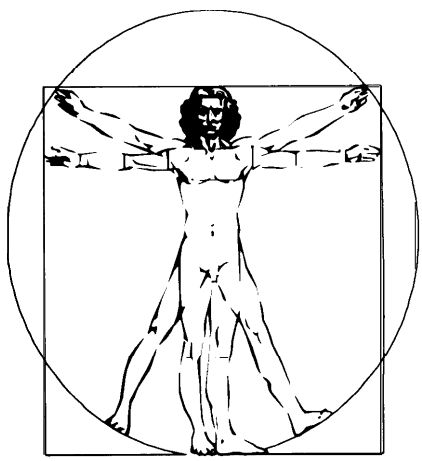
Implications for Society 3

Research involves people. People participate in research. People may benefit from research-driven improvements in clinical practice. And people face social perceptions and policies that stem from research.

Study of the genetic factors involved in mental disorders is no different. However, the polemics and controversy surrounding the genetics of mental disorders forestall reasoned discussion of what this research means to people with mental disorders and their families. The complexity of this research further compounds consideration of its clinical and social implications. And the uncertainty of the genetic mechanisms involved in mental disorders deters many from spending time (or money) on this topic.

It maybe unwise to devote a great deal of time and resources to the consideration of specific policies and implications of the genetics of mental disorders, given the early stage of research find-ings. But no discussion also seems an unwise choice. Clinicians, policy makers, people with mental disorders and their family members are left to decipher the complicated, confusing, and unevenly reported research results. No discussion also means that little opportunity for interdisciplinary dialogue exists among geneticists, mental health professionals, genetic counselors, ethicists, social analysts, and primary and secondary consumers.[1] People have no formal venue for voicing their concerns; experts outside of the mental health field have no official forum in which to share their experiences and knowledge.



[1] Primary consumers are individuals with mental disorders; secondary consumers are family members or others who help care for people with these conditions.

BOX 3-1: Abuses of Human Subjects in Research

Publicized abuses over the course of the 20th century remind us of the need to safeguard the rights and well-being of human subjects involved in research. In general, the withering eye of publicity served to vanquish studies where abuse occurred and often led to policy reform. A clarion call was sounded in the Nuremberg trials of Nazi physicians, who used prisoners of concentration camps as subjects of "biomedical experiments" during World War II. During the trials, the accused defended their actions by arguing that it was not common professional practice among physician-investigators to seek consent of research subjects. In response to this defense, in 1948 the judges crafted the Nuremberg Code, which sets forth 10 "basic principles to satisfy moral, ethical and legal concepts" in the conduct of human-subject research.

Scientific research involving human subjects became common in the United States shortly before the outbreak of World War II. By the 1960s, however, concerns about unethical research practices began to surface. A case in point was the intentional infection with hepatitis of residents of the Willowbrook State School for the Retarded, In a series of experiments, begun in 1956 and spanning over a decade, institutionalized children with mental disabilities were infected with live hepatitis virus in an effort to develop a vaccine. The scientists justified their procedures by noting that hepatitis ran rampant through the institution and that all of the children would eventually contract the disease. Further, they maintained that only children whose parents had given their written consent were included in the experiments. Critics challenged these arguments, suggesting that parents may have been coerced into volunteering their children as a means of procuring placement at Willowbrook. Moreover, parents were misled to believe their children were to receive a vaccine against the virus and they were not informed of the risk to their children of developing chronic hepatitis and the possible link to cirrhosis in later life. Criticism eventually brought the experiments to an end in the mid-1960s.

Perhaps the most notorious case of unethical research in the United States is the Tuskegee Syphilis Study. From 1932 to 1972, scientists conducting a U.S. Public Health Service study of 400 African American men suffering from syphilis deliberately withheld treatment from them in order to study the effects of allowing the disease to take its course. The men were told only that they were receiving free treatment for

The workshop hosted by the Office of Technology Assessment (OTA) and the National Institute of Mental Health (NIMH) in January 1993 provided one of the first opportunities for comprehensive discourse of the issues raised specifically by genetic studies of mental disorders. Experts within and outside of the mental health field, as well as consumer representatives, discussed ethical issues that emerge during this research, the clinical implications of what we know about the genetics of mental disorders, and how society views these topics. The panel's deliberations evinced the concerns many have about the genetics of mental disorders and characterized issues that have already emerged. This chapter documents the workshop discussion under three headings:

- **ethics and research,**
- **genetic counseling, and**
- **public perceptions and social implications.**

ETHICS AND RESEARCH

Diagnostic and treatment advances result from research, including studies involving human subjects. While few question the value of biomedical research in general, publicized abuses over the course of the 20th century highlight the need to safeguard the rights and well-being of research participants (box 3-1). Research of the genetic factors involved in mental disorders is no different; protection of research participants is a preeminent concern. However, the necessary involvement of whole families, the stigma and discrimination at-

BOX 3-1 continued: Abuses of Human Subjects in Research

'bad blood." The men received free physical examinations, hot meals on examination days, free treatment of minor ailments, and a guarantee that burial stipends would be paid to their survivors. Except for research procedures, including painful spinal taps offered as "cures," the men were denied treatment for syphilis. Treatment continued to be withheld even after it became apparent that penicillin was effective in treating the disease. In 1972, front-page news reports brought to public attention the deception and abuse surrounding the study. Critics regarded the denial of penicillin to treat the men's syphilis as the most egregious abuse. In addition, civil rights advocates pointed out the apparent practice of using vulnerable populations of poor, ignorant, imprisoned, or dying people as human subjects in scientific research. Critics also drew attention to the lack of a clearly defined protocol and the lack of uniform procedures or policies for reviewing experimental procedures or securing informed consent.

An ad hoc panel appointed by the U.S. Department of Health, Education, and Welfare (DHEW) to review the study recommended that it be terminated immediately. In 1973, Senator Edward M. Kennedy held hearings on human experimentation that presaged a complete revamping of federal policy on human experimentation. In May 1974, DHEW issued formal regulations governing the conduct of research involving human subjects. About the same time, Congress passed the National Research Act that created the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research. The Commission advised the then Secretary of DHEW, Congress, and the President about ethical issues related to human experimentation and proposed ethical guidelines for the institutional review board system to use to assess research involving human subjects.

SOURCES: R.R. Faden and R.L. Beauchamp, *A History and Theory of Informed Consent* (New York, NY: Oxford University Press, 1986); J.H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment* (New York, NY: Free Press, 1981); U.S. Congress, Office of Technology Assessment, *Neural Grafting: Repairing the Brain and Spinal Cord*, OTA-BA-462 (Washington, DC: U.S. Government Printing Office, September 1990); U.S. Congress, Office of Technology Assessment, *Biomedical Ethics in U.S. Public Policy—Background Paper*, OTA-BP-BBS-105 (Washington DC: U.S. Government Printing Office, June 1993).

tached to genetic and mental disorders, and the potential impact of mental disorders on reasoning and judgment compound and complicate ethical concerns. Workshop participants elaborated some of the difficult ethical issues that emerge from this research. In addition, several participants signaled the need for guidance on how to better deal with these situations.

The ethical conduct of research involving human subjects rests upon a bedrock of three values, first enumerated by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission): respect for persons, beneficence, and justice (46,65,68). Respect allows people to make and pursue their own decisions in an informed and voluntary manner. Beneficence seeks both to protect individuals from harm and to ensure benefits from research involving human subjects. Justice refers to the fair and uncoerced selection of human subjects for research, especially among vulnerable populations.

The regulatory translation of these ethical principles guides nearly all research with human subjects today. Specifically, federal regulations demand that all federally funded human research projects must be reviewed and approved by an Institutional Review Board, or IRB (45 CFR 46.103(b)). This multidisciplinary panel considers risks, benefits, subject selection, and consent issues for proposed studies involving human subjects. Federal regulations further require that informed consent be obtained from each subject, although this can be waived in certain circumstances. In order to provide informed consent, the anticipated benefits and potential risks associated

with an experimental procedure must be explained to the individual; he or she must understand these factors, rationally weigh them, and then make a voluntary decision as to whether or not to participate.

Informed consent, while straightforward in principle, can be challenging to obtain, especially in complicated research designs. Packed with technical information, lengthy, or even incomplete, consent forms may baffle all but those with specialized expertise. One workshop panelist described this concern and the need for one-on-one, ongoing discussion to achieve informed consent (8):

> We now have **a pretty impressive informed consent form for breast cancer genetic research after a lot of work. . . on two single typed pages.** Academically, we may have finally thought through many issues and anticipated some of them. But how do potential participants process all this and make a decision for themselves that they want to or do not want to participate in this research?. . . **Our most successful endeavors have been engaging individuals in one-on-one conversations. . .** True **informed consent is a discussion and a long, ongoing process.**

Although never translated into regulation, the National Commission acknowledged that mental disorders, which impact on cognitive processes, emotions, and behavior, may sometimes impair the ability to provide informed consent (65). The limited research data that exist fortify this observation. Severe symptoms of schizophrenia, including psychosis, paranoia, or delusions, can compromise an individual's competence to provide informed consent (3,32).

Of course, if a person is found incompetent to provide informed consent, proxy consent, given by a legally authorized representative, may be required and under certain circumstances requirements for informed consent may be waived (56). However, these approaches to consent are unlikely to be used commonly. For one, even hospitalized individuals with schizophrenia exhibit a considerable range of capacities to provide informed consent (32). And as one panelist noted, IRBs around the country may not be informed on this subject (57):

> **A** meeting held recently, jointly sponsored by the Office for Protection from Research Risks, the National Center for Human Genome Research, and NIMH . . . found that institution-wide IRBs know relatively little about mental disorders and they may need to be better informed about consent issues, substituted judgment issues and the like.

Perhaps most importantly, people with mental disorders and their families urge greater participation in research (24):

> I'm not at all certain that we have done all that we can or the best job we could in terms of really thinking appropriately about informed consent. I appreciate the difficulties and understand the concerns that people have about the impact on the research enterprise, but I also think that we have to respect what others are telling us about the increasing role that consumers are playing in their own lives and in shaping their own lives. My own information that we gather from talking to people in our office is that the work that's done is focused on getting a signature. Get the signature, get the paper signed. Sometimes there's a good description and discussion of what's going on and what may occur and what the research is pointing towards and sometimes it's not so good and not so thorough.
>
> In almost all cases it occurs once. I think we need to realize particularly in research of this type that we may want to see it as less an event and more a process. **We** may want to be sure as the research unfolds that those people most directly involved and affected continue to be updated and advised and understand what, in fact, is going on.
>
> So **I** think we need to think more comprehensively about a partnership with the people who are involved as research subjects and recognize there's a lot more to consent than getting someone who is now not under the protection of some of the rest of the field because they are specifically excluded. . . There is some unfinished business in that regard. **I** think we need to be par-

ticularly sensitive to respecting our duty to inform and perhaps inform more than one way more than one time so that people can be full participants and partners in the research.

The **conclusions of the workshop discussants—that informed consent requires more than a onetime paper signing event, that the issue of mental disorders and informed consent must be taken seriously, and that IRBs require support and education---echo the findings of a recent report from the Office for the Protection from Research Risks (OPRR)[2] (25,69). Panelists also urged greater sensitivity to the families of participants in research (34):**

> In mental illness the research subjects maybe fairly young . . . between the age of 18 and 21. . with serious mental illness, and the families may be very involved in the individual's life. . . I would maintain in that type of situation . . . that the . . . ethical obligation (for informed consent and ongoing communication) extends to the family as well.
>
> Let me give you an example. Say a family has identified a particular research protocol at a particular university and has informed the individual who has the mental illness of that program and they've made a collective decision that that program is an appropriate one and the individual goes to the program and at some point sits down and is informed about the research protocol and the risks of the research and the potential benefits of the research, et cetera.
>
> In that type of situation where there is no apparent disagreement between the individual and his or her family, it would be my contention and I believe it's NAMI's [National Alliance for the Mentally Ill] contention that the obligation on the part of the researchers to inform would extend to the family. In other words, they would have an obligation to sit down with the family as well as that individual.
>
> I realize that I just introduced a new subject, but that's something that we hear about a great deal, that families initiate a referral and then they're completely written out of the process.

Several panelists expressed the opinion that family members should be more involved in research, participating in the consent process, in ongoing contact with researchers, and as members of IRBs (5,18). In pedigree studies, families are necessary participants, which challenges the traditional vantage point of bioethics. Concern for the individual subject has directed the evolution of bioethical concepts of informed consent, confidentiality, and voluntary participation. Researchers and ethicists on our panel noted the difficulties of adapting these ethical principles to studies involving whole families. One such issue raised by genetic research and discussed at the workshop is disputed paternity (14):

> I feel privacy must be breached . . . in situations involving disputed paternity. I've had two cases where two daughters of two different individuals thought they were at risk for Huntington's when in fact they were not. That brings up two points. Obviously, they were told, in fact, in one case I had to tell the individual because the mother would not. In the other, the mother did eventually, after a lot of arm twisting, tell the daughter that, in fact, she was not at risk. In both cases, these two young women were pregnant. Now, that creates another issue and you might argue that the mother's privacy shouldn't be breached, but I feel that there's a right—that the daughter has a right to know something that impacts on the rest of her life, just as well as her mother has a right not to have anyone know what she did some 20 years earlier.

As the above example illustrates, pedigree research can reveal previously unshared information about biological relationships among family members. Such information pits the rights of some family members to their privacy against the rights of others to know if they or their children are at increased risk for a condition. Although researchers worry about discomforting and discour-

[2]This office is located in the National Institutes of Health, U.S. Department of Health and Human Services.

aging would-be research participants, several panelists gave voice to the opinion that pedigree research's ability to expose disputed paternity is required for true informed consent (18,46):

> **In discussing the business about informed consent, it's clear that unless that potential is brought out, one could be accused of violating the ethical principle of informed consent. In other words, if that's a possibility-even a relatively low risk-it must be revealed. And its not relatively low, it's relatively high. In some communities that I deal with, it's not five percent, it's more like** 15 or 20 percent. . . There are two ways of dealing with it. One is to have this in the informed consent form, and the other is to take the pedigree by asking, "Is this man the father of all your children?" (46).

Disputed paternity is not the only aspect of pedigree research that may incur conflict among family members. The very issue of informed consent becomes more complex, as described by one workshop participant (15):

> One of the things that is unique about pedigree studies is the fact that it's no longer a dyadic relationship between a patient and a person involved in a clinical trial or other research. There are other people involved in the family. Does every person on that pedigree have to have an informed consent statement before you publish it? Do you publish it? How much clinical information do you include? Should you alter the pedigree to prevent identification? All these questions about how to handle the information in pedigree research are being raised without much inspection except by the ethical norms of the people doing it.

Not only does a single individual consent to participate in a pedigree study, but the participant must be informed that relatives will be asked to participate (56,69). Family members participating in the study must be given the option to consent as well. Researchers must decide and inform participants of which information will be shared with family participants. A medical geneticist and ethicist on the workshop panel noted (46):

> Most IRBs I am familiar with . . . treat the pedigree as part of the patient record and therefore all the information related to that patient is considered confidential in the same way that clinical records are considered confidential. They don't approach any other members of the family for testing unless they get the permission from the proband or consultant in the pedigree.

Of course, problems can emerge if family members disagree about participation in a research project. An example from research in Huntington's disease is illustrative (14):

> **A young woman completed a Family History Questionnaire and signed an informed consent form placing her family on the Roster. When asked to identify family members who would be best suited to complete an affected questionnaire, she identified her brother. A packet of information concerning Huntington's disease and explaining the purpose of the Affected Questionnaire was sent to the brother. Several days after the questionnaire was mailed, a certified letter from the brother's attorney** was received stating that he wanted "his family" removed from the Roster.

Family members may have different feelings about a disease or about participating in research. Individuals may want to ignore the presence of a disease within their family, deny its existence, or may guard such information as a secret, even from other family members. Stigmatized genetic conditions and mental disorders are certainly sensitive issues for many families. These concerns highlight the unique kinds of risks that pedigree studies pose to individuals and families. While physical risks, such as possible side effects of a new medication, may be minimal or nonexistent in pedigree research, information about genetic status or mental disorder pose what a recent OPRR report calls *psychosocial risks.* **"Information can provoke anxiety and confusion, damage familial relationships, and compromise a subject's insurability and employment opportunities" (69). IRBs may not appreciate the nature of these risks and thus may dismiss them as insignificant, a neglect that OPRR cautions against.**

Because of the psychosocial risks presented by genetic research, confidentiality of information becomes paramount. Experts advise that as much

information as possible be kept private from other family members participating in genetic studies. Information that must be revealed should be disclosed only with the full knowledge and agreement of each participant. But privacy or confidentiality concerns extend beyond family members. Family and genetic studies of mental disorders can unearth a host of sensitive information, such as the presence of a mental disorder, increased family risk for a condition, other behavioral problems, substance abuse, and criminal history. This type of information in the hands of private insurers, employers, or others could pose grave risks to an individual participating in research. To address this concern, NIMH encourages the use of certificates of confidentiality to prevent access to individually identifiable research data by insurance companies, government authorities, or other third parties. Evolved in the context of substance abuse research, this certificate protects investigators from the compulsory revelation of potentially harmful research data (42 CFR Part 2a, 1991). Indeed, an NIMH scientist indicated that the mental health research community increasingly uses certificates of confidentiality (57).

The certificate of confidentiality does not preclude reporting cases of child abuse or imminent suicidal or homicidal behavior. Neither does the certificate of confidentiality inoculate against the inadvertent revelation of information by the research subject, as noted at the meeting (57):

> Let me warn you that there's a potential leak in the system. Not so much in the system, but in the way in which it's used practically. Individuals who go for testing before they enter a research protocol may be told, "Well, we'll be happy to enter you in our protocol, but we need to be sure about the diagnosis. We need to have certain blood tests," and the person goes in to their private physician and says, "I want to get a blood test to check out X, Y, and Z, and the reason is that I'm about to participate in a research study on the genetics of Alzheimer's disease." So, the physician writes down, "To participate in research study on Alzheimer's disease, ordering the following studies," and files for insurance reimbursement. The person himself has already let out of the bag information which can and will go to the insurance company.

Apprising research participants about this potential problem is yet another important component of informed consent. Finally, a representative (12) from one consumer organization—the National Depressive and Manic-Depressive Association—notes that:

> [a] Confidentiality Statement serves no purpose if the storage of research data is accessible. Any data storage device that has telecommunication ability, or that is networked to such a main server is vulnerable. ALL RESEARCH DATA WITH ANY FORM OF PATIENT IDENTIFIER, INCLUDING "INTERNAL CODE," MUST BE ISOLATED DURING WORK AND KEPT IN A STAND-ALONE DATA BASE WITH NO TELECOMMUNICATION INTERFACE AT ALL [capitalization in original letter]. We feel this is absolutely necessary, absolutely imperative to protect information from incursion by 1) government at any level, 2) insurance companies, 3) current or prospective employers, 4) media snoops, 5) current or prospective families, and 6) hackers. Should the research data for any particular individual be requested, that patient should be asked to execute a specific Release of Information.

While not discussed in great detail, workshop participants also raised concerns about how to handle data and biological materials after a research subject withdraws from a study or in future studies, for which informed consent was not specifically garnered. Federal regulations clearly require that subjects be free to withdraw from a research project without penalty or loss of benefits to which they are otherwise entitled. Regulations do not address the use of data or tissue samples should a participant decline further study participation. A panelist noted that the ruling in a 1990 California Supreme Court *case—John Moore v. The Regents of the University of California—pro*vides guidance (57). In that case, the court held that cell lines transformed from a donated blood sample are not the property of the person who donated the sample. In line with this ruling, work-

shop participants speculated that people who withdraw from a genetic research project might not necessarily be able to require destruction of all of the information and biological materials previously provided. There are questions about this case's applicability, however. For example, could a withdrawing research subject request that all identifiers linking the data or samples to him or her be purged? Also, *Moore* constitutes binding legal authority only in California. As of this writing, it has not been adopted in other jurisdictions.

Having invested considerable time and resources into the collection of data and biological materials from extended families, researchers may desire to test new genetic markers or hypotheses as they arise. Must researchers seek renewed informed consent? Most experts do not advise the destruction of valuable and perhaps irreplaceable resources. On the other hand, relevant ethical concerns raised by a new study may make renewed informed consent indispensable. A Huntington's disease researcher described his approach to this problem (14):

> I would be concerned if I collected DNA on people and then simply discarded it when it might be very useful to them. So I would suggest that you have an informed consent saying that we 're going to keep this DNA and it will on] y be used with your written consent, like we do in our Huntington's disease DNA bank.

OPRR offers similar guidance (69):

> Where a new study proposes to use samples collected for a previously conducted study, IRBs should consider whether the consent given for the earlier study also applies to the new study. Where the purposes of the new study diverge significantly from the purposes of the original protocol, and where the new study depends on the familial identifiability of the samples, new consent should be obtained.

What if research results become clinically relevant? Should someone be informed if it becomes clear that he or she has a 90 percent risk of developing a serious medical disorder, for which preventive interventions or effective therapies exist? Several obstacles preclude a simple yes in response to this question. An individual who participates in research may not want to know such information. A researcher in a laboratory, who has had no contact with the subject, may make the health risk discovery. In this situation, who contacts the research subject? Researchers assert that the question should be put to subjects directly: if we discover that you are at risk for a severe disease which is preventable, do you want us to inform you? NIMH's approach to this topic offers one example. It advises its grantees that consent documents clearly indicate whether subjects will be given the results of genetic tests used in research (56).

GENETIC COUNSELING

The standing room only crowds at seminars hosted by NAMI hint at the desire—among family members and people with mental disorders—for more information about the genetics of mental disorders (24). "[W]hat invariably happens is that people line up from the audience and they say, "Let me tell you about my history. I have this, this, and that. What's the risk [to me and my family]?" (28). While genetic counseling for mental disorders apparently occurs rarely (29,63)—an informal survey of genetic counselors in the New York area indicated that only a small number of people request counseling on mental illness (42)-consumer representatives at the OTA-NIMH workshop testified to a hunger for knowledge about genetics among people with mental disorders and their families (5).

> [T]here is a tremendous hunger for knowledge. Not for it to be packaged to us, but for us to be given both the uncertainty and the certainty. . . Consumers want to know. The first thing that almost every consumer said [in a survey of 650 consumers in Virginia] is "I want to know, even if it's uncertain, even if it's complicated, I want to know," because mental illness for so many people has been presented as a mystery or as something that we are responsible for. To have information, even well-informed guesses given to us as that, is something we hunger for.

The relay of genetic information occurs formaly in the context of genetic counseling. A recent report from the Institute of Medicine (35) defines genetic counseling as:

> the process by which individuals and families come to learn and understand relevant aspects of genetics; it is also the process for obtaining assistance in clarifying options available for their decisionmaking and coping with the significance of personal and family genetic knowledge in their lives.

The first question that needs to be addressed is whether genetic counseling is appropriate for mental disorders at all. A variety of factors would seem to answer no. The genetic contribution to these conditions is complex and incompletely understood. Certainly, there are no genetic tests for mental disorders. Even what is inherited is unclear. And genes by no means account for the whole picture. As indicated in chapter 2, mental disorders are generally considered multifactorial conditions; genetic and nongenetic factors are both involved. Furthermore, there is no known way to prevent the mental disorders considered in this report (although treatment may prevent relapse of symptoms in some conditions).

The enumerated rationale against genetic counseling for mental disorders neglects both the strengths and common application of genetic counseling as well as the desire for information among consumers. Genetic counseling is not simply about single gene disorders, disorders for which there are genetic tests, or the certain prediction of disease; it has a much broader application. The whole field of genetic counseling evolved around the concept of relaying risk information, probabilities, and uncertainties. Principles derived from genetic counseling-concerning risk communication and respect for client autonomy-can inform the relay of genetic information concerning mental disorders (8). As noted in a recently published psychiatric genetics text: "[A]n informed and responsible genetic counseling service has a small but definite current role, and this is likely to increase in the future" (43).

It is true that no known interventions can prevent the development of the mental disorders discussed in this background paper. But, once again, mental disorders are not unique in this regard. Treatments effective for many people with mental disorders are available. Awareness of increased risk for a condition can help alert individuals to the earliest signs of a condition, permitting early treatment that may prevent the most debilitating symptoms and long-term impairment. Genetic counseling also offers an opportunity to correct common misperceptions about disorders with a genetic component: namely that genetic conditions are impossible to treat or that these conditions require biological treatment (43).

Many times a person with a severe mental disorder or his or her family members fear that children or siblings face a similar fate: a severely disabling and chronic condition. Not infrequently, severe mental disorders afflict generation after generation in a family. In this situation, information about the genetic risk for a condition can relieve fears. As noted at the workshop by the executive director of NAMI, and the mother of a daughter with schizophrenia (24):

> Family members attending workshops and lectures on the genetics of mental illness almost always bring questions "This is my family. What do you think?" Peoples' levels of anxiety are enormously high and almost always their reaction is "It's not as bad as I thought. We're not fated to have these dreadful illnesses in their most dreadful form just because we want to have a human experience and reproduce and have an extended family.
>
> So, there's an enormous amount of misunderstanding and partial understanding, even among families, and certainly families in the Alliance are as well educated and knowledgeable about these disorders as any. So that the provision of knowledge offers an enormous amount of relief.

Recurrence risk is the most elementary information transmitted in genetic counseling (7,8,35,61)—an individual's risk of inheriting a condition. For mental disorders, no genetic test

TABLE 3-1: Averaged Risks of Mental Disorders

	Schizophrenia	Bipolar disorder	Major depression	Obsessive-compulsive disorder	Panic disorder
General population	1.070	0.8%	4.9%	2.6%	1.6%
First-degree relative (parent, child, or sibling)	9.0-1 13.0%a	4.0-9.070	5.9-1 8.4%	25.O%	15.O-24.7%

[a]Risk is 46 percent when both parents are affected.

SOURCE: K. Berg and D.G. Kirch, National Institute of Mental Health, National Institutes of Health, U.S. Department of Health and Human Services, Bethesda, MD, 1992.

can lead to an individualized assessment.[3] Rather, estimates of risk reflect pooled data from family studies, with varying levels of information available for different disorders (tables 3-1, 3-2, and 3-3). Empirical risk estimates convey the probability of mental disorder among family members. For example, while approximately 1 percent of the general population will develop schizophrenia, nearly 10 percent of those with a first-degree relative with schizophrenia will become afflicted. First-degree relatives in general face a tenfold increased risk for schizophrenia.

Individuals with mental disorders and family members may find comfort in knowing that a mental disorder is not inevitable for loved ones. But recurrence risk estimates do present difficulties. The concept of empirical risk can be difficult to understand and act upon, which is why experts in genetic counseling emphasize the importance of risk presentation and interpretation (4,35,64). How an individual interprets risk estimates varies depending on how the risk is perceived and communicated. Research into several genetic conditions shows that a variety of factors influence the perception of recurrence risk, including the nature of the illness and its perceived burden. While little research has focused on the perception of risk or perceived burden of mental disorders, existing data suggest diverging experiences among primary and secondary consumers. In one small study, 92 percent of well family members versus 25 percent of affected individuals viewed schizophrenia as a severe, debilitating disorder entailing extreme burden (55). Only 29 percent of the well family members, versus 66 percent of individuals with schizophrenia, reported that they would have children. In another study, 19 people with bipolar disorder and their well spouses were asked about their perception of the disorder: approximately 50 percent of well spouses compared with 5 percent of the bipolar patients indicated that they would not have married and would not have had children if they had known more about bipolar disorder (59).

Perceptions of risk and mental disorders are not the only obstacles to genetic counseling. Simplified, recurrence risk data itself can be misleading. Recurrence risk estimates do not distinguish the severity of disorder or the age of onset among family members. They provide no information about the genetic mechanisms at play. Recurrence risk in a particular family may greatly exceed or fall below the tabulated estimates. For example, if several members of a family have a particular mental disorder, usually with an early age of onset and severe course, other family members are more

3 Even when genetic tests are available for a disorder, predictive ability can fall short of the absolute, reflecting the **specific genetic** factors at play and always present possibility of human error.

TABLE 3-2: Risk of Mood Disorder Among Siblings of Individuals With a Major Mood Disorder by Status of Parents[a]

Study	Proband diagnosis	Sibling diagnosis	Risk to sibling when neither parent has a mood disorder (percent)	Risk to sibling when at least one parent has a mood disorder (percent)
Rudin, 1920	Mood disorder	Mood disorder	7.4%	23.8%
Schulz, 1930s	Mood disorder	Mood disorder	14.3	26.1
Luxenburger, 1930s	Mood disorder	Mood disorder	3.4	16,1
Pollock, Malzberg, and Fuller, 1939	Mood disorder	Mood disorder	1.3	3.8
Stendstedt, 1952	Mood disorder	Mood disorder	13.5	17,9
Reich, Clayton, and Winokur, 1969	Bipolar disorder	Mood disorder	10.0	21.0
Johnson and Leeman, 1977	Bipolar disorder	Mood disorder	18,4	23.2
Angst et al., 1980	Bipolar disorder	Bipolar disorder	1.2	5.6
	Bipolar disorder	Unipolar disorder	4.1	8,4

[a] Summary of data presented in reference number 62. Authors note in text that empirical risks available on mood disorders generally do not take into account the multiple occurrence of such disorders in families. The exception is demonstrated in the table: the risk for mood disorders among siblings of individuals with these conditions when the status of the parents is known. All of the available studies indicate that the risk to a sibling is substantially increased if one of the parents is also ill.

SOURCE: M.T. Tsuang and S.V. Faraone, *The Genetics of Mood Disorders* (Baltimore, MD: The Johns Hopkins University Press, 1990).

likely to develop the condition than average estimates of risk suggest.

Several implications flow from the limits on recurrence risk information for mental disorders. **Sensitivity to varying understanding of illness and probability, as well as personal and cultural factors, must imbue genetic counseling. Average estimates of recurrence risk cannot stand alone; a careful diagnosis and family history provide an essential framework for the individualized interpretation of recurrence risk data (box 3-2). Finally, workshop participants concurred that more data are needed to better characterize specific risks that family members face in order to inform genetic counseling.**

Genetic counseling extends beyond communicating recurrence risk. A complex tangle of concerns and questions impel the pursuit of information on genetics and mental disorders. One workshop participant, who is an expert in genetics and mental disorders, described a typical scenario (20):

A couple, who was contemplating having a family, sought genetic counseling on depression. The wife had experienced her first bout of severe depression. She expressed concern that symptoms may flair up postpartum, jeopardizing her job, the income from which was crucial for the family. They worried aloud about their relationship which was shaken by the depressive episode and the husband's ambivalence about having a child. These are common concerns expressed in genetic counseling: people are generally confronting a new diagnosis, fear the worst, not just in terms of risk to a child, but also in terms of the impact of the disorder on the family and the impact of a pregnancy and child-rearing on the health of a parent dealing with mental illness.

The panoply of concerns surrounding mental disorders and genetics underscores what genetic counselors are realizing increasingly: the relay of genetic information occurs in a therapeutic relationship (4,8,35). Support, counseling, and followup services can assist individuals and their

TABLE 3-3: Familial Risk of Schizophrenia[a]

Relationship	Percentage of risk
General population	1%
Spouses	2
Third-degree relatives	
First cousins	2
Second-degree relatives	
Uncles and aunts	2
Nephews and nieces	4
Grandchildren	5
Half-siblings	6
First-degree relatives	
Parents	6
Siblings	9
Children	13
Siblings with one schizophrenic parent	17
Dizygotic twins	17
MonoZygotic twins	48
Children of two parents with schizophrenia	46

[a]Risk estimates based on pooled data from the more than 40 systematic family and twin studies between 1920 and 1987,

SOURCE. 1.1. Gottesman, *Schizophrenia Genesis: The Origins of Madness (New* York, NY W.H, Freeman, 1991).

families in coping with a diagnosis of mental disorder, the risk family members face, and life decisions that may follow. Sensitivity to an individual's willingness and ability to receive genetic information is but the first demonstration of this psychotherapeutic component of genetic counseling. The provider of genetic services needs to be sensitive to the concept of the "teachable moment," the point at which an individual, couple, or family is most able to comprehend and absorb the information being given. A primary consumer at the OTA-NIMH workshop described the framework for the delivery of genetic information—the realization that one's life is altered by a mental disorder (5):

> I need to know that . . . the information is there if I need it. . . As somebody with a primary psychiatric diagnosis, I will say that it is a process **that** one goes through of accepting that one first of all has an illness of this sort. I think that we go through stages that are almost like Kubler-Ross' stages of accepting death because who I believed I would be, who my family believed I would be, is not who I am, We die to ourselves. We die to our hopes, we die to our family's hopes and somehow we have to begin to find life beyond that. And we need to know that there is some information out there and we would like to draw from it because we also reconstruct our lives. We reconstruct who we are in the shifting ground of our disorder.

Providing information only upon request is an overriding principle of genetic counseling. It signals not only a sensitivity to consumer receptivity, but the value placed on individual autonomy in making life choices. Respect for individual autonomy drives nondirective counseling, which does not explicitly or implicitly make judgments on such personal decisions as marriage and childbearing. Medical geneticists harken to the wisdom of helping people at higher risk for a disorder to make decisions for themselves, by detailing the experiences and decisions that others have made (14):

> Invariably I'm asked "Should I have children or not?" When that happens I tend to use Yogi Berra's edict. When you come to a fork in the road, take it. What I mean by that is that people confronting similar risks make different decisions and I provide them examples.
>
> One was Marjorie Guthrie. When she was invariably asked: Why did you have children, she would say, "Well, Woody had 45 fantastic years of life, very productive, etc., and I had three children. I am delighted I had them." That one perspective.
>
> The other side is the case of the president of our Huntington's disease association; we had her come to talk to our medical students. She would say when asked that question: "Oh, I would never dream of bringing children into the world."
>
> I would point out both sides of these situations to this person and say "By the way, there are a lot of people on both sides and therefore whichever decision you're going to make and

BOX 3-2: Genetic Counseling for Mental Disorders

In 1978, Tsuang enumerated several steps required in genetic counseling for mental disorders. These guidelines were the first published information on the subject. While genetic counseling has evolved since that time, it is useful to review this earlier set of recommendations, which makes clear the need for accurate diagnosis, the limitations of genetic risk information, and the need to dispel any myths that may exist.

Dispel any myths. Many people have erroneous beliefs about mental disorders and genetics. They often equate genetic risk with the certitude of disease and believe that a genetic disorder is untreatable. At the outset of any counseling session, it is incumbent on the care-provider to dispel such myths, clarifying the multifactorial nature of most mental disorders and the availability of effective treatments.

Establish an accurate diagnosis. Accurate prediction of genetic risk rests on accurate diagnosis, sometimes difficult to obtain in mental disorders. Necessary resources for a diagnosis include information from personal interview, available medical records, and relatives.

Obtain a comprehensive family history. While collecting family history data—via interview of the individual seeking genetic information, direct interview of relatives, and medical records—poses difficulties, family history is essential for genetic counseling. It permits a more individualized risk assessment.

Estimate recurrence risk. Based on diagnostic information and family history, a counselor can estimate the risk of mental disorder to an individual and his or her family members. In conveying the recurrence risk that an individual faces, a counselor discusses the limits of empirical risk estimates, Including the lack of knowledge on genetic mechanisms involved and severity of condition that may arise.

Provide a framework for decisionmaking. Individuals seeking genetic information often do so in the context of personal decisions on marriage and childbearing. What the genetic counselor can provide is an objective and accurate portrait of the disorder, its treatment, related disability, and the financial supports and other services available and required. While advice on family planning is inappropriate, information on different decisions and experiences regarding genetic information may help clarify the factors involved in such personal decisions. Simply listening to the concerns and desires of individuals seeking genetic information also may help them cope with their illness and its impact on their lives.

Follow up the counseling session. Followup of a counseling session is integral to the process. A followup contact confirms accurate recollection of genetic information, can address any new questions that have arisen, and in general demonstrates support and sensitivity. Finally, a written record of the information derived in genetic counseling, for any future use, should be forwarded to the individual and/or his or her primary mental health care provider.

SOURCE M.T. Tsuang, "Genetic Counseling for Psychiatric Patients and Their Families, " *American Journal of Psychiatry 1351465-1475, 1978*

> I'm certainly not going to tell you which one to make, there are a lot of people who would agree with you and leave it at that.

Many people with a mental disorder (or any condition that is genetic) **and their family members confront the decision of whether that individ**ual should have a child. Indeed, information on genetics is often sought in the context of family planning. In this context, highly charged issues can emerge for people with mental disorders (24).

> When I talk to and listen to many consumers, they are not all nearly as supportive of this kind **of effort as we might like them to be. The reason** is because we have an unfortunate history in psychiatry, in public psychiatry in particular, of coercion, control, and sterilization in state hos-

pitals. These things, we feel, have receded into the misty past but they're right up close to folks who are living with these disorders. So, when they hear you talking about genetic counseling, they think what you're really saying in code is, "I'm going to tell you how you should not have children. If I talk to you long enough and strong enough, you will believe me and you will do what I am counseling you to do."

I certainly understand that's not what the goal of genetic counseling is, but that's how it's understood and that's how the public wants it to be done for people with these disorders. . . The outcome that many people are seeking is exactly the eugenic outcome that you described. . . That's what the whole incredibly powerful disability rights movement opposes. Mentally ill people are now part of that movement. The disability rights movement is not at all warm toward this aspect of your work because there's a very strong implicit statement about the value of their life as a disabled person. . . The way it's received by disabled people, and certainly I think the way many mentally ill people receive it, is that it's part of keeping them separate. It's part of saying, "You're not really normal. For instance, we don't think you should have a family life with children. . ."

So, we have to be aware of what stigma in society has done, the high degree of defensiveness that it has created to the kind of information that we're trying to bring and the sense that many people have in the disability movement that there's a political undertone here of social control that is very, very worrisome. Having been so recently released from second-class status, having so recently seen themselves as full participants, they're very sensitive to anything that would seem to discount their value as whole people, real people, responsible people who can and should make judgments for themselves about their life.

The principle **of nondirectiveness, so deeply embedded in genetic counseling, opposes the eugenic interventions that consumers fear. Psychiatric geneticists generally spurn directive counseling against childbearing as well, not only out of respect for consumer autonomy, but also on scientific grounds (27,28). "It needs to be said at the outset that there is no place for public health campaigns persuading people with psychiatric disorder or a strong family history of psychiatric disorder not to have children" (43). Recurrence risk for family members is usually low for mental disorders (except when both parents are afflicted, for example, with schizophrenia). These conditions are often treatable. And the factors producing increased recurrence risk are not well understood. Thus, the avoidance of childbearing is not scientifically supportable as a means of primary prevention-eliminating mental disorders from the population.**

While experts largely eschew eugenic principles and directive counseling on reproductive decisions for mental disorders, it would be dishonest to ignore the difficult, indeed imperfect, translation of these principles into practice. In the clinical realm, nondirective counseling, that does not reveal the clinician's own view of the burden of illness or what best for the consumer, requires considerable skill (4,8,46). Society's negative view of mental disorders also thwarts freedom of reproductive choice (54,64). Possible stigmatization can influence the reproductive decisions by creating a sense of public disapproval (see next section). Secondarily, it may result in depleted public resources and services for people with mental disorders. Having a child with an increased risk of a mental disorder, when services are inadequate for their care, is hardly an unhampered decision (50).

Many experts take explicit exception to nondirective counseling of people with a mental disorder when extremely disabled, raising questions about decisionmaking and child-rearing capabilities. For women with severe mental disorders, childbearing presents several other issues, including birth complications, potential teratogenic and other negative effects of some psychotropic drugs on offspring, the effect of pregnancy and the postpartum period on the mother's mental disorder, the mother's ability to handle the additional stress of raising a child, and the risk of adversely affecting the child's development. One workshop participant, a primary and secondary consumer, noted

that all too often a mother with a severe mental disorder—in the midst of a symptom crisis—also faces the loss of custody of her children, a devastating reality that might be avoided with parental supports and adequate treatment (6). In light of these concerns, a small body of research addresses issues around family planning for women with severe mental disorders (17,33,44,53).

Workshop participants raised several other issues concerning genetic counseling and mental disorders: 1) the provision of genetic services, 2) multiple consumers of genetic counseling services, and 3) adoption and genetic counseling.

The provision of genetic services. While genetic counselors and mental health care providers both have skills and expertise important for the relay of information on the genetics of mental disorders, professionals in neither field are fully trained to do so. Genetic counselors have knowledge of human genetics, are experienced in risk communication, and are steeped in a professional culture that respects individual autonomy. They typically do not have expertise in mental disorder diagnosis and treatment. Mental health care providers, on the other hand, offer expertise in the diagnosis and treatment of mental disorders; their knowledge of genetics and genetic counseling is limited. Given the dearth of genetic counselors—there are approximately 1,500 genetic counselors in the United States, half of whom concentrate on prenatal counseling (8)—the most realistic solution to this knowledge gap is the transfer of competencies among professionals. Genetic counselors and experts in medical genetics can help educate mental health professionals about the relay of genetic information; also, they may increasingly form partnerships with mental health care providers.

Workshop participants noted another impediment to the delivery of genetic services: the way in which it is financed. Private insurance rarely reimburses genetic counseling as an independent service (42,46). Thus, most genetic counseling occurs in the context of a health care delivery team. Also, the reimbursement system is not geared to services that go both to an individual with a disorder and their families. Finally, any extension of genetic counseling to people with mental disorders will have to ensure that expertise reaches the public system of care, on which so many individuals with the most severe conditions rely.

Multiple consumers of genetic counseling services. The client or consumer of genetic counseling services includes not only an individual with a disorder, but also his or her family members and prospective spouses. All have an interest and may seek information on the inheritance of a condition. One workshop panelist noted the tensions that exist (18): "I don't have one client, I always have the family. So, I'm always juggling a lot of different balls in terms of who am I actually addressing, different issues for everybody in the family." Ideally, the provision of genetic information will not pit relatives, future spouses, and individuals with mental disorders against one another. In practice, however, information on diagnosis and the inheritance of mental disorders can lead to serious interpersonal conflict as well as raise legal and ethical concerns. In general, providers of genetic services try to balance their duties to maintain confidentiality-a primary but not absolute concern in the eyes of the law—against disclosing information, when confidentiality could cause harm to a third party (2,30,58; see previous discussion).

Adoption and genetic counseling. It is not uncommon for women with severe psychiatric disorders to give up their children for adoption. Prospective parents therefore may have an interest in learning the risk for serious mental disorder in their adopted offspring. One workshop panelist indicated that "probably the most frequent call I get is from a prospective adoptive parent who goes through regular adoption agencies in the United States and finds out that the child has a mother with schizophrenia (19)." Adoptive parents face barriers to information. In addition to the limited number of professionals able to give genetic information on mental disorders, access to information on the mental health history of biological parents may be lacking(11).

PUBLIC PERCEPTIONS AND SOCIAL IMPLICATIONS

Research does not move forward in a social vacuum, simply unveiling new knowledge. Obviously, biomedical research has as one primary goal the improvement of clinical care. But the interface between research and society goes beyond clinical practice. Scientific advances become the tools of public opinion and social policy (51). Conversely, the social perception of a scientific approach can fuel popular support opposition. The subject of the workshop-genetics and mental disorders—invokes powerful images and arouses intense public reactions. This section considers public perceptions of genetics and mental disorders, how they intermingle, and some of the social and public policy issues that emerge.

Molecular genetics has become a modem-day celebrity (49,52). Featured on the front pages of newspapers and popular magazines, molecular genetics is often described as instruction manual, crystal ball, and pharmacopoeia all rolled up into one (for a recent example, see reference 23). This air of expectation that surrounds genetic research has led many commentators to express the hope that human diseases will be vanquished and even many social ills will be eliminated (16,37,40). The general public apparently accepts this expectation, with national surveys showing enthusiasm for genetic testing and gene therapy (41).

Some analysts worry about the hyperbole and value-laden symbols used to describe molecular genetics. Genes are characterized as good or bad; there are popular references to people "going shopping" for genes when choosing a mate or adopting a child; complex traits and behavior are boiled **down to DNA fragments. Many liken genetics with invariable or unchangeable characteristics. In an analysis of** *The Social Power of Genetic Information,* **one workshop participant characterized how gene-talk has infiltrated the public's psyche (49):**

> You can be sure that genetic ideas have been popularized when you see a button saying "Gene police! You—Out of the Pool"; or a Mother's Day card, to a daughter who is herself a mother, that says on the front, "What a good Mother you are," and on the inside, "It's all in the genes." Even the advertising industry seems to have assimilated genetic concepts: an ad for a BMW boasts its "genetic advantage."

Slogans by themselves are hardly dangerous. But their influence on public attitudes may be, especially among people unfamiliar with genetic principles—as is the norm (67). Perhaps most ironically, expressed genetic "triumphalism," as the editor of the prestigious journal *Nature* **termed it (40), fuels a backlash against the very science it once celebrated. A recent article in***Time* **magazine noted that "[t]here is already talk of a genetic backlash, a revolt against the notion that we are our genes, or, as one critic put it, 'that our Genes R Us'" (23). Data from surveys also convey public fears and concerns about genetic testing and genetic engineering (23,41). Researchers of the genetics of mental disorders, who participated in the OTA-NIMH workshop, described how just a few years transformed them from scientific heroes to pariahs among their peers (19). In a recent manuscript, a scientist who participated in the workshop notes that genetics is often equated with Nazism. "Critics of this enterprise are quick to associate contemporary strategies with the lurid and disquieting past abuses of biology by the Nazis, resulting in the sterilization or murder of thousands of mental patients, the physically handicapped, and millions of 'non-Aryans' during the Holocaust" (31). Similarly, a researcher into twins who are discordant for schizophrenia notes in a recent text that he was "publicly called 'anew Mengele' by a psychiatrist at a national conference" (60). He concludes that "[f]or a few people it seems that anybody who studies twins is automatically assumed to be a fascist or worse" (60).**

Withered support for research is not the only worrisome result of exaggerated or simple-minded claims about genetics. The public's perception of genetics is a primary thread in the fabric of public policy. Many analysts express alarm at the potential discriminatory use of genetic information, falsely perceived as forecasting a certain, unyielding, or completely incapacitating fate

(1,48). A preliminary case study describes some of the discriminatory consequences of such viewpoints (9):

> Genetic conditions are regarded by many social institutions as extremely serious, disabling, or even lethal conditions without regard to the fact that many individuals with "abnormal" genotypes will either be perfectly healthy, have medical conditions which can be controlled by treatment, or experience only mild forms of a disease. As a result of this misconception, decisions by such institutions as insurance companies and employers are made solely on the basis of an associated diagnostic label rather than on the actual health status of the individual or family. . . Once labeled . . . an individual may suffer serious consequences. . . These include inability to get a job, health insurance, or life insurance, being unable to change jobs or move to a different state because of the possibility of losing insurance, and not being allowed to adopt a child.

Genetic discrimination has received considerable attention from policy makers and analysts. In fact, 5 percent of the National Institutes of Health's National Center for Human Genome Research budget—$5 million in fiscal year 1992—is devoted to the task of addressing the Ethical, Legal, and Social Implications (ELSI) of genetic information (see chapter 1). Among the most discussed issues are insurance and employment discrimination on the basis of genetic test results (box 3-3).

While genetic information and the perception of genetics may serve to limit access to health care, its social influence may be more insidious. Public pressure may mount against individuals viewed as passing on disease genes to their offspring. Citing survey results, a recent OTA report concluded that "stigmatization of carriers [of the gene for cystic fibrosis] is likely to focus on beliefs that it is irresponsible and immoral for people who could transmit disability to their children to reproduce" (64). In response to a 1990 general population survey, 39 percent said "every woman who is pregnant should be tested to determine if the baby has any serious genetic defect." Nearly 10 percent of those surveyed expressed the belief that a woman should be required bylaw to have an abortion rather than have the government help pay for the child's care. Public opinion may even turn against bringing a child into the world with a benign genetic condition. The public response to TV anchorwoman Bree Walker Lampley's pregnancy is illustrative. When she became pregnant with her second child, she found herself the focus of Los Angeles radio talk show attacks. Ms. Lampley has a genetic condition-ectrodactyly-which manifests as the absence of one or more fingers or toes. Because her offspring are at a 50 percent risk of inheriting the condition, the radio talk show callers and host criticized Lampley's pregnancy.

Mental disorders are among the most stigmatized of health conditions. Although attitudes toward mental disorders appear to be improving (12,13), data continue to show that the public is uneducated about mental disorders, fearful of it, and hostile to people with these conditions (63,66). For example, a recent national survey of public attitudes toward people with disabilities shows that from the public's perspective mental disorders are the most disturbing of all disabling conditions (47). Many individuals harbor beliefs that bad parenting, personal inadequacy, weakness of character, or sinfulness lie at the root of severe mental disorders (63). The news and entertainment media promote these stigmatizing views with their routine presentation of people with mental disorders as incompetent, ineffectual, and violent (63,66).

Ignorance and negative attitudes, combined with other factors, wreak havoc on the lives of people with mental disorders. Data from surveys and other research show the tragic consequences: people with severe mental disorders suffer poor self-esteem and discrimination in employment, housing, and access to health care (39,66).

The negative attitudes attached to mental disorders aggrieve family members as well. In addition to becoming the most significant care-provider, family members suffer psychological consequences.

BOX 3-3: Policy Protection Against Genetic Discrimination

As genetic tests for a host of diseases become available, analysts worry that insurers and employers will increasingly discriminate on the basis of genetic test results. For example, insurance companies may discriminate by denying life, health, or disability insurance to people found to carry disease-related genes. Employers may use genetic screening to eliminate job applicants or current employees who are likely to be frequently absent from work, be less productive than other workers, or would increase costs of employer-funded insurance and benefit programs.

Given these concerns, protection from genetic discrimination is at the top of many analysts and advocates agendas. Review of current policies suggests that existing protections are limited. At the federal level, the Rehabilitation Act of 1973 and the Americans With Disabilities Act (ADA) of 1990 prohibit employment discrimination on the basis of disability. *Disability* is defined to include both actual disabilities and conditions that are perceived as being disabilities. The Rehabilitation Act of 1973 applies to federal employers, contractees, and grantees. Although no cases involving genetic discrimination have been decided under the Rehabilitation Act, the law has been held to apply in cases involving discrimination based not on the employee's present condition but on the employer's fear that at some time in the future the employee's real or perceived disability may affect his or her ability to perform the job adequately or safely.

The ADA applies the employment discrimination provisions of the Rehabilitation Act to all private sector employers with 15 or more employees. The ADA limits inquiries about health or medical conditions in several ways. It prohibits all preemployment inquiries and medical examinations except examinations conducted after a job offer has been made. The examination may include all types of tests, including genetic tests. However, the results of the tests may not be used to exclude an individual from the job unless the exclusion is shown to be job-related, consistent with business necessity, and not amenable to reasonable accommodation (29 C.F.R. 1630.14(b)(3)).

The ADA's impact on health insurance is intentionally limited. Indeed, under the ADA, an insurer is free to limit benefits on the basis of demonstrable risk as long as no state law prohibits such discrimination. Further, an employer or other entity covered by the ADA may limit the insurance coverage provided to its employees without violating the provisions of this law. As long as the employer provides the same coverage to all employees, there is no requirement that the insurance covers services needed for a specific disability. In general, the federal government leaves regulation of the insurance industry largely to the states.

All states have laws prohibiting employment discrimination on the basis of handicap; many define handicap broadly enough to extend protection to people regarded as being impaired because they are at risk of developing a genetic disease. In addition to the laws common to all or most states, a small but growing number of states have laws that specifically restrict the use of genetic information by employers or insurers.

Given the limited protection from genetic discrimination currently offered by federal and state laws, the Joint Working Group on the Ethical, Legal, and Social Implications in Human Genome Research (ELSI) developed recommendations to prevent the negative impact of genetic information on access to insurance. The working group expressed concerns that genetic discrimination is not mentioned specifically in the ADA and the law does not protect carriers of genetic diseases from employment discrimination. In regard to health insurance, ELSI recently published a series of recommendations to address concerns that access to health care may be denied or preexisting conditions excluded from coverage. The group listed the following recommendations in its report: "Information about past, present, or future health status, including genetic information, should not be used to deny health care coverage or service to anyone."

SOURCES: J.M. Miller, "Genetic Testing and Insurance Classification: National Action Can Prevent Discrimination Based on the 'Luck of the Genetic Draw,'" *Dickinson Law Review* 93:729-757, 1989; National Center for Human Genome Research, "Insurance Task Force Makes Recommendations," *Human Genome News* 5(2):1-2 July 1993; M.R. Natowicz, J.K. Alper, and J.S. Alper, "Genetic Discrimination and the Law," *American Journal of Human Genetics* 50:465-475, 1992; H. Ostrer, W. Allen, L.A. Crandall, et al., "Insurance and Genetic Testing: Where Are We Now?" *American Journal of Human Genetics* 52:565-577, 1993.

> Subjective burden—the family's distress over the pain and altered life prospects of their mentally ill relative—is exacerbated by these stigmatizing events. Reactions to perceived social censure become intertwined with responses to the sorrows and demands of the illness itself. Emotional reactions to major mental illness in a family member frequently include bewilderment, fear, denial, self-blame, sorrow, grieving, and empathic suffering. The added perception of stigma may elicit rage and resentment or intensify depression and social withdrawal (38).

It is on this stage of stigmatization and discrimination that the social influence of genetic models of mental disorders will play out. What is or will be the result of the co-mingling of public perceptions of genetics and mental disorders? Although few research data address this issue, workshop participants and other commentators describe the complex blend of views. On an undercurrent of fear, many primary and secondary consumers express relief and optimism concerning genetic research of mental disorders.

> I think it's a complex issue but if you look at the kind of stigma that is most painful to people who have chronic psychiatric disabilities, discovering the scientific substrate and the underpinnings of these disorders has been profoundly destigmatizing, I would say, in the last decade. And I think it will continue to function that way (5).

Clinicians echo this perception, as the words of Dr. Raymond DePaulo show (20):

> Families . . . do express fears. But I think, by and large, they're greatly relieved right now that we're seriously going at this enterprise. And they take hope, not just from the fact that Freud was wrong and it isn't mother's fault, but even more from the fact that people are seriously working on finding the causes of these disorders.

Many people with mental disorders and their families look forward to the results of genetic research, because it offers promise of improved understanding of their condition and hope for improved treatment (70). The very image of mental disorders as biological—genetic—is viewed as destigmatizing, thus offering comfort for some.

"Proliferation of biogenetic research findings. . . has somewhat softened the older prejudices against families (38)."

A note of caution was sounded at the OTA-NIMH workshop, in terms of the potential discriminatory consequences of genetic data and the backlash against research described above (10):

> I think that it's quite right that in general . . . families affected with mental disorders have a great belief in the value of research . . . [that it will] change their status for the better. And I think that's a realistic and hopeful and good thing. I think that it must be tempered, however, by a realistic appraisal of the immediate impacts of that research. For instance, the results of research becoming diagnostic tools can have an immediate negative impact on them, let's say, with employers or insurers or whatever, using the information in a discriminatory way. The other thing I would say is that. . . I think that there's an issue of how research gets transmitted to the public as well. You know, I see a lot of people who are in cystic fibrosis groups or whatever, who are disillusioned at some level with research, with genetic research. It's clearly true in mental disorders as well. . . I think that there has to be, within the research community, some recognition that crummy linkage studies have an impact and it's not always so good.

Recognizing the destigmatizing influence of genetics research, one workshop participant evoked the lessons of history in his note of caution (15):

> There's a two-edged sword here. One of the roles of genetics in the 1980s has been to use genetics as a destigmatizing force. That is, the ability to say that there are genes involved in a disorder proves that it is more like heart disease or cancer because it's a physical disorder. There's something broken in your brain. In essence, it's an assault on the Freudian determinism of parenting causing schizophrenia. That's very powerful. But at the same time, we've got a carryover of genetic determinism from the past where, after all, in Germany, it was the folks with psychiatric disorders who were believed to have the disorders for genetic reasons who were the first victims of eugenics. . . So. . . we've got

> a very strange mix of cross currents going on here. We've got one social current that says "We need genetics to de-stigmatize" but we seem to have forgotten the history that suggests that genetics can be used as a label effect-once that label is imposed, it sticks and can be used against the individual and family.

History teaches us that science and prejudice can combine in ways ruinous to people with stigmatized conditions and their families. The history of screening for sickle cell anemia in this country provides one example (64). Sickle cell anemia impairs red blood cell flow through the circulatory system, causing complications in organ systems throughout the body. This painful, incurable, and sometimes fatal genetic condition has a high incidence among African Americans, with one in 400 newborns having sickle cell anemia. One in 10 or 11 have the sickle cell trait. Individuals with the sickle cell trait have a normal and healthy life but if they marry another carrier can have a child with sickle cell disease. A massive screening program for sickle cell trait was undertaken in the 1970s, so that couples could be informed of their risks of having affected children. While at first glance, screening programs offered an inexpensive benefit to African American citizens—indeed, most laws were drafted and promoted by African American legislators at the height of the civil rights movement-early programs suffered from misinformation and discrimination against carriers. Some state statutes consistently contained blatant medical and scientific errors. Almost every state law failed to insist on using the most sensitive assay available. Controversy also focused on the racial distribution of sickle cell mutations and the target screening population. The laws were seen by many citizens as racist eugenic measures aimed at reducing the number of marriages between carriers and decreasing the number of pregnancies at risk for affected children of a minority population. The fact that the programs were largely designed and operated by Caucasians fueled fears of genocide. Most state laws failed to provide adequate education and counseling for persons with sickle cell anemia or the trait. Those diagnosed with sickle cell trait were often told they should not have children, that childbirth would be hazardous, or other untruths. State laws also failed to provide public education to guard against discrimination and stigmatization. Stories of job and insurance discrimination multiplied as screening programs proliferated. Other screening programs have had similar consequences for the insurability and employability of those identified as predisposed to genetic conditions (51).

The eugenics movement earlier this century offers an even more terrifying example of the potentially dangerous mix between genetics and prejudice against mental disorders. In Nazi Germany and the United States, people with mental disorders were among the initial targets of eugenic policies (22,26,30,45). A number of scientific discoveries planted the seeds of eugenic policies in the 19th and 20th centuries. Sir Francis Galton, a cousin of Darwin who coined the term *eugenics,* observed that many accomplished men of his day were linked by bloodlines, which led to his belief that proper matings could produce a race with enhanced intellectual, behavioral, and physical characteristics—positive eugenics. In addition, Galton and others developed statistical techniques that permitted the quantitative analysis of inherited traits. Social, political, and economic factors fertilized the growth of the eugenics movement. National attention was increasingly focused on social issues of unemployment, criminality, prostitution, and chronic alcoholism. Also, concerns arose that increased immigration from southern and eastern Europe was drawing the United States away from its "Anglo-Saxon superiority."

Public policies executed these scientific and social developments. At the federal level, eugenic policies took the form of increasingly restrictive immigration laws. Eugenicists, asserting the simple inheritance of such traits as lunacy, epilepsy, alcoholism, pauperism, criminality, and feeblemindedness, proffered scientific rationales for excluding individuals from entry to the United States. While authentic advances in genetics seeded the eugenics movement, they provided no evidence for the simple inheritance of the traits mentioned above. Eugenic considerations also

prompted states to enact laws regarding compulsory sterilization. In 1907, Indiana passed the first law legalizing the compulsory sterilization of inmates at the state reformatory. By 1931, 30 states had passed compulsory sterilization laws applying to individuals categorized as feeble-minded, alcoholic, epileptic, sexually deviant, or mentally ill. Individuals with mental disorders made up half of the 64,000 persons in this country sterilized for eugenic reasons between 1907 and 1964. When eugenic sterilization laws were challenged in 1927, the U.S. Supreme Court ruled the practice constitutional.

Many consider that the current application of immigration and compulsory sterilization laws suggests that eugenics is no longer a major concern. Furthermore, the understanding that mental disorders do not have a simple genetic basis and that nongenetic factors play an important role would seem to limit the potential of eugenic policies. Perhaps most important, American repulsion by the Nazi legacy and the emphasis in this country on individual reproductive rights also make state-determined eugenic policies unlikely. But, as noted above, indirect pressure not to have children may well come to bear on individuals seen to have a greater genetic risk of mental disorders; society may brand them irresponsible or immoral for transmitting disorders to their children. And eugenic policies are moving forward abroad. In China, a draft law on "eugenics and health protection" presented to the Eighth National People's Congress (NPC) in 1993 proposed that people with diseases such as mental illness "which can be passed on through birth" be banned from marrying (21).

SUMMARY AND CONCLUSIONS

People with mental disorders and their families participate in research, benefit from its results, and feel the impact of its social dissemination. Workshop participants discussed these clinical and social implications of research of the genetics of mental disorders. At least three issues stand at the fore of any attempt to bridge the gap between research and society: family involvement, the nature of mental disorders, and the need for education.

Involvement of family members. Historically, ethical guidelines and public policy largely have focused on the well-being of the individual, as research participant, consumer of clinical services, and member of society. Genetic research broadens this approach, extending the circle of concern to family members in addition to the afflicted individual. Family members are necessary participants in research raising issues around consent and confidentiality. Family members often seek information on genetic status, which raises potential conflicts. Any social effect of genetic research-for example, its use to limit access to health care—will obtrude on individuals with mental disorders and family members alike. While workshop participants recognized the potential clash of interests between family members and affected individuals, many expressed the belief that a framework of benevolence could lead to relevant guidance for research, clinical practice, and public policy-developments that are sorely needed.

The nature of mental disorders. Two features of mental disorders color genetic research and its translation into practice and policy. First, mental disorders can sometimes circumscribe an individual's decisionmaking ability. The impact of some mental disorder symptoms raises issues around informed consent for research participation and informed clinical decisionmaking. Advocating the importance of individual autonomy, workshop panelists strongly asserted the need to take seriously and perhaps foster further guidelines and policies that increase the meaningful participation of people with mental disorders in research and clinical care, so as to better protect their rights and well-being.

The second feature of mental disorders that permeates genetic research is the stigma attached to these conditions. The ignorance and negative attitudes attached to mental disorders encumber research and clinical care, heightening concerns about confidentiality. The stigma also drives support for this research among many consumers,

and, paradoxically, could fuel its abusive application. This social reality animates the final issue put forth by workshop participants: the need for education.

Educational needs extend to several spheres. Researchers and individuals participating in the review of research need information about the clinical and ethical issues raised by research of the genetics of mental disorders. Mental health care providers need information about the genetics of mental disorders and the practice of delivering such information to requesting consumers. Similarly, genetic counselors need information on the nature, diagnosis, and treatment of mental disorders. Finally, society at large needs information about the nature of genetics and mental disorders, in order to diminish fears and stigmatization and to help inoculate against discriminatory policies.

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