Chapter 2

# Introduction

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# Chapter 2
# Introduction

People want-expect-perfectly healthy babies. When a child is born with a genetic condition, parents suffer anxiety, endure anguish, and experience guilt: "This baby is sick because of us. "

This report is about one of these inherited conditions: cystic fibrosis (CF). CF is a life-shortening disorder. It is a genetic condition—i.e., one that follows a clear pattern of inheritance in families-and is the most common, lethal recessive disorder in American Caucasians of European descent. Each year in the United States, about 1 in 2,500 babies is born with CF (10,35,47 )---i.e., about 1,700 to 2,000 babies with CF are born annually (25). Approximately 1 in 9,600 Hispanic, 1 in 17,000 (9) to 19,000 (50) African American and 1 in 90,000 (50) Asian American newborns have CF.

Medicine has long recognized the consequences of CF (table 2-1) on several organ systems, particularly the lungs and pancreas. Only recently, however, have scientists pinpointed the most common change, or mutation, in the genetic material-DNA—that accounts for the majority of CF cases (44,66,68). Because CF is a recessive trait, a child with CF must receive two mutant CF genes, one inherited from each parent, who are CF ''carriers, ' but who do not have the disorder (figure 2-l). Thus, while approximately 30,000 people in the United States have CF, as many as 8 million people could be carriers of one CF mutation. What are the implications of informing this latter pool of individuals--a a subset of those of reproductive age and younger-about tests that reveal CF carrier status?

## TERMINOLOGY

Human genetics, like all scientific disciplines, is rife with jargon, and subtle distinctions in language can matter a great deal. People, reports, or institutions rarely define terms of art in precisely the same manner. To avoid confusion, OTA uses several terms as follows.

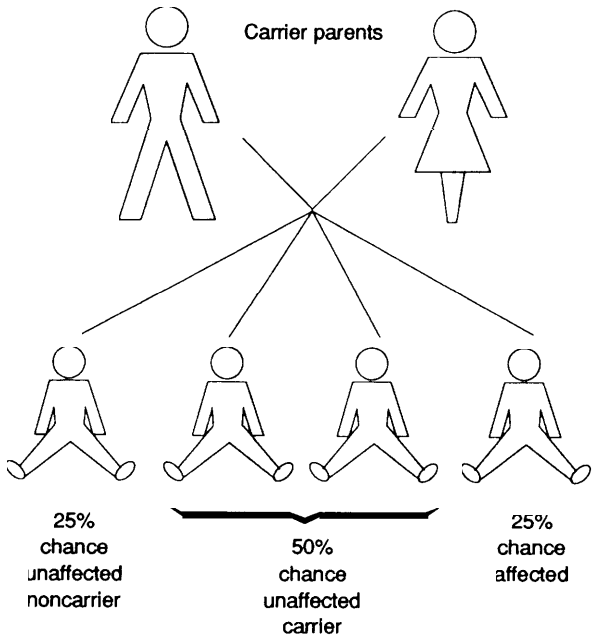
OTA defines ***genetic testing*** as the use of specific assays to determine the genetic status of individuals already suspected to be at high risk for a particular inherited condition. While any individual can be

**Table 2-l—History of Cystic Fibrosis: Selected Highlights**

| | |
|---|---|
| 1650. . . . . | Literature refers to now characteristic CF pancreatic and lung symptoms association with salty skin and early death. |
| 1705. . . . . | A book of folk philosophy states that a salty taste means a child is bewitched. |
| 1857. . . . . | *The Almanac of Children's Songs and Games,* Switzerland, quotes from Middle Ages: "Woe is the child who tastes salty from a kiss on the brow, for he is hexed, and soon must die." |
| 1938. . . . . | First reported description of disease, calling it "cystic fibrosis of the pancreas." |
| 1946. . . . . | Antibiotics found effective for treating CF-related lung infection. |
| 1946. . . . . | Inheritance pattern-autosomal recessive-suggested. |
| 1953. ....., . . . . | Sweat abnormality in CF first described. |
| 1955. . . . . | First review of use of pancreatic enzymes to treat CF. |
| 1959. . . . . | Safe and accurate way to diagnose CF, "sweat testing," reported. |
| 1960 to present. . . . | Accelerated improvement in survival. |
| 1968. . . . . | Mechanism underlying CF-related male infertility demonstrated. |
| 1981 to 1983. . . . . | Basis for sweat abnormality (i.e., electrolyte transport problems) described. |
| 1986. . . . . | CF gene localized to chromosome 7. |
| 1989. . . . . | CF gene and its most common mutation identified. |
| 1990. . . . . | CF mutation assays available from selected genetic laboratories, companies, and medical centers. |
| 1990. . . . . | CF mutation corrected in laboratory cells. |
| 1991 . . . . . | Functions of CF gene described. |

**SOURCE:** Office of Technology Assessment, 1992, based on L.M. Taussig, Cystic *Fibrosis (New* York, NY: Thieme-Stratton, Inc., 1984).

**Figure 2-1—inheritance of Cystic Fibrosis**




SOURCE: Office of Technology Assessment, 1992.

considered ‘‘at high risk’ for a particular unknown trait, and hence be “tested,” ‘ ‘at high risk” here denotes the presence of a family history or clinical symptoms. The terms ***genetic test, genetic assay,*** and ***genetic analysis are*** used interchangeably to mean the actual laboratory exarnination of samples.

***Genetic screening*** usually uses the same assays employed for genetic testing, but is distinguished from genetic testing by its target population. OTA uses the term ‘screening’ selectively. In this report, it refers to analyzing samples from individuals without a family history of the disorder, groups of these individuals, or populations. ***Carrier screening for CF*** (or ***CF carrier screening),*** then, involves performing tests on persons for whom no family history of the disorder exists to determine whether they have one normal and one aberrant copy of the CF gene, but not the disorder (which results from having two aberrant CF genes).[1]

Many individuals are CF carriers but do not have a positive family history. In fact, 4 of 5 babies born with CF each year-as many as 1,600---are cases where there was no known family history for CF. The difference between *testing* and *screening* is illuminated by considering a person contemplating procreation. He or she could inquire about the availability of an assay to determine the probability that he or she could have a child affected with CF. If there are no relatives with the disorder, the individual could be informed that a test would provide information about his or her genetic status for CF. The person could then elect to be *screened* to determine whether or not he or she is a carrier for CF. If, however, there is a family history of the disease, a practitioner would ideally inform the individual and his or her partner about CF carrier assays and they might choose to be ***tested*** to determine if they are both carriers.

***Genetic counseling*** is a clinical service that includes providing an individual (and sometimes his or her family) with information about heritable conditions and their risks. When centered around genetic testing and screening, it involves both education and psychological counseling to convey information about the ramifications of possible test outcomes, prepare the client for possible positive or negative analyses, and discuss actual test results. Many types of health professionals perform genetic counseling. OTA reserves the term ***genetic counselor*** for master’ s-level individuals certified (or board-eligible) by the American Board of Medical Genetics to clarify the discussions of the legal distinctions in licensing and third-party reimbursement among the different types of practitioners. But, OTA uses the term ***genetic counseling*** more generically to refer to the educational and informational process that is performed by genetic specialists, including physicians, Ph.D. clinical geneticists, genetic counselors, nurses, and social workers.

OTA avoids using the term “program” in discussing CF carrier screening in the United States. For many, the term connotes a formal public health effort led or sanctioned by Federal, State, or local governments. In analyzing CF carrier screening, OTA’s premise is that large numbers of Americans might be screened for their CF carrier status. OTA remains neutral on whether the assays will be a component of a fixed, regulated scheme or another facet of general medical practice.

[1] In contrast, OTA uses the term *CF screening* (or *screening for CF*) to mean screening individuals to diagnose the presence or absence of the actual disorder, in the absence of medical indications of the disease or a family history of CF. Such screening usually involves newborns (ch. 3), but is rarely done for CF except in Colorado and Wisconsin. CF testing of infants is common if a family history of the condition exists.

***Box 2-A—Eugenics At the Turn of the Century***

Eugenics refers to processes or policies to either discourage or prevent reproduction by members of society with ''undesirable" heritable traits or to encourage or require procreation by individuals who have ''desirable" genetic characteristics. Put more broadly, it involves efforts that interfere with individuals' reproductive choices in order to attain a ''societal' goal. Drawing on roots developed by Francis Galton, a cousin of Charles Darwin, in England in the late 1800s, eugenics movements flourished in the United States at the turn of the century.

Compulsory sterilization laws were an outgrowth of the U.S. eugenics movement. The Model Eugenics Act, from which many States drafted their laws in the early 1900s, targeted institutionalized tuberculosis patients, people who were blind or deaf, and chronic alcoholics among those who should be sterilized. In 1927, the U.S. Supreme Court upheld the Commonwealth of Virginia's sterilization law, Justice Oliver Wendell Holmes writing:

> We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be *strange if* it could not call upon those who already sap the strength of the State for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetence. . . . Three generations of imbeciles are enough (16).

Despite the fact that compulsory sterilizations continued into the 1970s, the eugenics movement per se waned in the United States during the 1930s, largely from distaste with Hitler's embrace of eugenics. Wariness over past abuses of genetic information led to the emphasis on nondirective genetic counseling in clinical practice. Nevertheless, the legacy of eugenics—though by and large renounced-continues to color perceptions about large-scale genetic screening, and thus to subtly influence decisions surrounding human genetics and public policy,

SOURCE: Office of Technology Assessment 1992, based on N.A. Hoi_ *Proceed With Caution: Predicting Genetic Risks in the Recombinant DNA Era (Baltimore, MD: The* Johns Hopkins University Press, 1989); D.J. Kevles, *In the Name of Eugenics* (Berkeley, CA: University of California Press, 1985); K.M. Ludmerer, *Generics and American Society: A Historical Appraisal* (Baltimore, MD: The Johns Hopkins University Press, 1972); P, Reilly, *Generics, Law, and Social Policy* (Cambridge, MA: Harvard University press, 1977); and P. Reilly, *The Surgical Solurion* (Baltimore, MD: The Johns Hopkins University Press, 1991).

## RECENT HISTORY OF HUMAN GENETICS AND PUBLIC POLICY

The science of human genetics is embedded in this country's consciousness, and has manifested itself---vertly and covertly-in public policies throughout U.S. history (box 2-A). Race and skin color, for example, are genetically influenced, and have played a direct role in official and unofficial decisionmaking. In some respects, identifying carriers of CF mutations—invisible genetic characteristics—is just another twist in the history of genetics and U.S. public policy, but one that has implications for the majority population in this Nation.

To provide background and perspective for today's debate about CF carrier screening, this section briefly describes watershed events in U.S. politics and human genetics. Not intended to be comprehensive, it focuses on a few, discrete events in the 20th century that place the questions raised by CF carrier screening in context and help frame the issues and options addressed by this report. The impact of broader U.S. laws, such as Title VII of the Civil Rights Act (42 U.S.C. 2000e) and the Americans With Disabilities Act (Public Law 101-336; 42 U.S.C. 12101), are discussed elsewhere in the report.

### *U.S. Law and Genetic Disease*

Most U.S. legislation related to genetic disease is State law covering newborn screening (2,63,78,89). During the 1970s, however, Congress enacted three measures involving carrier screening for several genetic conditions (Public Laws 92-294, 92-414, and 94-278). Today, most State newborn screening laws (and the programs and practices established by them) operate, for the most part, unchallenged. In contrast, the Federal Government's role in public health and genetics has changed historically.

In the late 1960s and early 1970s, sickle cell anemia received prominent attention as a health concern. The African American community felt that sickle cell anemia was a neglected condition, with little Federal research funding directed toward it. As the debate progressed, Federal interest, along with State interest, developed. President Nixon made an appeal for an effort to combat sickle cell anemia in his 1971 health address to Congress (39), and the following year he signed into law the National

Sickle Cell Anemia Control Act (Public Law 92-294). While the act focused on detecting sickle cell anemia, the mechanics of the test also identified carriers for sickle cell. Later that year, Congress moved a second time to enact legislation directed at another genetic disease, ß-thalassemia, with the National Cooley's Anemia Control Act (Public Law 92-414).

Both programs represented a significant expansion of Federal support for nonresearch genetic initiatives. Federal programs supported only State efforts with voluntary participation, a measure designed to defuse ongoing controversy over mandatory, coercive screening. And although the statutes' intent was to reduce stigmatization of and discrimination against carriers, these practices continued unabated (64).

In 1976, Congress amended the sickle cell legislation, broadening it to the National Sickle Cell Anemia, Cooley's Anemia, Tay-Sachs, and Genetic Diseases Act (Public Law 94-278; hereinafter the National Genetic Diseases Act). In doing so, it expanded both the scope and authority of activities, as well as the range of genetic disorders for which Federal grants and contracts were awarded. The legislation emphasized voluntary participation and the use of proper guidelines for confidentiality of results; it also stressed that genetic counseling for all participants should be available-goals that experts agree are desirable for CF carrier screening (18,54). In 1978, Congress reauthorized the program, which continued to provide funding for basic and applied research, training, screening, counseling, and information and education programs (Public Law 95-626).

In 1981, the role of the Federal Government in genetic services, education, and training dramatically altered (61). Authorization for programs operated under the National Genetic Diseases Act was replaced by the Maternal and Child Health Block Grant (Public Law 97-35). No longer were Federal funds for genetic services, professional training, and public education programs guaranteed: The majority of fund allocation decisions have since been left to individual States. Programs for genetic services, research, and professional training now compete with other maternal and child health services (box 2-B). And while many States have responded with State or regional programs, the reduced Federal role led a presidentially appointed commission to voice concern about the adequacy and effectiveness of genetic services, education, and training (61).

While difiicult to quantify, decreased Federal attention to genetic services, training, and education might have left the country less than well prepared to handle the rapid integration of molecular genetics research into clinical practice. From the late 1970s to the present, basic research in genetics has enjoyed generous Federal sponsorship and returned the dividend of increased knowledge about many genetic conditions. In contrast, Federal funds for projects relating to genetic services show a steady decline since 1981. These genetic services provide the link to translate basic research developments into clinical practice.

A void in Federal funding for genetic services might have exacerbated at least one issue raised by the prospect of routine CF carrier screening: the inadequacy of training-related monies to ensure sufficient genetic counseling services. Similarly, decreased Federal spending for genetic services likely contributed to the initial scrambling to fired pilot studies for CF carrier screening (17,67). In fact, it was left to the National Center for Human Genome Research (NCHGR), National Institutes of Health (NIH)---a research, not service, agency—to step forward and coordinate clinical assessments of genetic services for CF carrier screening (90).

In October 1991, NCHGR funded six 3-year clinical assessment studies to examine education and counseling issues related to CF carrier screening. The National Institute of Child Health and Human Development and the National Center for Nursing Research also funded one project each (53). The Cystic Fibrosis Foundation, which took a lead role in funding investigations to find the CF gene and its mutations, declines to participate in any decisions about pilot projects for CF carrier screening, saying its mission is not prevention, but improving treatment and finding a cure (67).

### *The 1983 President's Commission Report*

***In 1980,*** Congress created the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (Public Law 95-622; 42 U.S.C. 300). Among the topics Congress mandated that the Commission examine was the ethical, social, and legal implications of genetic screening, counseling, and educa-

### *Box 2-B-Genetic Services: Federal-State Partnership*

Funding for genetic services derives from a medley of Federal and State sources, and varies greatly from State to State. During the 1970s, genetic services enjoyed substantial Federal funding, in part through congressional mandate. The Omnibus Budget Reconciliation Act of 1981 (Public Law 97-35), however, led to the consolidation of genetic services funding-along with seven other programs—into the Maternal and Child Health (MCI-I) Block Grant. Overall, funding for maternal and child health services was cut, and the responsibility for distributing the monies and for providing services was passed to the States, which also had to begin using $3 in State funds for every $4 of Federal money received. Prior to the block grant, no matching funds were required.

Under provisions of the MCH block grant, 85 percent of funds go directly to the States for maternal and child health services. States must decide how to allocate the funds among a number of areas, such as general prenatal care, infant nutritional supplementation, and other maternal and child health needs. MCH funds maybe used for health care services, education, and administration. In fiscal year 1990, less than 2 percent of MCH funds were used by States to support genetic services other than newborn screening.

In general, MCH funds account for a small portion of State genetic services. Under terms defined by the block grant, each State decides whether or how much money to designate for genetic services. In 1990, 34 States used MCH funds to support some aspect of general genetic services other than newborn screening, including nonpatient-related activities such as administration and planning. In the majority of States, however, MCH funds accounted for less than 25 percent of fiscal year 1990 funding for genetic services (51). In fiscal year 1990, MCH funding for genetic services other than newborn screening totaled approximately $8 million; State funding accounted for approximately $22 million (51).

Fifteen percent of the MCH block grant is administered as direct grants for Special Projects of Regional and National Significance (SPRANS). SPRANS monies are grants for specific projects and are not given to each State. SPRANS provides seed money for demonstration, or pilot, projects in a number of areas. After the demonstration period ends, usually in 3 years, alternative funding must be found.

In fiscal year 1990, genetic services received about 9 percent of all SPRANS funds. When adjusted for inflation, however, constant dollar funding for genetic services under SPRANS has decreased almost every year since the block grant's inception. Moreover, SPRANS support of genetic services has decreased born about 90 percent of the SPRANS genetic services budget in 1981 to about 66 percent in 1991. Initially, most of the SPRANS genetic services budget established statewide genetics programs, with each State receiving seed money for at least 4 years. The last State received funding in 1990 (27). Other areas of genetic services delivery receiving SPRANS support include ethnocultural projects to increase utilization of genetic services by undersexed populations; psychosocial studies; and support groups for young adults and families. In fiscal year 1990, 16 States used approximately $4 million from SPRANS grants to support demonstration projects in clinical genetic services other than newborn screening (51). In fiscal year 1990, just over one-third of SPRANS' genetic services budget went to the regional networks and the Council of Regional Networks for Genetic Services (CORN) (27). CORN and the regional networks-comprised of genetic service providers, public health personnel, and consumers-serve as resources for communication and coordinate data collection and quality assurance, but do not provide direct services to patients.

In addition to block grant and SPRANS awards, States also fund genetic services from other sources. In fiscal year 1990, at least 26 States derived $46 million in genetic services funding exclusive of newborn screening from provider in-kind and service charges, third-party reimbursement, grants, contracts, newborn screening fees, health insurance surcharges, and mental health/mental retardation reds. For some States, such funding accounts for most of their genetic services funding. For example, newborn screening fees generated 93 percent of genetic services funding in Colorado and 86 percent in Michigan in fiscal year 1990. Similarly, prenatal screening service fees accounted for more than 83 percent of the genetic services budget in California in fiscal year 1990 (51).

All States, the District of Columbia, and Puerto Rico coordinate genetic services statewide; nearly half experienced a decrease in funding for genetic services from fiscal years 1988 through 1991 (51). Individual ***State*** genetic service programs face yearly uncertainty about how much—if any-funding they will receive, which makes planning difficult. As general knowledge and public awareness about genetic diseases continues to emerge out of the Human Genome Project, uncertainty in genetic services funding will be increasingly problematic.

SOURCE: Office of Techology Assessment, 1992.

***Box 2-C—The 1975 National Research Council Report, "Genetic Screening: Programs, Principles, and Research"***

***In*** response to a letter from the American Society of Human Genetics, the National Research Council (NRC) of the National Academy of Sciences convened a committee in 1972 specifically to analyze neonatal screening for phenylketonuria and generally to assess the relation between genetics and preventive medicine. In particular, the committee was charged with addressing the questions: To what degree has genetics played a part in thinking about and practice of disease prevention? How should this relationship be fostered and extended?

Key recommendations of the committee were that participation be left to the discretion of the person tested and that information obtained as a result of a test not be made available to others except with the consent of the patient The committee also advised that professionals responsible for screening programs be aware of and regularly assess potentially damaging effects of screening, including invasion of privacy, breach of confidentiality, civil rights violations, and psychological effects from being labeled a genetic carrier. Principles described in the report still underlay genetic screening and testing today.

The NRC report was not ubutuated by the Federal Government, but it was supported with Federal funds from the National Science Foundation. It made a critical impact in shaping future discussions, such as the 1983 President's **C**ommission report, ***Screening and Counseling for Genetic Conditions:*** *The Ethical, Social, and Legal Implications of Genetic Screening, Counseling, and Education Programs.*

*SOURCE: Offuce* of Technology Assessment 1992, based on Committee for the Study of Inborn Errors of Metabolism, National Researeh Council *Genetic Screening: Programs, Principles, and Research (Washingtom DC:* National Academy of Sciences, 1975).

tion programs. In 1983, the Commission published the results of its deliberations (61).

In carefully weighing the advantages and disadvantages of applications of advances in medical genetics, the Commission found, on the whole, that these advances have greatly enhanced health and well-being (62). Drawing on the literature (55) (box 2-C) and public hearings, the Commission reached 15 conclusions, including recommendations about the confidentiality of genetic information and mandatory versus voluntary screening (61).

The Commission's report on genetic screening is noteworthy for its examination of past experience with screening programs (e.g., for Tay-Sachs disease, sickle cell anemia, and phenylketonuria) and its prescience in using CF carrier screening as a specific case study. The Comrnission's analysis explored ethical aspects of genetic screening in anticipation of issues it predicted would be raised by large-scale carrier screening for CF. It concluded that the fundamental value of CF carrier screening lies in its potential for providing people with information they consider beneficial for autonomous reproductive decisionmaking (61,62). Nine years ago, the Commission identified some of the same controversies being discussed today.

### *The Human Genome Project*

As the 21st century approaches, Congress and the executive branch have made a commitment to support scientific efforts to determine the location on the DNA of all genes in the human body (as has been done for CF)--in short, to map the human genome. The Human Genome Project is estimated to be a 15-year, $3 billion project. It has been undertaken with the expectation that enhanced knowledge about genetic disorders, increased understanding of gene-environment interactions, and improved genetic diagnoses can advance therapies for the 4,000 or so currently recognized genetic conditions; a premise supported by the fact that even prior to the Human Genome Project, advances in medical genetics have guided the development of new treatment strategies and incrementally improved the management of some genetic conditions over the years (22,23).

In many respects, the Human Genome Project served as the catalyst for congressional interest in this OTA assessment. Despite scientifuc and technological promises of the project, fears have been raised about how information gained from it—such as identification of CF mutations—will be used (37,52,56,57,80). These concerns will involve policy decisions for Congress.

To address gaps in knowledge and perhaps forecast the social consequences of the Human Genome Project, NIH and the Department of Energy (DOE) each fund an Ethical, Legal, and Social Issues (ELSI) Program. Funds for each agency's ELSI effort derive from 3 to 5 percent of appropriations set aside from the total genome initiative budget. In fiscal year 1991, DOE's ELSI spending was $1.44 million (3 percent). Fiscal year 1992 spending is targeted at $1.77 million (3 percent) (26). NIH-ELSI spending for fiscal years 1990 and 1991 was $1.56 million (2.6 percent) and $4.04 million (4.6 percent), respectively. For fiscal year 1992, NIH-ELSI aims to spend 5 percent of the NCHGR appropriation ($4.98 million) (45). Table 2-2 lists the types of efforts that have been funded to date by the ELSI program.

**Table 2-2—Research Grants Funded by the Ethical, Legal, and Social Issues Program, National Institutes of Health and U.S. Department of Energy (May 1991)**

| Source | Description |
|---|---|
| DOE. . . . . | Project to prepare 50 selected science teachers per year for 3 years to become State resource teachers in human genetics. Workshops will also update and expand curriculum materials. |
| DOE. . . . . | Project to examine legal protections of confidentiality y of genetic information and to study the availabilit y of and need to collect genetic data to plan public health service programs. |
| DOE. . . . . | Study to assess the significance of discrimination directed against individuals and family members because of real or perceived differences in their genetic constitution. |
| DOE. . . . . | Project to survey ethical attitudes toward the medical applications of genetic information and to conduct a legal study of confidentiality of genetic data. |
| DOE. . . . . | Report examining the current funding mechanisms in the biological and biomedical sciences of major Federal agencies and private organizations to determine the impact of funding on the ability to recruit and retain young investigators. |
| DOE. . . . . | Eight-part television series, "The Secret of Life." |
| DOE. . . . . | Curriculum development module and instructional activities, "Mapping and Sequencing the Human Genome: Science, Ethics, and Public Policy," for first-year high school biology students. |
| DOE. . . . . | Conference and laboratory workshop for nonscientists drawn from four groups: public policy makers, civic leaders, program officers of health-related foundations, and science journalists. |
| DOE. . . . . | Conference: "Justice and the Human Genome Project." |
| NIH. . . . . | Study, including public education and participation, to determine the impact of the Human Genome Project on women and to identity ways of avoiding or reducing potential gender injustice. |
| NIH. . . . . | Historical analysis of the relevance of eugenics to genomics for the specific case of cancer theory and policy. |
| NIH. . . . . | Study to examine the ethical and legal implications of genetic information on understanding health, normality, and disease causation. |
| NIH. . . . . | Project to develop a human molecular genetics curriculum module for honors, main-stream, and low-achieving high school students and adults in a continuing education program. (Cofunded with the NIH Center for Research Resources.) |
| NIH. . . . . | Series of projects to update and inspire secondary school science teachers in genome technologies and their implications, including newsletter for educators, "hands on" demonstrations to the public and at schools, and workshops. |
| NIH. . . . . | National survey of public knowledge and perceptions of genetic testing and the Human Genome Project. (Cofunded with the National Science Foundation (NSF).) |
| NIH. . . . . | Survey of physicians' and master' s-level genetic counselors' knowledge of and attitudes toward genetic testing. Survey and interview of commercial interests in and impact on human genetics research. |
| NIH. . . . . | U.S.-Canadian survey of geneticists', genetic counselors', and genetic clinic patients' views on a variety of situations in genetics that pose ethical dilemmas. A separate grant involves a survey of geneticists from 34 additional nations about the same situations. |
| NIH. . . . . | Sociological study exploring the meaning of human genetics in popular culture (e.g., fiction, film, news accounts) to understand lay interpretations of genetic concepts. |
| NIH. . . . . | Comparison of feminist, medical, and bioethical analyses of impact of genetic testing on parent-child relationships. (Cofunded with NSF.) |
| NIH. . . . . | Study of the concept of genetic susceptibility y and the basis and limits of privacy of genetic information about individuals. |
| NIH. . . . . | Ethnographic study of the impact of genome research on the social organization of biological science. |
| NIH. . . . . | Report on professional standards for forensic DNA typing. (Cofunded with NSF, Federal Bureau of Investigation.) |
| NIH. . . . . | DNA sequencing of mitochondrial DNA to define the technical and statistical limits of this approach to human identification applications (e.g., identifying victims of accidents, natural disasters, and wars; reuniting separated families; investigating claims of identity; and aiding criminal investigations). |

*(Continued on next page)*

**Table 2-2—Research Grants Funded by the Ethical, Legal, and Social Issues Program, National Institutes of Health and U.S. Department of Energy (May 1991)-(Continued)**

| Source | Description |
|---|---|
| NIH. . . . . | Study of the impact of genetic testing and counseling on medicine and the doctor-patient relationship. |
| NIH. . . . . | Paradigm analysis to develop a comprehensive and systematic framework to resolve ethical issues raised by genomic information in clinical genetics. |
| NIH. . . . . | Study of the historical and social impact of amniocentesis. |
| NIH. . . . . | Study examining historical case studies to examine the potential risks of stigmatization associated with genetic testing, screening, and diagnosis. |
| NIH. . . . . | Interdisciplinary study of the implications for insurance of increasing information from the Human Genome Project. |
| NIH. . . . . | Study of the impact of genetics on access to health care. |
| NIH. . . . . | Historical analysis of the impact of the genetics of human leukocyte antigens on criminology and the genetics of race. |
| NIH. . . . . | Training manual and communication materials to train geneti conunselors to, in turn, conduct courses for primary care providers. |
| NIH. , . . . . . | Intensive short course for scientists and bioethicists on the ethical, legal, and social implications of the Human Genome Project. |
| NIB. . . . . | Education workshop series for State legislators and other State officials. |
| NIB. . . . . | Public lecture series on the ethical, legal, and social implications of the Human Genome Project. |
| NIB. . . . . | Forum for genetic disease support groups on the Human Genome Project and its ethical, legal, and social implications. |
| NIB. . . . . | Eight CF pilot screening projects (six by National Center for Human Genorne Research, Ethical, Legal, and Social Issues Program, and one each by the National Center for Nursing Research and National Institute of Child Health and Human Development.) |
| NIB. . . . . | Conferences: "Strategies for Documentation of Research on the Human Genome," "Human Genome Workshop: Ethics, Law, and Social Policy, ""bgal and Ethical Issues Raised by the Human Genome Project," "A Legal Research Agenda for the Human Genome Initiative," "The Genetic Prism: Understanding Health and Responsibility," "Ethics, Values, Professional Responsibilities," "Biotechnology and the Diagnosis of Genetic Disease," "Testing for Germ Line p53 Mutations in Cancer Families," "Human Genome Research in an Interdependent World," "Ethical and Legal Implications of Genetic Testing," "Computers, Freedom, and Privacy," "The Human Genome Project: A Choices and Challenges Forum," "A Conference on Human Genorne Research Implications," and "Genetic Factors in Crime: Findings, Uses, and Implications." |
| NIH/DOE. . . . . | Conference: "Genetics, Religion, and Ethics." |
| NIH/DOE. . . . . | Project to examine issues of privacy, stigma and discrimination, particularity as they relate to culturally diverse groups--both those who have and have not used genetic services. |
| NIH/DOE. . . . . | Study investigating newborn genetic screening programs and policies governing State-sponsored genetic screening. Minority populations' access to and use of genetic services will be examined, including the nature of services available to rural populations. |
| NIH/DOE. . . . . | Television documentary, "The Future of Medicine." |
| NIH/DOE. . . . . | Report addressing a variet y of issues presented by the rapid proliferation of genetic tests capable of predicting future disease. |

SOURCE: Office of Technology Assessment, 1992.

## THE INTERESTED PARTIES: PRESSURES FOR AND AGAINST SCREENING

Why is carrier screening for CF a controversy? Experts agree that persons with a family history of CF should have the opportunity to avail themselves of the new, DNA-based tests. No one espouses mandatory screening. Who opposes voluntary screening, and on what grounds? Who supports CF carrier screening, and why? Do past experiences with large-scale genetic screening (e.g., maternal serum alpha-fetoprotein, sickle cell, or Tay-Sachs) provide a framework to answer questions raised by routine CF carrier screening? What is the role of genetics in public health (box 2-D)?

Many parties have a stake in resolving questions raised by our increased understanding of human genetic disease, including CF. These stakeholders include consumers, health care providers, and commercial ventures. Also weighing in on the evaluation of the technical, legal, ethical, and economic considerations are experts and professional societies in each of these fields. This section briefly describes the tensions that have arisen and identifies areas

### *Box 2-D---Genetic Screening and the Practice of Public Health*

***In*** some respects, friction over routine carrier screening for CF reflects different notions of public health and its interaction with genetics. What is public health, today? How do genetic testing and screening for CF fit in its practice? Do they fit at all? Does the evolving practice of clinical genetics challenge many common assumptions about the limitations on, and aims of, public health authorities?

Public health is a dynamic field, and its history records struggles over the limits of its mandate. Public health attempts to prevent disease, prolong life, promote physical health through sanitation of the environment, control contagious infections, educate individuals and whole populations about health, and organize medical services for the early diagnosis and preventive treatment of disease. Since it can involve social machinery to ensure maintenance of health (59,69), such institutional mechanisms might sooner or later violate-or be perceived to violate---private beliefs, private property, or the prerogatives of other institutions (73). Today, some public health initiatives, such as quarantine or immunization, are mandatory. Compulsory components, however, are only a narrow slice of what constitutes the practice of public health. There is nothing inherently coercive or mandatory about public health per se: Witness, for example, public education about drug abuse, sanitation, or voluntary cholesterol or blood pressure screening.

Debates surrounding public health issues, such as the spread of infectious disease, often involve an adversarial model focused largely on balancing individual rights against community rights, on the assumption that the two are in conflict (1,60). For public health issues like genetic testing and screening, however, individual interests might be in harmony with public interests, and thus cooperative models of individual and governmental action (3,34,59) could be more appropriate. On the one hand, who better to make the choice of whether to conceive a child with a genetic disorder than the individuals who will both gain from and provide support to the child. At the same time, as the Human Genome Project project continues to identify genetic risks that everyone faces in procreation, genetic diagnosis and counseling becomes an aspect of personal health for the entire community-and hence perhaps governmental action.

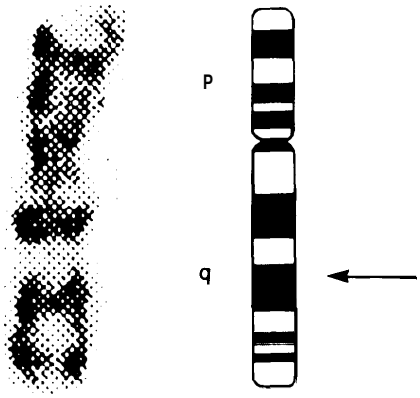
Nevertheless, disputes about the role of public health practices in genetics arise and often adopt polemic tones. The balance between individual freedom, individual responsibility, and government responsibility for health is especially delicate in areas such as carrier screening for CF. If examined from the view of public health measures to control disease, CF and other genetic illnesses are fundamentally different from infectious disease. Unlike familiar public health measures such as vaccination or sanitation policies, CF carrier screening does nothing to protect individuals from the causes of disease, nor does it directly improve personal health. CF carrier screening conveys information about future scenarios—i.e., the potential of CF occurring in one's offspring, not oneself. Viewed negatively from this perspective, some maintain that public health and genetics equate with eugenic motives. Still others take a dim view of a public health role for CF carrier screening, not because of eugenic overtones, but because they believe that consumers are best served by having CF carrier tests available through general medical practice. They argue that formal effort translates to regulated medicine, which they oppose.

Balanced against these perspectives, however, are beliefs of others that public health currently centers on identifying, educating, and counseling individuals and populations about achieving good health. From this perspective, genetic screening falls squarely beneath the public health rubric, which should play an important and appropriate role in CF carrier identification. These voices argue that there is nothing inherently eugenic about the role of public health in genetics. To the contrary, many believe public health's historical tradition with institutional mechanisms and social approaches is appropriate and necessary for quality assurance and consumer protection.

It is easy to see how a formal CF carrier screening policy could be perceived as a form of eugenics if it were assumed that all persons found to be carriers would, or should, act to prevent the birth of a child with a genetic condition. Thus, while some maintain that such is not the case and that the public health goal met by routine CF carrier screening is to provide information and options, others assert that early diagnosis or reducing incidence of genetic illness on a population basis is also an implicit goal. In any case, whether information about carrier status affects the incidence of CF ultimately depends on how individuals use information provided by screening, and reducing incidence of the disorder might not be a goal per se of carrier screening, but could be a consequence.

SOURCE: Office of Technology Assessment, 1992.

**Figure 2-2-Chromosome 7 and the Cystic Fibrosis Gene**




**In humans, DNA is associated with protein, in bundles called chromosomes. Each chromosome contains many genes, but only the chromosomes-which can be ordered in pairs by their size and shape-are microscopically identifiable. Humans have 46 chromosomes: 1 pair of sex chromosomes (two X chromosomes for females; an X and a Y for males) and 22 pairs of autosomes. In 1986, scientists discovered that the CF gene was on chromosome 7. Left: Chromosome 7, as visualized by light microscopy. Right: Schematic of chromosome 7; arrow denotes location of CF gene on the long arm of the chromosome.**

**SOURCE: Office of Technology Assessment, 1992.**

about which concern has been expressed. Subsequent chapters elaborate on and analyze these issues.

### *Scientific and Clinical Tensions*

Elucidation of the location of the CF gene and the most common mutation leading to the condition—commonly referred to as delta F508 (DF508) (figure 2-2) (44,66,68)-has been quickly followed by a widely available, direct-DNA assay for carrier testing and screening. Using today's technology, it is usually a one-time test that can inform an individual whether he or she carries a CF mutation and could thus pass it to his or her offspring (who would be affected if it also received a CF mutation from the other parent). In theory, carrier screening for CF could encompass 100 to 125 million Americans of reproductive age, but will probably involve significantly fewer numbers.

Routine CF carrier screening will likely integrate into medicine in the reproductive context first—chiefly obstetric/prenatal, but also preconceptional. A focus on pregnant women, however, is not without controversy (13,20,48,49). Some have concerns about abortion, and some have reservations that prenatal testing negatively shapes perceptions of pregnancy, disability, and women (48,49). Nevertheless, based on the annual number of births (4.2 million) (31,88) and spontaneous abortions (an estimated 1.8 million) (31), there are approximately 6.0 million pregnancies per year for which CF carrier screening might be performed. Twenty-four percent of women giving birth receive no prenatal care until the third trimester (88), however, so CF carrier screening in the obstetric/prenatal context would involve, at most, 10 million[2] men and women per year, depending on who is screened. Followup carrier screening that focused on relatives of people identified as carriers initially, rather than mass screening, also significantly reduces the number who theoretically must be screened to identify a majority of carriers (24).

The current test, however, leaves ambiguity when results are negative. About 1 in 25 Caucasians carry a CF mutation, but the DF508 test identifies only 70 to 80 percent of actual CF carriers[3] in this population, depending on a person's ethnicity (30,47). More than 170 additional genetic alterations in the gene also cause CF—i.e., a person with CF can have the same mutation on his or her chromosomes or two different mutations. Assays using DF508 plus 6 to 12 other CF mutations (DF508+6-12) identify 85 to 90 percent of CF carriers, depending on the population being screened (21,58). (In Ashkenazic Jews, DF508+6 identifies nearly 95 percent of carriers (71).) Thus, a negative test result does not guarantee that a person is not a carrier. He or she could carry one of the rare CF mutations that was not assayed and hence still be a carrier. For a test that detects 85 percent of carriers, about 1 in 165 individuals who test negative using DF508+6-12 will have an undetected mutation; at 90 percent sensitivity, 1 in 246 individuals who test negative will be a carrier (47).

[2] This figure does not account for the estimated 2.4 million infertile couples who are trying to conceive and might be interested in CF carrier screening (would increase overall figure). Nor does it estimate the number of men and women not involved in a pregnancy (would increase), the number of individuals involved in more than one conception per year (would decrease), or those who might have been screened during a previous pregnancy (would decrease).

[3] It should be emphasized that the ΔF508 DNA-based test is not 70 to 80 percent accurate. Evidence indicates that the test per se is specific, and that DNA tests yield accuracy greater than 99 percent (1 1,46). That is, if the ΔF508 mutation is present in the individual's genome, the test detects it, absent laboratory error. Like all diagnostic tests, a certain number of false positive or false negatives can arise during the course of testing. Quality control and quality assurance, discussed in chapter 5, are designed to reduce this number to a small figure.

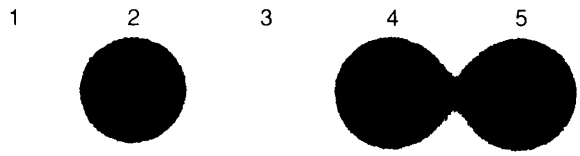



Photo credit: IG Laboratories, Inc.

**DNA analysis for the most common mutation responsible** for CF, DF508. **A dot indicates the individual has a DF508 mutation. The absence of a dot means the person does not have a DF508 mutation, but he or she could carry one of the other 170+ CF mutations.**

Couples where each partner is a carrier are sometimes referred to as carrier couples, or couples who are positive/positive (+/+). For these couples, the chance of having a child with CF is 1 in 4 for each pregnancy. If the CF test detected 100 percent of mutations, a couple in which one partner is positive and one negative (+/-) would not beat risk of bearing a child with CF. Tests to detect 170+ mutations are impractical, however, and even if they were feasible, not all CF mutations have been identified. Using DF508+6- 12 means that for +/-couples, the negative partner could carry one of the rare mutations that the assay is not structured to detect. Couples where one partner is a carrier and the other's result is negative might misunderstand that their reduced risk is not zero risk.

For example, if 100,000 random couples were screened, 160 couples would be identified as +/+ if the test were 100 percent sensitive; one-fourth of frost-time pregnanices for these 160 couples (i.e., 40) would be expected to result in CF-affected fetuses. Instead, at 85 percent sensitivity, about 116 couples will be identified as +/+ and with each pregnancy have a 1 in 4 risk of a child with CF. Results for 93,315 will be -/-, and about 6,569 couples will have +/- results. In fact, approximately 41 of the 6,569 couples with +/- results are at 1 in 4 risk of bearing a child with CF in each pregnancy, while the remaining 6,528 have no risk-but these two groups cannot be distinguished with an 85 percent test sensitivity (6,47).

About 4 of the 93,315 couples with -/- test results are also actually at 1 in 4 risk with each pregnancy of having a child with CF. Thus, of the theoretical 160 +/+ couples, 116 are dectable and 44 are not when the test is 85 percent sensitive. In other words, if all 100,000 couples experience a first-time pregnancy, 40 fetuses with CF are expected. But with an

**Table 2-3-Test Sensitivity and Risk of Child With Cystic Fibrosis**

| Percent mutations detected | Couples at 1 in 4 risk with each pregnancy | | | | Affected fetuses in first pregnancy | | |
|---|---|---|---|---|---|---|---|
| | Actual | +/+[b] | +/h | -/-[b] | Actual | Detectable | Missed |
| 85 | 160 | 115.6 | 40.8 | 3.6 | 40 | 28.9 | 11.1 |
| **90** | **160** | **129.6** | **28.8** | **1.6** | **40** | **32.4** | **7.6** |
| **95** | **160** | **144.4** | **15.2** | **0.4** | **40** | **36.1** | **3.9** |

[a] per 100,000 couples.
[b] Test results.

**SOURCE: A.L. Beaudet, Howard Hughes Medical Institute, Houston, TX, personal communication, March 1992.**

*85* percent sensitive test, 29 are detectable and 11 missed. If the assay elucidates 95 percent of carriers, 144 of 160 couples would be detected. In this case, if all 100,000 couples experience a frost-time pregnancy, only 4 couples at 1 in 4 risk of having a child with CF would be missed (table 2-3) (4,6).

With a test that detects 85 percent of CF carriers, a couple with a +/- result has approximately a 1 in 661 risk of having an affected child with each pregnancy (compared to a general population frequency of about 1 in 2,500). At a 95 percent detection rate, a couple whose result is +/- faces a 1 in 1,964 risk of an newborn with CF with each pregnancy (47). When the test detects a greater proportion of mutations, +/- couples can be told with greater confidence that their risk of having a child with CF is more remote; hence they might be less anxious about uncertainty. Couples who both test negative, while not having zero risk, would have a 1 in 109,200 risk of an affected child with each pregnancy (85 percent sensitivity) (47).

Some scientists, clinicians, and organizations argue that even achieving detection levels of 90 to 95 percent is insufficient to justify routine CF carrier screening-that other requirements must be met (4,7,12,18,29,32,41,54,93). They assert that CF mutation tests are appropriate only for testing individuals or families with a known history of CF or in pilot projects. Another view holds that individuals should not be advised about CF carrier screening, but for those who actively seek it and who receive sufficient education and counseling, screening is acceptable (42). Others, while also advocating pilot studies, believe the current state-of-the-art is sufficient for the test to now be offered routinely to persons of unknown risk during the course of general or obstetric/prenatal care (5,12,14,33,65,70). The latter proponents argue that consumers should be informed about the test and be given an opportunity

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to choose whether to take it or not. Related to the issue of informing individuals about CF carrier assays is concern on the part of some physicians that withholding information about their availability leaves them vulnerable to malpractice suits.

### *Social Pressures*

Science is so much a part of society that it is no longer useful, or helpful, to consider its impact in isolation (36). While CF carrier screening is first a question of science, it is also a question of personal values (28). Not surprisingly, then, pressures for and against CF carrier screening do not center solely on scientific issues. Intertwined are matters of law, ethics, and economics. Compelling arguments that assess, weigh, and consider these factors are being made for and against routine CF carrier screening, This section briefly touches on the social pressures involved; the ensuing chapters analyze them in greater detail.

For some questions, the debate is highly charged, emotional, and divisive+. g., prenatal testing and the option of abortion. The extraordinary tensions in the United States about abortion affect, to a certain extent, the analysis of the implications of CF carrier testing and screening. A couple where both partners are positive for DF508+6-12 can undergo prenatal testing to determine whether the fetus will have CF. The Cystic Fibrosis Foundation, for example, divorces itself from the CF carrier screening debate, and the abortion issue apparently played a major role in this policy (67). Nevertheless, although abortion tinges the debate, reproductive aspects of CF carrier screening encompass broader choices, including avoiding conception, seeking adoption, or choosing artificial insemination by donor.

Another concern expressed by opponents of CF carrier screening is that market pressures will drive widespread use of tests before the potential for discrimination or stigmatization by other individuals or institutions (e.g., employers and insurers) is assessed (8,15,93). This view contends that commercialization and advertising will lead some to opt for screening without fully realizing the implications of, for example, insurance considerations. On the other hand, patient demand is a major element of market forces. Thus, some point out that commercialization of genetic tests is not the factor responsible for increased interest in genetic assays, but rather

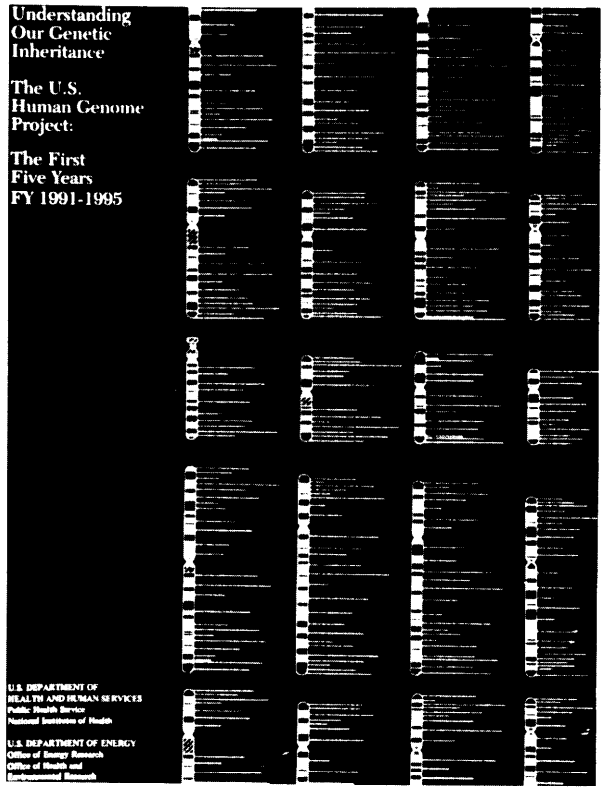



*Photo credit: Office of Tehnology Assessment*

**Five-year plan for the U.S. Human Genome Project, jointly funded by the U.S. Department of Health and Human Services and the U.S. Department of Energy.**

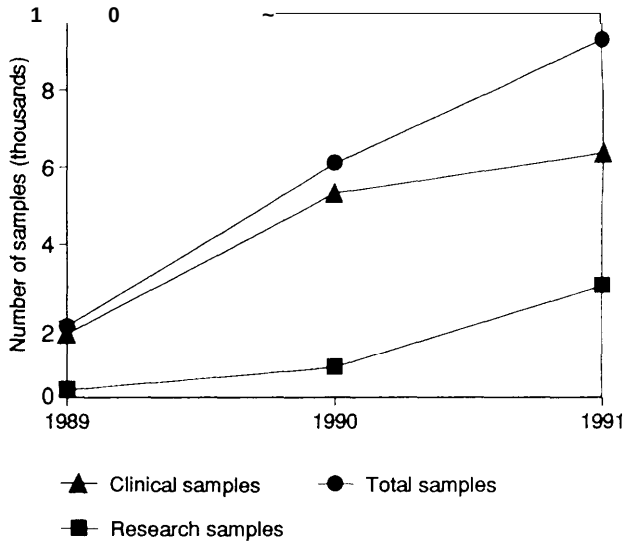
that commercialization is the response to public demand.

Because the price to consumers for CF tests averages about $170 per test, opponents also raise questions about costs. While some clients can afford out-of-pocket payments for CF carrier assays, issues of access arise for those who cannot pay but wish to use the tests. Moreover, even with less expensive tests, CF assays, like all diagnostic tests, are subject to limitations defined by laboratory quality control and quality assurance. Thus, what standards should prevail? How should quality be monitored? Finally, opponents of widespread CF carrier screening ask: How can the limited genetic services delivery system in the United States handle the swell of CF carrier screening cases, let alone cases of other genetic conditions arising from increased knowledge from the Human Genome Project? These voices express concern on both quantitative and qualitative fronts: that inadequate numbers of personnel exist (93) and that optimal methods for

educating and counseling related to CF carrier screening need definition for those personnel who are available (40).

Those who advocate CF carrier tests for use beyond affected families are no less concerned about the issues just raised. Rather, proponents argue on other legal and ethical grounds that screening should move forward and individuals routinely informed about the assays so they can voluntarily choose to avail themselves of the tests (12,33,65,70). They assert that the tests are sensitive enough for current use and will, like most tests, continually improve. Since 80 percent of babies born with CF are to couples with no previous family history (42), these voices believe that failing to inform patients now about the availability of CF carrier assays denies people the opportunity to make personal choices about their reproductive futures, either prospectively---e.g., by avoiding conception, choosing to adopt, or using artificial insemination by donor--or by using prenatal testing to determine whether a fetus is affected.

**Figure 2-3-Trends in the Number of Samples Screened for Cystic Fibrosis Carrier Status, 1989-91**




SOURCE: Office of Technology Assessment, 1992.

## THE OTA ASSESSMENT

For years, scientists, clinicians, lawyers, ethicists, and policymakers theorized about the potential consequences that increased knowledge of human genetics would bring. In the early 1990s, CF mutation tests move the debate from the theoretical to the practical. With this report, OTA assesses both the current technical capability of direct, DNA-based tests to detect mutations in the CF gene and what this capability means for individuals and society.

For some, the key question hovering over routine carrier screening for CF is if, not when. For others, the debate has shifted to when, not if. Without making judgment on its appropriateness or inappropriateness, OTA finds that the matter of CF carrier screening in the United States is one of when, not if. The expansion in the number of tests for CF carrier status will likely continue (figure 2-3); OTA estimates that as many as 63,000 individuals could be screened for their CF carrier status in 1992. A rapid upward trend is not entirely unexpected, however, given the nascent stage of the technology's movement into U.S. medical practice. What is unclear is the extent to which its integration will be sustained.

Regardless of the number of individuals actually screened, it is clear that, increasingly, patients will be informed about the availability of CF carrier assays and a proportion will opt to be screened. Nevertheless, the timeframe for physicians to begin routinely informing patients about CF carrier tests is uncertain. It could be within a year or two, but more likely will be a gradual process over several years—time enough, perhaps, for policymakers to address the issues raised by this report.

Leaving the precise timing of CF carrier screening aside, the number of DNA-based tests for genetic disorders and predispositions unquestionably will increase rapidly over the next decade, almost certainly by an order of magnitude. OTA considers it likely that the time available, if any, for debate and discussion on dissemination and use of new genetic tests will be compressed, as pressure to use them rises. Given this scenario, some of the policy questions raised in this report extend beyond implications for CF carrier screening.

[4]This number is based on a canvas of 41 facilities performing CF mutation analysis (30 responding) and tests performed in federally and privately funded pilot studies. It underestimates the number of individuals who will be informed about CF carrier screening, since: not all who are informed agree (o screening, standards of care will evolve, and not all facilities responded.

### *OTA Surveys*

*In* collecting information for this assessment, OTA found specific details were needed to answer questions about two areas covered by the report:

- What are the attitudes of genetic counselors and nurses in genetics toward CF carrier testing and screening? To date, what have been their experiences with CF mutation analyses? What are their current caseloads and what changes do they expect with routine CF carrier screening? Have their patients had difficulties with health insurance coverage due to results from genetic tests?
- What are the attitudes and policies of health insurers toward genetic testing and screening for CF carriers? Do these differ by provider type, i.e., commercial health insurers, Blue Cross/Blue Shield (BC/BS) plans, and health maintenance organizations (HMOs)? How does genetic information, including information from genetic assays, affect underwriting? What role do they envision for genetic tests in their future business practices?

OTA addressed these questions by conducting mail surveys. First, OTA surveyed the June 1991 members of the National Society of Genetic Counselors and the International Society of Nurses in Genetics. OTA focused on genetic counselors and nurses in genetics to avoid duplication with, and to compare its results to, other surveys of medical and clinical geneticists (38,91). A separate background paper describes this survey's approach and presents data OTA collected that are not directly related to CF carrier screening (86).

Second, to address questions related to practices and attitudes toward genetic information for individual health insurance policies or medically underwritten groups, OTA sent tailored questionnaires to three survey populations: medical directors of commercial insurers; medical directors and chief underwriters of all BC/BS plans; and medical directors at the 50 largest HMOs, largest HMO within a State, or largest by HMO model type. This report summarizes these data and examines their implications for the policy issues surrounding carrier screening for CF. As with the results from the genetic counselors/nurses in genetics survey, a separate OTA background paper describes this survey's methods and results in greater detail (87).

**Table 2-4-Public Attitudes About Making Genetic Tests Available Through Physicians**

**Question:** If there were genetic tests that would tell a person whether they or their children would be likely to have serious or fatal genetic diseases, would you approve or disapprove of making those tests available through a physician?

| | Percent[a] |
|---|---|
| Approve | 89 |
| Disapprove | 9 |
| Not sure | 2 |

[a] Percentages are presented as weighted sample estimates. The unweighted base from which the sampling variance can be calculated is 1,273.

SOURCE: Office of Technology Assessment, *New Developments in Biotechnology: Public Perceptions of Biotechnology*, OTA-BP-BA-45 (Washington, DC: U.S. Government Printing Office, May 1987).

Paralleling the paucity of information about counselors' and insurers' attitudes toward genetic testing and screening is our lack of knowledge about how consumers view these practices today. A new OTA survey of Americans' attitudes toward genetic testing and screening was not feasible for this report, however. Nor was a comparative analysis possible of the views of the general population versus CF-affected individuals or families. Other studies, however, have surveyed certain aspects of consumer attitudes toward prenatal diagnosis of CF (43,92) and neonatal and carrier screening for CF (19).

A 1986 OTA telephone survey (77) of a national probability sample of adult Americans reported that about 9 of 10 Americans approved of making genetic testing available through doctors (table 2-4). Furthermore, 83 percent of respondents reported they would take a genetic test before having children if such a test would tell them whether their children would probably inherit a fatal genetic disease (table 2-5). Survey respondents were not, however, specifically questioned about CF.

An independent survey in 1990 queried Americans about their attitudes toward genetic tests in a different manner, but found overall public opinion toward them was favorable. Sixty-six percent of respondents believed ''genetic screening will do more good than harm. Even when informed as part of a question that treatment was impossible for most serious genetic conditions despite the availability of prenatal diagnosis, 69 percent said they would want prenatal testing if they (or their partner) were pregnant (72).

**Table 2-5—Consumer Attitudes Toward Genetic Tests**

| Question: If genetic tests become available that would indicate whether or not it was likely that your children would inherit a fatal genetic disease, would you personally take such a test before having children or not? | Percent[a] |
|---|---|
| Would take test. . . . . | 83 |
| Would not take test. . . . . | 15 |
| Not sure. . . . . | 3 |

[a] Percentages are presented as weighted sample estimates. The unweighted base from which the sampling variance can be calculated is 1,273. Percentages do not add to 100 due to rounding.

SOURCE: Office of Technology Assessment, *New Developments in Biotechnology: Public Perceptions of Biotechnology*, OTA-BP-BA-45 (Washington, DC: U.S. Government Printing Office, May 1987).

### *Scope and Organization of This Report*

As mentioned earlier, the primary focus of this report is the implications of routine carrier screening for CF. Secondarily, the report analyzes the appropriateness of using CF as a model for policy decisions raised by tests for other genetic conditions: To what extent is there an algorithm that describes the policy implications of the broad array of current and potential genetic tests? Where possible, the report analyzes how experiences with CF carrier screening can be used to construct a generic set of policy issues. Conversely, where concerns and possible solutions for CF carrier screening are inappropriate or less relevant, the report identifies these areas.

To provide a perspective on CF, medical information about the disease—its diagnosis, its therapy, and its prognosis-is presented in chapter 3. To set the stage for the legal, economic, social, and policy analyses of CF carrier screening, chapter 4 describes the genetics of CF: It covers the technical basis for—and limitations of—DNA tests for CF mutations. Chapters 5 through 9 analyze five key aspects of CF mutation analysis: quality assurance, education and counseling facets, financing, social and legal dimensions of discrimination issues, and costs and cost-effectiveness. CF carrier screening programs in the United Kingdom are described in chapter 10, which also analyzes if lessons learned from these efforts can aid decisionmaking in the United States. Appendixes A and B describe the international epidemiology of CF mutations and case studies of other carrier screening efforts, respectively.

This report does not present an ethical analysis per se of the implications of routine CF carrier screening because the fundamental principles identified in the 1983 President's Commission report remain unchanged (61,62). And although the boundary of this report encompasses carrier screening for CF, previous OTA reports analyze other issues related to new genetic technologies, including: genetic monitoring and screening in the workplace, the implications of the Human Genome Project, the commercial development of tests for human genetic disorders, human gene therapy, forensic uses of DNA tests, and technologies to detect heritable mutations (74-77, 79,80,83-85). Finally, detailed analyses of allied issues, such as safety and efficacy of amniocentesis, prenatal care and pregnancy management (78), termination of pregnancy, and assisted conception (81,82) are beyond the scope of this report.

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