit.mcs.anl.gov/MPW), the coding, based on the pathways' logical structure, is represented by objects commonly used in electronic circuit design. Such design facilitates diagram drawing and editing and enables automation of basic simulation operations.

the practice of utilization review, which tracks each physician's referral and test-ordering practices and sometimes even treatment protocols. She observed that the MCO setting presents some unique ethical dilemmas because physicians and other personnel are MCO employees or contractors and because payor and provider functions are contained within the same entity. Physicians, no longer free agents, may be caught between competing MCO and patient interests.

She suggested that traditional concepts of interpersonal morality with regard to confidentiality may not apply to institutional decisions because institutions are not moral beings. Organizational decisions are made for the institution's good, and values implied by such decisions may differ from those held by individuals in their personal lives.

DNA-based predictive tests for adult-onset disorders or predispositions may, therefore, be used by insurance companies to discriminate in the interest of cutting costs. Kotval emphasized that cost-tracking is not restricted to for-profit, market-driven managed care.

Kotval's group seeks to (1) understand the context in which DNA-based tests will be used by MCOs, (2) identify policy gaps that could allow misuse of confidential medical information, and (3) make practical recommendations to remediate these gaps. She stressed that genetic information increasingly will be an inseparable part of the medical record. If individuals are to avail themselves of the benefits of genetic testing, however, they must be assured that the medical record is confidential.

"In the popular imagination," she said, "one's genetic makeup is perceived as fundamental and integral to the self, revealing something deep, basic, and even final about a person, adding to [the genetic data's] sensitivity and raising concerns about its possible misuse. Our genes are fraught with both personal and cultural significance."

Anguish of Genetic Testing

Gene testing's profound challenges to a person's sense of self, family, and future were well illustrated in A

Question of Genes, last fall's 2-hour nationally televised Public Broadcasting Service special sponsored by the DOE Human Genome Program and SmithKline Beecham. At the Santa Fe meeting, producer and director Noel Schwerin (NoelEye Documentaries) presented a short excerpt. The program follows the lives of several individuals and families as they confront genetic testing for such conditions as heart disease, Alzheimer's disease, breast cancer, and cystic fibrosis. The decisions and dilemmas of a range of personalities and perspectives are explored, including those of the sole survivor of four sisters who experiences tremendous guilt on learning that she does not harbor the gene mutation associated with a rare inherited form of breast cancer. [A print copy of the free educators' guide can be ordered from 800/991-1441 or through the extensive Web site (www.pbs.org/gene), which contains numerous additional resources for teachers. Discussion guides to accompany the video can be downloaded from the Web (www.pbs.org/gene/educator/41_discussion.html).]

Mental Retardation Organization Viewpoint

Sharon Davis represented The Arc, a national organization of 140,000 members concerned with the welfare of people with mental retardation and their families. The Arc, funded by the DOE ELSI program to increase awareness of the Human Genome Project, is examining critical issues related to new genetic discoveries. More than 750 genetic disorders have been identified as causing mental retardation; two of the most common are Down's and Fragile X syndromes.

In discussing the future possibility of gene-based cures, Davis noted that most of The Arc's workshop participants support increased funding for research to cure mental retardation and that this does not devalue those already affected. Davis emphasized the need for education to (1) promote widespread discussion before policy is enacted to govern the use of future technologies and (2) allow informed personal choices regarding testing

and participation in research. She concluded her presentation by reminding the audience that "the potential for cure for some must not make us less accepting of those living with the condition." See www.ornl.gov/hgmis/resourceware.html for the full text of Davis's talk.

Physician Education

Transitional periods can be uncomfortable, noted Sara Tobin (Stanford University) as she described the current context in which genetic advances are emerging: changes in the health-care system; marketing pressures; uneven distribution of genetic resources, especially of genetic counselors; limited public understanding;

and inadequate training of physicians in the "new genetics." A study published last year in the *New England Journal of Medicine* reported that most physicians who ordered a particular DNA-based test did not obtain prior informed consent and that one-third interpreted the results incorrectly to their patients.

Tobin is developing an interactive CD-ROM course to aid physicians who have had little or no training in clinical applications of molecular genetics. This course, "The New Genetics: Courseware for Physicians: Molecular Concepts, Applications, and Ramifications," will provide continuing medical education credits for practicing physicians in basic genetics, molecular techniques,

Abstracts of Research in Progress

DOE Human Genome Program research in progress since 1991, including research abstracts from the 1997 Santa Fe meeting, can be found on the HGMIS Web site (www.ornl.gov/hgmis/research.html). Print copies of the workshop proceedings are available from HGMIS (see address on p. 10). ◊

clinical applications, and ELSI. Probable release date is spring 1999 (www.leland.stanford.edu/dept/scbe/cdrom.htm).

In the News (from p. 4)

Palmisano Joins DOE OBER



Anna Palmisano
DOE OBER

On July 20 Anna Palmisano, a microbiologist and microbial ecologist, joined the Environmental Sciences Division of the DOE Office of Biological and Environmental Research. In her new position, Palmisano will continue her program management activities for the Natural and Accelerated Bioremediation Research program, the Microbial Genome Program, and such biological aspects of ocean sciences as the Biotechnological Investigations—Ocean Margins Program. She worked on these projects for 9 months in 1997 as a detailee from the Office of Naval

Research (ONR), where she served as a program officer in environmental biology for 6 years. Before joining ONR, she conducted research on biodegradation in freshwater streams, soils, and landfills for the Environmental Science Department of Procter & Gamble company.

Palmisano received her B.S. in microbiology from the University of Maryland and M.S. and Ph.D. in biology from the University of Southern California, where she studied the physiological adaptation of microorganisms in Antarctica. She was a National Research Council postdoctoral fellow in planetary biology at the National Aeronautics and Space Administration—Ames Research Center, investigating the biogeochemistry of mat-like structures formed by microbes. ◊

DNA Files on National Public Radio

The *DNA Files: Unraveling the Mysteries of Genetics* is a series of nine 1-hour nationally syndicated documentaries to be distributed this fall by National Public Radio (www.best.com/~ringo/strp). Hosted by NBC *Date-line* reporter John Hockenberry and supported in part by the DOE Human Genome Program, the series will explore both the science and the social, ethical, and legal implications of genetic developments. The voices of prominent researchers, people affected by advances in the clinical application of genetic medicine, members of the biotechnology industry, and others from related fields will provide real-life examples of the impact of genetic discoveries. In addition to public radio audiences, the series will target educators, scientists, and involved professionals.

The programs will include such topics as DNA and behavior; prenatal genetic testing; predictive genetic tests; gene therapy; law and the genetics of identity; genetics and biotechnology; genetics of human evolution; plants, animals, and transgenics; and the Human Genome Project. The series will be available after November 5 to local public radio stations, which should be contacted for broadcast schedules. *The DNA Files* Web site will be expanded by November 1 to feature program information, audio excerpts, resources, and interactive scenarios (www.dnafiles.org). [Contact: strp@aol.com or mills015@tc.umn.edu] ◊

Human Genome News

All current and past issues of *Human Genome News* are archived and searchable on the HGMIS Web site (www.ornl.gov/hgmis/publicat/publications.html#hgn). Articles and other text prepared for HGN after 1995 are indexed according to subject. ◊

Appendix F

* The Arc

* Mental Retardation

* HGP's Importance

* The Arc's Issues

- Discrimination
- Privacy
- Testing, Screening, and Counseling
- Gene Therapy

* Conclusions

The Human Genome Project: Examining The Arc's Concerns Regarding the Project's Ethical, Legal, and Social Implications

Following is the text of an address presented by Sharon Davis, Ph.D., on November 12, 1997, at the DOE Human Genome Program Contractor-Grantee Workshop VI (abstract). Dr. Davis represents The Arc, a 140,000-member national organization on mental retardation. A 2-year project at The Arc is being funded by the DOE Human Genome Program's Ethical, Legal, and Social Issues (ELSI) Program. This project will develop and disseminate educational material for members and leaders of The Arc's 1100 affiliated chapters to inform them about the Human Genome Project and mental retardation and to conduct training through The Arc's existing training vehicles.

Dr. Davis can be reached at The Arc of the United States; 500 E. Border St., Suite 300; Arlington, TX 76010 (817/261-6003, Fax: /277-3491, sdavis@metronet.com).

[Return to top](#)

The Arc

I represent The Arc, a national organization on mental retardation whose members are united by a concern for the welfare of people with mental retardation and their families. These members work through 1100 state and local affiliated chapters throughout the United States to develop services and to advocate for full community participation by people with mental retardation. One in ten families is touched by mental retardation in this country, and our members come from all walks of life.

In February 1996, the DOE ELSI Program granted funds to The Arc to conduct an educational program with two major purposes. The first is to make our members aware of this scientific undertaking, the Human Genome Project. The second is to examine the critical issues related to new genetic discoveries affecting people with mental retardation and their families. We want as many people as possible to begin to understand that this research affects all of us. Working with me on this project is Leigh Ann Reynolds, who is here in the audience.

[Return to top](#)

Mental Retardation

Mental retardation is attributable to any condition that impairs the development of the brain before birth, during birth, or in the childhood years.

It is caused not only by the genetic makeup of the individual but also by the possible influences of environmental factors. These factors can range from drug use to childhood diseases to poverty and cultural deprivation. A person is considered to have mental retardation when his intellectual functioning level (intelligence quotient or IQ) is below 70 to 75; significant limitations exist in two or more such adaptive skill areas as self-care, communication, functional academics, and work; and the condition is present from childhood (age 18 or below).

Roughly 90% of people with mental retardation have IQs above 50. In 50% to 75% of these children, the cause is unknown. Most identifiable causes (up to 60%) of severe mental retardation (IQ 50 and below) originate from genetic disorders. Two of the most common genetically transmitted forms of mental retardation are Down syndrome (a chromosomal disorder) and fragile X syndrome (a single-gene disorder). Chromosomal disorders affect about 7 out of 1000 infants. Single-gene disorders affect about 1 in 1500 births. More than 750 genetic disorders have been identified that cause mental retardation.

[Return to top](#)

The Human Genome Project's Importance to The Arc

When we began our education program, we surveyed The Arc's Board of Directors and learned that only 2 of 24 had heard of the Human Genome Project. While I'm told this is typical of the general public, we believe the leaders and members of The Arc should be more knowledgeable because so many are affected personally. Represented on the board are individuals who have a family member with Down syndrome, fragile X syndrome, Angelman's syndrome, Cri du Chat, and perhaps other genetic disorders. Not only had they not heard of the Human Genome Project, they were generally unaware of the ethical, legal, and social issues affecting families with genetic disorders.

To remedy this general lack of knowledge among our leaders and members, we developed educational materials that have been furnished to our chapters and members on such topics as these:

- Overview of the Human Genome Project,
- Genetic causes of mental retardation,
- Genetic discrimination,
- Genetic testing, screening, and counseling, and
- Genetic privacy.

We also have produced fact sheets on such specific disorders as PKU, Prader-Willi syndrome, and fragile X syndrome. We're still working on others. Interested persons can access materials through our Web site (<http://TheArc.org/welcome.html>).

Workshop presentations at chapter conferences are another part of our educational efforts. We introduce the Human Genome Project using clips

from the video developed by the NIH National Human Genome Research Institute. We review the ELSI Program and specific issues we are addressing. Workshop participants have an opportunity to discuss issues and present their views in small groups as they discuss case scenarios designed to elicit a range of perspectives. We conduct pre- and post-testing to gather our members' views on various issues. This information is provided to our Board of Directors to give them a sense of the views of the members they represent. So far, about 500 people have participated in these sessions. Today, I would like to present an overview of issues being addressed by The Arc's leaders and members.

After we review the Human Genome Project's scientific undertaking and the ELSI Program, we tell people that the project deserves our attention because it has a direct impact on individuals and families affected by mental retardation. Researchers are rapidly discovering new genes. We need to consider the impact of such information on society.

The lack of current treatments and emerging gene therapy research raise ethical dilemmas regarding such areas as privacy, fairness, and discrimination. We point out that we are ALL affected. We need to educate ourselves and speak out on the issues that will eventually, either directly or indirectly, affect us all.

[Return to top](#)

The Arc's Issues

Even though there is a wide range of issues important to families, we decided to focus on these three topics:

- Insurance and employment discrimination based on a person's genes.
- Decisions involving genetic testing, screening, and counseling (including prenatal and newborn testing).
- Ethical issues involving genetic therapies that may eventually "cure" mental retardation.

[Return to top](#)

Genetic Discrimination

The first issue we address is genetic discrimination. Discrimination based on the presence of a disability has always been an issue of great concern to The Arc. People with mental retardation have long been discriminated against in both insurance and employment. Now a new, less-known type of discrimination is emerging due to the increasing use of genetic tests that can reveal the presence of defective genes. This new phenomenon is called genetic discrimination.

Genetic discrimination occurs when people are treated differently because they have a disease gene or genes, even when they show no symptoms of disease. Men and women who are carriers for a genetic condition may also be discriminated against because of their potential to have a child with a genetic condition.

An example of genetic discrimination was reported in *Newsweek* last December. A pediatrician who suspected that a 2-year-old boy (David) had fragile X syndrome ordered lab tests that confirmed his suspicion. The family spent several years learning to deal with David's condition. At age 6, David visited a neurologist who scribbled "fragile X" on a health insurance company claim form. The company responded promptly by canceling coverage for the entire family of six. There is no medical treatment for fragile X, and none of David's siblings had been diagnosed with the condition.

The *Washington Post* cited a case in which a pregnant woman whose fetus tested positive for cystic fibrosis was told that her health maintenance organization (HMO) would be willing to cover the cost of an abortion but would not cover the infant under the family's medical policy if she elected to carry the pregnancy to term.

The denial of health insurance based on a person's genes is one of the most common forms of discrimination. Insurance companies gather and use medical information to predict the risk of illness and death. They then determine which individuals and groups to insure and at what price.

Genetic discrimination has been documented in other settings as well. A recent study identified cases in which healthy people were fired from jobs, treated differently in school, or barred from adopting a child because they carried genes that could potentially result in disease or disability.

Legislation Banning Discrimination. The Americans with Disabilities Act (ADA) offers some protection to those currently affected or predisposed to a genetic disorder. ADA does not, however, cover the insurance industry as long as its decisions on coverage are based on experience that demonstrates people's risk of illness, disability, or death.

As the number of genetic tests increases, discrimination will increase. That's why legislation banning discrimination has been proposed. The Arc's Board of Directors passed a resolution last year calling for such legislation. The U.S. Congress made a beginning step to deter genetic discrimination when it passed the Federal Health Insurance and Accountability Act of 1996. This law limits the use of preexisting-condition exclusions by health insurers and specifically mentions "genetic information." Other legislation is being considered by the U.S. Congress.

A number of states also have laws banning genetic discrimination in health insurance. Some states also are examining discrimination in employment and

passing laws banning such discrimination based on genetic information. Much of this legislation, however, has serious deficiencies.

[Return to top](#)

Genetic Privacy

Legislators are beginning to address issues of genetic privacy. Medical records are not private. If you have ever applied for individual life, health, or disability insurance, information about you may be in the Medical Information Bureau (MIB), a computerized database of medical and some nonmedical information. Originally created to prevent consumer fraud, MIB holds information on 10 million to 20 million Americans. If an insurance applicant has a condition pertinent to health or longevity, such information must be provided by insurance companies to MIB. Nonmedical information that could affect insurability, such as an adverse driving record or participation in hazardous sports, also can be reported.

You must give consent to MIB to establish your record or for an insurance company to search your MIB record. If you don't give consent, the insurance company may automatically deny coverage. Next time you fill out an insurance application, examine it carefully. I recently received a letter urging me to apply for mortgage insurance, and sure enough, if I signed the application, I was giving permission for the company to access my MIB file. An individual in one of our recent workshops informed the group that he was denied mortgage insurance because of diabetes, a condition listed in his MIB file. As this database grows, some people are concerned that corporations, agencies, and others will have access to our medical records and genetic information just as they do to our credit histories.

[Return to top](#)

Genetic Testing, Screening, and Counseling

Issues related to genetic testing, screening, and counseling are another area of concern to The Arc. Thanks to the Human Genome Project and the identification of new genes, specific laboratory tests are being developed that can determine whether or not an individual is at high risk for a particular genetic condition.

More and more people will be able to know whether or not they will develop a disorder or possibly pass a disease gene on to their children. How will having this information impact society? Do most of us want to know about future genetic information that could change our lives? For example, if you could find out today that you have an 80% to 90% chance of developing a rare and untreatable form of colon cancer in the future, would you want to know?

Other issues of concern include the following: Must a physician offer prenatal

genetic screening to all pregnant women or risk medical malpractice liability if he doesn't? Should a woman have a right to refuse prenatal screening? What if she's already had a child with a serious genetic condition? One of our workshop participants reported that her 3-year-old son's serious genetic condition had already cost more than \$1 million, paid for by the state. She expressed her intention to have another child and her strong belief that she would refuse prenatal testing. What about testing infants and children for genetic conditions when there is no treatment available?

Positive and Negative Consequences of Testing. Genetic testing can have both positive and negative consequences. On the positive side, testing can help people make more informed decisions about their future. Another advantage of testing is that it provides an opportunity to seek genetic counseling so that the risk of passing on a disease gene is reduced.

On the other hand, anxiety runs high when individuals are confronted with a positive test result confirming a genetic condition. Are people prepared to deal with such news? Also, testing does not provide clear-cut answers. A positive result does not guarantee and a negative result cannot completely rule out the possibility that a person will become ill or be affected by the condition. Environment and other factors play a role. Another problem is that physicians may misinterpret the results of genetic tests now available.

If positive test results are not kept private, the individual risks the possibility of losing health insurance and employment for herself, the children, and other family members.

This concern was expressed to me at a recent meeting by a woman who is president of a local chapter of The Arc in Massachusetts. She learned recently that her two older brothers, now in their 60s, have fragile X syndrome, a genetic condition that causes mental retardation. Her two grown sons are unaffected. She could be a carrier, however, and so might they. There's now a simple test for fragile X, but she has read The Arc's educational materials and is concerned about genetic discrimination. She doesn't want any positive test results on her record or her sons', so she has decided to take the fragile X test and pay for it herself. If she is not a carrier, her sons won't have to make a decision regarding testing. Furthermore, her insurance company won't know the results.

Testing of Children. One major area of concern regarding genetic testing is the testing of children. Parents often want to have their children tested to plan for the future or reduce the anxiety of not knowing. Yet, receiving positive test results may actually restrict the child's future in many ways. Children suffer the possibility of being stigmatized for their condition, with a resulting loss of self-esteem. They may also face discrimination by family, employers, insurance companies, educational institutions, and others. What rights does a child have to agree to or refuse testing?

There are currently no universal standards among physicians for testing

children. Health professionals usually recommend that testing be conducted only when there is a clear benefit to the child. Family members, on the other hand, may feel testing should be considered if it can benefit others. For example, a member of our project's advisory committee had a daughter with severe disabilities but no diagnosis. He had his daughter tested because his sister, who wanted to have a child, wished to rule out a genetic condition in the family.

[Return to top](#)

Gene Therapy

The third issue area we're discussing as an organization is the use of gene therapy, which potentially could cure some genetically caused mental retardation. Gene therapy is an experimental treatment in which normal genes are introduced into the body's cells to correct or modify the cell's function.

We inform our members that, although gene therapy holds great promise for treating some genetic diseases and conditions that have not been treatable previously, no one has ever been "cured" of their condition by gene therapy. Much more scientific research is needed for gene therapy to have a significant impact on the treatment of genetic conditions.

At this time, the most promising use of gene therapy for mental retardation is to treat single-gene conditions involving enzyme defects. Most of these defects cause significant disability that cannot be treated satisfactorily by such other approaches as modifying the diet or supplying the enzyme. Some examples include adrenoleukodystrophy, galactosemia, and the urea cycle disorders.

At some time in the future, it may also become possible to apply gene therapy to fragile X syndrome. Scientists, however, say that more knowledge is needed about the function and control of the fragile X gene before such studies are undertaken.

Gene Therapy and Ethical Issues. Gene therapy also raises some ethical questions related to the quality of life of people with diseases and conditions. We asked our members if The Arc should be advocating the development of gene therapies that can "cure" people with mental retardation. Some people say that disabilities are not diseases and, therefore, do not need to be cured or repaired. They feel that people with conditions such as mental retardation can cope with their condition and lead meaningful lives, not in spite of their disability but with it. Yet, The Arc always has supported efforts to prevent mental retardation. Should we, as an organization, support gene therapy that could one day cure mental retardation?

We ask this question because in some groups, people with disabilities say they don't want to be cured. A segment of deaf people refers to itself as the deaf culture and prefers to have children who are deaf. Some people with

physical disabilities say that calls for cures demean them as individuals. These people are very critical of Christopher Reeve, who advocates funding to cure spinal cord injuries. They say he hasn't accepted his disability. Others have difficulty with the idea of no longer being disabled.

This is what Ted Kennedy, Jr., said in a recent interview: "I think of myself as a person with a disability. In fact, going through the 2 years of chemotherapy and the cancer, losing my leg--it was probably the defining event of my life. It shaped who I am. And, you know, if someone offered me a pill today that would somehow magically grow my leg back, I would say no."

We asked members of The Arc what they believe about curing mental retardation if it were possible. Some 90% participating in our workshops across the country said advocating for a cure did not devalue those with the condition. About 85% agree that The Arc should advocate for more funding for research to cure genetic conditions. This information will help guide our Board of Directors in its decision-making regarding these issues.

Arguments in Favor of Gene Therapy. The major argument in favor of gene therapy is based on its potential for treating individuals severely affected by their condition. A perfect example is Lesch-Nyhan disease, which is characterized by communication deficits, writhing movements, and involuntary self-injurious behavior. Males who have this disorder have to be restrained constantly to prevent them from inflicting severe damage on themselves. Most have their teeth removed to keep from biting their lips off. If we have a new medical technology that will cure this condition, don't we have an obligation to use it?

Arguments Against Gene Therapy. A number of arguments are offered against gene therapy, including the concern about the potential for harmful abuse if we don't distinguish between good and bad uses of gene therapy. The eugenics movement of the 1920s to the 1940s found people with mental retardation being involuntarily sterilized, along with others considered less desirable. Another concern is that in mental retardation gene-therapy research, many candidates are likely to be children who are too young or too disabled to understand the ramifications of the treatment. Finally, gene therapy is very expensive and may never be sufficiently cost-effective to merit high social priority. Opponents say that if those who can afford gene therapy are the only ones to receive it, the distribution of desirable biological traits will widen the differences among various socioeconomic groups.

Genetic Enhancement. Another relevant issue is genetic enhancement, using gene therapy to supply a characteristic that a parent might want in a child but which does not involve the treatment or prevention of disease. Such physical characteristics as height, weight, and enhanced cognitive abilities are common areas mentioned.

What about cognitive enhancement for children with mild mental retardation? If cognitive enhancement could increase the IQ of such a child to allow

functioning in the normal range, should it be considered? Currently, it is not considered acceptable to use gene therapy to treat conditions that are not diseases. Is mild mental retardation a disease that needs to be cured or a condition or trait that does not justify a need for cure? This is a topic we haven't addressed as an organization yet. We have raised it as an issue in our forthcoming report on ethical issues related to gene therapy. Even though such a cure does not exist yet and may never exist, we believe we should be involved proactively in discussing genetic enhancement before any policy is enacted governing use.

[Return to top](#)

Conclusions

The Arc's goal is to create an adequate level of awareness among its members on the issues I've outlined, so that our voices can be heard before harmful policy is created. There are differences of opinion on many of the issues we have addressed and general agreement on others.

We conclude by telling our members that genetic research is changing the world in which we live. As families potentially affected by the knowledge gained from research, we must become involved by being educated and expressing our views when appropriate. Even though ethical, legal, and social issues have been debated widely by scientists, ethicists, and others, few voices have been heard from families directly affected by a genetic condition. We urge our members to keep informed about the issues so they also can make informed personal choices regarding testing, participation in research, and gene therapy if it becomes available in the future.

We are also reaching out beyond our membership. The American Association of University Affiliated Programs for People with Developmental Disabilities is disseminating our materials to its member university-affiliated programs and research centers for mental retardation and developmental disabilities. The director of the Frank Porter Graham Child Development Center and Mental Retardation Research Center in Chapel Hill, North Carolina, who wrote the fragile X syndrome report for us, is sponsoring a conference for early childhood educators and is distributing all our reports to attendees. These professionals in the field often work closely with families and seek to collaborate with us in our common mission.

Finally, The Arc will continue to advocate for understanding and acceptance of the condition of mental retardation and fair treatment for citizens with mental retardation. The potential for cure for some must not make us less accepting of those living with the condition.

[Return to top](#)

Last modified: Wednesday, March 17, 1999

Appendix G



The Arc's Human Genome Education Project

A two-year project funded through the U.S. Dept. of Energy to create awareness of the ethical, legal and social concerns arising from The Human Genome Project (HGP).

The international HGP is mapping our human genome (all the genes in our bodies) to begin finding out what genes cause certain diseases and conditions. The Arc has created materials (Q&As, reports, training materials) to aid our members in having a better understanding of this incredibly exciting research and to begin thinking about what it could mean to families and others directly impacted by having genetic information.

All materials produced by the project can be downloaded from The Arc's Home Page. If you do not have access to the internet and would like to receive reports, please indicate this below by filling out the spaces provided and mailing or faxing your request to:

The Arc of the U.S.
500 E. Border, Suite 300
Arlington, Texas 76010
<http://TheArc.org/> ♦ Fax (817) 277-3491

For specific questions, contact project staff:
Sharon Davis, Ph.D., Principal Investigator ♦ sdavis@metronet.com
Leigh Ann Davis, Project Associate ♦ ldavis@metronet.com
(817) 261-6003 ♦ TDD (817) 277-0553

The following materials are available. Check any you would like to receive:

SPECIAL REPORTS *(Genetic Issues in Mental Retardation)*

- An Introduction to Genetics and Mental Retardation
- Genetic Discrimination
- Genetic Testing, Screening and Counseling - An Overview
- Protecting Genetic Privacy
- Fragile X Syndrome
- Gene Therapy and Mental Retardation
- Participating in Genetic Research: Considerations for People with Mental Retardation and Their Families
- Mental Retardation & Developmental Disabilities Research Centers: An Overview of Current Genetic Research

Q&As *(two-page fact sheets)*

- Genetic Causes of Mental Retardation
- Genetic Discrimination
- Newborn Screening to Prevent Mental Retardation
- Down Syndrome
- Prader-Willi Syndrome
- PKU

COST: Reports - \$25/100
Q&As - \$15/100
Single copies free with SASE.
For more than 10 items, send \$5 to cover postage & handling.

Name: _____

Address: _____

Phone: _____

E-Mail: _____