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DEPARTMENT OF HEALTH & HUMAN SERVICES

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Elke Jordan, Ph.D.
Deputy Director
Office of the Director
National Human Genome Research Institute
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Dear Dr. Jordan:

Enclosed is the final version of the consensus statement on Genetic Testing for Cystic Fibrosis. We plan to have it printed by the Government Printing Office, and as you know, the statement has been submitted to a major medical journal for possible publication.

The printed version of the statement will be mailed to you as soon as it is available.

Sincerely,

William H. Hall
Director of Communications
Office of Medical Applications
of Research

Enclosure

NATIONAL INSTITUTES OF HEALTH

CONSENSUS DEVELOPMENT CONFERENCE STATEMENT

GENETIC TESTING FOR CYSTIC FIBROSIS

April 14–16, 1997

NIH Consensus Statements are prepared by a nonadvocate, non-Federal panel of experts, based on (1) presentations by investigators working in areas relevant to the consensus questions during a 2-day public session; (2) questions and statements from conference attendees during open discussion periods that are part of the public session; and (3) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the NIH or the Federal Government.

Abstract

Objective. To provide health care providers, patients, and the general public with a responsible assessment of the optimal practices for genetic testing for cystic fibrosis (CF).

Participants. A non-Federal, nonadvocate, 14-member panel representing the fields of genetics, obstetrics, internal medicine, nursing, social work, epidemiology, pediatrics, psychiatry, genetic counseling, bioethics, health economics, health services research, law, and the public. In addition, 21 experts from these same fields presented data to the panel and a conference audience of 500.

Evidence. The literature was searched through Medline and an extensive bibliography of references was provided to the panel and the conference audience. Experts prepared abstracts with relevant citations from the literature. Scientific evidence was given precedence over clinical anecdotal experience.

Consensus Process. The panel, answering predefined questions, developed its conclusions based on the scientific evidence presented in open forum and the scientific literature. The panel composed a draft statement that was read in its entirety and circulated to the experts and the audience for comment. Thereafter, the panel resolved conflicting recommendations and released a revised statement at the end of the conference. The panel finalized the revisions within a few weeks after the conference.

Conclusions. Genetic testing for CF should be offered to adults with a positive family history of CF, to partners of people with CF, to couples currently planning a pregnancy, and to couples seeking prenatal testing. The panel does not recommend offering CF genetic testing to the general population or newborn infants. The panel advocates active research to develop improved treatments for people with CF and continued investigation into the understanding of the pathophysiology of the disease. Comprehensive educational programs targeted to health care professionals and the public should be developed using input from people living with CF and their families and from people from diverse racial and ethnic groups. Additionally, genetic counseling services must be accurate and provide balanced information to afford individuals the opportunity to make autonomous decisions. Every attempt should be made to protect individual

rights, genetic and medical privacy rights, and to prevent discrimination and stigmatization. It is essential that the offering of CF carrier testing be phased in over a period of time to ensure that adequate education and appropriate genetic testing and counseling services are available to all persons being tested.

Introduction

Genetic testing is available for a variety of diseases and will soon be available for many more. Furthermore, genetic predispositions to common diseases are becoming known and potentially will affect large segments of the population. This consensus conference considered cystic fibrosis (CF), a well-characterized, serious genetic disease for which testing is becoming available, and a series of recommendations for genetic testing in the population is presented. The analysis and recommendations may prove relevant to genetic testing in other situations.

At the beginning of this decade, a test was developed that could identify individuals who carry the genetic mutation associated with CF. Concerned that this test might be inappropriately or prematurely used, several genetic and health professional organizations issued recommendations on its use. These groups considered the circumstances under which the tests should be offered and the populations that would potentially benefit. Almost all of their recommendations were against using the test for large-scale, population-based screening until more sensitive tests were developed and until more had been learned about the risks and benefits of genetic testing for individuals and their families. Several statements called for additional support for research on the educational, laboratory, counseling, ethical, and cost/benefit issues associated with the delivery of population-based screening for CF. Since that time, new research has yielded a large body of data on these issues.

This conference brought together the research investigators, health care providers, epidemiologists, geneticists, ethicists, and other experts, as well as representatives of the public, to present and discuss the latest data.

Following 1-1/2 days of presentations by experts and audience discussion, an independent, non-Federal consensus panel composed of experts in the fields of genetics, obstetrics, internal medicine, nursing, social work, epidemiology, pediatrics, psychiatry, genetic counseling, bioethics, health economics, health services research, law, and the public weighed the scientific evidence and developed a draft statement in response to the following five key questions:

1. What is the current state of knowledge regarding natural history, epidemiology, genotype-phenotype correlations, treatment, and genetic testing of cystic fibrosis in various populations?

2. What has been learned about genetic testing for cystic fibrosis regarding (public and health professional) knowledge and attitudes, interest and demand, risks and benefits, effectiveness, cost, and impact?

3. Should cystic fibrosis carrier testing be offered to: (1) individuals with a family history of cystic fibrosis; (2) adults in the preconception or prenatal period; and/or (3) the general population?

4. What are the optimal practices for cystic fibrosis genetic testing (setting, timing, and the practices of education, consent, and counseling)?

5. What should be the future directions for research relevant to genetic testing for cystic fibrosis and, more broadly, for research and health policies related to genetic testing?

The primary sponsors of this meeting were the National Human Genome Research Institute and the NIH Office of Medical Applications of Research. The conference was cosponsored by the National Institute of Diabetes and Digestive and Kidney Diseases; the National Heart, Lung, and Blood Institute; the National Institute of Child Health and Human Development; the NIH Office of Rare Diseases; the National Institute of Mental Health; the National Institute of Nursing Research; the NIH Office of Research on Women's Health; the Agency for Health Care Policy and Research; and the Centers for Disease Control and Prevention.

1. What Is the Current State of Knowledge Regarding Natural History, Epidemiology, Genotype-Phenotype Correlations, Treatment, and Genetic Testing of Cystic Fibrosis in Various Populations?

CF is a multisystem genetic disease in which defective chloride transport across membranes causes dehydrated secretions. This leads to tenacious mucus in the lungs, to mucus plugs in the pancreas, and to the characteristically high sweat chloride levels. Intelligence and cognitive function are typically normal. A survey in 1995 reported that 35 percent of young adults with CF worked full-time, and almost 90 percent had completed a high school education. More than 25,000 Americans have CF, with approximately 850 individuals newly diagnosed each year. CF is inherited as an autosomal recessive disorder; the responsible gene, the CF transmembrane conductance regulator (CFTR), was mapped to chromosome 7 and identified in 1989.

Natural History

CF has a highly variable presentation and course. Median age at diagnosis is 6–8 months; nearly two-thirds of individuals are diagnosed before 1 year of age. Some individuals have severe pulmonary and/or gastrointestinal disease, whereas others have relatively mild disease with presentation during adolescence and young adulthood. Outcomes range from early death from pulmonary complications to mild atypical disease in the second and third decades, and a rare normal length of life. Even though median survival increased from 18 years in 1976 to 30.1 years in 1995, there has been little life-span extension between 1990 and 1995. Survival has improved, thus far, through aggressive management of pulmonary, pancreatic, and intestinal complications. Despite advances in treatment, there is no cure for CF.

Severity of lung disease is the key to the quality of and length of life. Ninety percent of persons who have CF die from pulmonary complications. Pulmonary function tests, especially forced expiratory volume (FEV_1), are predictive of mortality: when the FEV_1 is $\leq$30 percent, mortality is 50 percent in 2 years. Poor prognosis is related to respiratory complications before 1 year of age, malnutrition, and denial of the condition. Better prognosis is indicated from mild symptoms at diagnosis, pancreatic sufficiency, and atypical presentation. There are suggestions in the literature that early diagnosis and treatment may result in improved growth of young children; however, data are limited about whether early treatment decreases morbidity as measured by hospitalizations and pulmonary function tests and, ultimately, mortality rates.

Treatment

The major goals of traditional treatment of CF are to improve pulmonary, gastrointestinal, and pancreatic outcomes. Pulmonary treatment is focused on physical therapy to decrease obstruction of the airways, antibiotics to decrease colonization by *Staphylococcus aureus* and *Pseudomonas aeruginosa,* and nonsteroidal anti-inflammatory drugs to decrease the inflammatory cascade and resulting tissue damage. Gastrointestinal and pancreatic treatments include high protein–high caloric diets, pancreatic enzymes, and fat-soluble vitamins.

New modalities include the use of inhaled DNase, which breaks down the DNA from neutrophils, and pharmacologic modification of ion transport to loosen secretions. Pharmacologic activation of mutant CFTR protein to stimulate chloride channel activity is being investigated. Double lung transplantation extends life, but is not curative.

There are new findings regarding human beta defensin-1, a factor responsible for innate immunity. The natural bactericidal activity of human beta defensin-1 is inhibited on CF epithelia because of high extracellular sodium chloride, and correction of the sodium chloride concentration of extracellular fluid holds promise for therapy in CF. Finally, although the feasibility of gene therapy is currently under investigation, this potential "cure" is not anticipated in the near future.

Epidemiology

Incidence

CF is one of the most common genetic diseases in Caucasians, with an incidence of about 1 in 3,300. The disease also has a fairly high incidence among Hispanics, 1 in 9,500. CF is a rare disorder in native Africans and native Asians, estimated to occur in less than 1 in 50,000, but higher incidences are observed in American populations of these ethnic groups (1 in 15,300 and 1 in 32,100, respectively), suggesting Caucasian admixture. Recent surveys of some Native-American populations also indicate high incidences: 1 in 3,970 in the Pueblo people, and 1 in 1,580 among the Zuni. These data are summarized in Table 1. The relatively high incidence and concomitant high frequency of carriers motivate the proposal of population-based screening.

CF Mutation Analysis

Since the identification of the gene and the major mutation responsible for CF, more than 600 mutations and DNA sequence variations have been identified in the CFTR gene. The ΔF508 mutation is represented in almost all populations, although its relative frequency varies among different geographic locations. The highest frequency is observed in Caucasian populations, where it accounts for approximately 70 percent of the CF alleles (Table 1). ΔF508 mutation

TABLE 1

Group	Incidence	Carrier Frequency	% ΔF508	% Common Caucasian Alleles	% Group-Specific Alleles	Sensitivity
Caucasians	1/3,300	1/29	70	13	–	80
Hispanics	1/8–9,000	1/46	46	11	–	57
Ashkenazi Jews		1/29	30	67	–	97
Native Americans	1/3,970 1/1,500		0	25	69	94
African-Americans	1/15,300	1/60–65	48	4	23	75
Asian-Americans	1/32,100	1/90	30			30

Source: Modified from Cutting GR. Genetic epidemiology and genotype/phenotype correlations. In: Program and abstracts. NIH Consensus Development Conference on Genetic Testing for Cystic Fibrosis, 1997 Apr 14-16, Bethesda, MD.

accounts for large portions of the alleles in other racial/ethnic groups: 48 percent in African-Americans, 46 percent in Hispanics, and 30 percent in Asian-Americans and Ashkenazi Jews. Some 15–20 other "common" mutations account for 2–15 percent of CF alleles, depending on the ethnic composition of the patient group studied. Most of the remaining mutations are rare.

The proportion of detectable mutations is an important indicator of the utility of a population-screening program. Combining detection of the ΔF508 with other mutations common to specific ethnic groups, it appears that there are several populations for which 90–95 percent sensitivity can now be achieved with the current technology: Ashkenazi Jews, Celtic Bretons, French Canadians from Quebec, and some Native Americans. In Caucasians in the United States, it is feasible to approach 90 percent sensitivity at the current time. The detection rate in African-Americans is about 75 percent. Despite the relatively high incidence in Hispanics, the detectable alleles account for only 57 percent of the CF mutations in this group. The promise appears to be weak in Asian-Americans, at 30 percent sensitivity. Because the remaining mutations are rare, expanding the panel of screened mutations is expected to achieve only marginal gains in sensitivity.

Genotype-Phenotype Correlations

The discovery of the gene has enabled evaluation of specific mutations in relation to the observed clinical heterogeneity. The correlation of genotype with phenotype is substantial for pancreatic function; however, identification of the specific CFTR mutation has not been highly predictive of the severity and course of pulmonary disease, which is the major factor affecting patient quality of life and longevity. Furthermore, there is evidence to suggest a role for modifier genes and environmental factors that are as yet unidentified.

Virtually all males with classic CF have congenital bilateral absence of the vas deferens (CBAVD). However, there is a population of otherwise healthy males with CBAVD who have a high frequency of CF mutations. It appears that more than half of these males have one or two specific mutations, which identifies these genotypes as the most common cause of CBAVD. Some women with these genotypes are normal or develop chronic sinusitis or bronchitis as the extent of their morbidity. It is unclear whether such mildly affected individuals can be reliably identified by their genotype.

Thus, it appears that knowledge of the genotype is as yet of limited value in making predictions about the anticipated course of disease in an individual, although research to identify genotypes associated with relatively mild presentation such as CBAVD may prove useful in informed decisionmaking.

Genetic Testing in Various Populations

Genetic testing has been performed for CF carriers in various racial and ethnic groups, mass and focused screening, and different types of organized medical settings. At this time, there is limited spontaneous public request for this testing. Although testing has not met with enthusiasm, there has been little or no group opposition to offering testing to African-Americans, Asian-Americans, Caucasians, Hispanics, Native Americans, and persons of Jewish ancestry. Most experience has been gained with Caucasians and Ashkenazi Jews, where incidence is highest. Mass screening has resulted in the least response. Pregnant patients appear to be motivated to obtain genetic information. Nonpregnant patients and those with a family history have exhibited only moderate acceptance rates. In the United States, mass screening of newborns has occurred in only two states, Colorado and Wisconsin; otherwise, newborn testing has been limited to those with a family history. The logistics of testing have been successfully implemented in various settings such as HMOs and primary care settings, including fee-for-service settings. With the exception of one fee-for-service setting and the newborn state

programs, all testing has been free of charge. Direct provider recruitment has proven more effective than less personal approaches.

2. What Has Been Learned about Genetic Testing for Cystic Fibrosis Regarding (Public and Health Professional) Knowledge and Attitudes, Interest and Demand, Risks and Benefits, Effectiveness, Cost, and Impact?

Knowledge and Attitudes Toward Cystic Fibrosis and Genetic Testing

As with most genetic diseases, the public's knowledge is very low regarding CF, its genetic basis, and its variable course and prognosis, and understanding of genetic testing is poor. Moreover, among those who have heard of CF, inaccurate impressions often exist, because people are generally not familiar with the progress in treating the disease over the past 40 years. Understanding genetic testing for CF involves learning complex concepts such as test sensitivity, carrier status, patterns of inheritance, risk/probability, and genotype-phenotype correlations. These gaps in the public's genetic knowledge suggest that genetic testing programs must include written informed consent and educational and counseling components.

There are only approximately 2,000 genetic professionals nationally, so implementation of widespread genetic testing must rely heavily on primary care providers and prenatal providers. Some research efforts, however, have shown that many office-based physicians are not interested in participating in genetic testing programs involving CF because of lack of familiarity and concerns with unreimbursed time. Medical practitioners need to become more knowledgeable about genetics, genetic testing, and nondirective counseling as genetic tests become more widely available.

Public Interest and Demand

Notwithstanding the limits of public understanding of genetics and genetically related diseases, prospective parents have enormous interest in the health and well-being of children to be. In an Office of Technology Assessment survey of a decade ago, 83 percent of Americans said they would take a genetic test before having children, if it would tell them whether their children would likely inherit a fatal genetic disease. Many genetic counselors and nurse geneticists report that they are frequently asked about DNA-based CF tests. However, studies have shown that interest in CF genetic testing is limited in the general population, and that agreement to participate in genetic education and testing procedures occurs primarily among pregnant women and persons with positive family histories.

In the prenatal testing context, participation rates have varied widely in studies to date because of variability of methods used, with acceptance of offers for testing ranging from about 50 percent to a high of 78 percent in one HMO population. Participation has been affected by factors relating to convenience, education, cost, views regarding abortion, concerns about the low sensitivity of the test, and the manner of presentation of the testing opportunity. Concerns about confidentiality and insurability are often mentioned in the genetic testing context. There also is evidence of reluctance to engage in carrier testing on the psychological grounds of "not wanting to know," as has occurred in studies where some people with positive family histories chose not to participate.

The reasons for interest in prenatal genetic testing are diverse. Some participants in studies have sought information in anticipation of a decision about pregnancy termination in the case of a fetus with CF. Others wished to know only their carrier status, perhaps to make emotional and practical plans for parenting a child with CF.

Risks

Research has assessed initial concerns among providers of genetic services that genetic testing might have adverse psychological consequences, such as anxiety and depression caused by the difficulty of conveying the uncertainties inherent in genetic testing or the challenge of adjusting to identification as a carrier. The research to date has shown such problems to be transitory; the topic, nevertheless, may warrant additional research incorporating comprehensive psychological assessment tools. The risks of misinformation or misunderstanding highlight the need for a high level of competence in conveying the results and meaning of information derived from genetic testing. Problems retaining complex genetic concepts highlight the need for broad-based public education.

Another concern is the fear that disclosure of genetic test results might affect one's family relationships, employment, educational or other opportunities, or ability to maintain or obtain health insurance. This is a more general problem and needs to be addressed at a broader level to ensure patient access to genetic services and other opportunities without threat of harmful consequences.

Impact and Effectiveness

The effectiveness of genetic testing can be judged in terms of its ability to convey information that patients find useful. The experience to date reports high levels of patient satisfaction after undergoing genetic testing for CF. In the prenatal situation, because of the rarity of the disease, over 99 percent of couples tested receive reassuring information regarding the improbability of having a child with CF.

Several studies have reported significant increases in knowledge of CF among couples who have undergone genetic testing and participated in the educational programs connected with it. Although there was some drop in knowledge after several years, knowledge levels still were higher than in the pretesting period. A decline in understanding has been reported in some research, where a considerable portion of the individuals who were carriers did not retain the meaning of the test results. In some instances, this meant that people incorrectly believed they were no longer at risk for having offspring with CF.

In addition to the educational and psychological benefits of CF testing, the effectiveness of testing can be judged in terms of how the information is used. This is most germane in situations in which a test produced a positive result. Most couples in whom the woman was found to be a carrier chose to have the partner tested as well. The inability of current DNA testing technology to detect all possible mutations and the difficulty in conveying the concept of residual risk temper these positive effects.

Another indicator of impact occurs in the rare instances in which a fetus with CF is identified. In the limited studies to date, most couples with no positive family history in this circumstance choose to terminate the pregnancy. It should be noted that some couples do not undergo final stages of testing because of their intention to continue the pregnancy.

Cost

Assessment of the costs associated with testing, screening, and treatment of CF is challenging because technology and treatment modalities are changing rapidly. Nonetheless, there is general agreement about the magnitude of many of the key cost variables and the likely future direction of change in these costs.

In terms of treatment, options for care for many individuals with CF have expanded over the past decade with implications for the average cost of care. Although the Office of Technology Assessment estimated in 1992, based on 1989 data, that the annual treatment costs were approximately $10,000 per year per individual with CF, current estimates exceed $40,000 per year in direct medical costs and $9,000 per year in ancillary costs. Using a 3 percent discount rate, this implies a net present value of approximately $800,000 for direct and ancillary costs associated with a CF birth.

The technology and cost of DNA diagnostic testing for a CF mutation are changing rapidly. At present, the cost of DNA diagnostic testing for CF is between $50 and $150 per test, testing for between 6 and 72 CF mutations. Rapid progress is being made in cost of testing, however, because of improvements in instrumentation. These costs will likely decline and the number of mutations screened will quickly increase.

In terms of the cost of prenatal testing, the costs of informed consent procedures, educational and counseling services, associated administrative costs, and so forth must be added to the laboratory testing costs per se. These costs will vary as a function of the level of various educational and counseling services accompanying the testing according to evolving professional standards for genetic testing procedures.

Regarding cost savings from neonatal testing, currently no definitive data demonstrate medical benefit and cost savings associated with population-based neonatal screening. However, there is suggestive evidence that differences in height, weight, and nutrition of youngsters with CF are a function of whether they had neonatal screening and early diagnoses. These may well translate into future health outcomes and treatment savings, but the magnitude of such benefits is not known.

Broader assessment of the costs of a voluntary, broad-based prenatal screening program depends on variables such as the number of individuals deciding to participate in the test, the incidence of CF carriers in the population involved, the testing method (e.g., sequential or couple-based), the proportion of couples with an affected fetus who choose to terminate the pregnancy, and the number of children the couples wish to have. Although assumptions about these variables differed, studies showed that the cost per identified CF fetus averted ranged from $250,000 to $1,250,000 for a Caucasian population of Northern European ancestry. Estimates on the high end of this range come down substantially if one considers couples who plan to have more than one child or if identified carriers inform siblings and other relatives.

A broad educational effort is essential to create a level of genetic literacy in the population and among health care professionals that will allow individuals to utilize genetic and other information in making important life decisions. An estimate of the costs of this effort is not available.

3. Should Cystic Fibrosis Carrier Testing Be Offered to: (1) Individuals with a Family History of Cystic Fibrosis, (2) Adults in the Preconception or Prenatal Period, and/or (3) the General Population?

The first two sections of this report summarized the knowledge base for the recommendations that follow. Objectives for CF testing and reasons for and against testing are different for each population, but in all cases individuals' acceptance of testing must be entirely voluntary. Each population is considered separately.

1. *Individuals with a family history of CF and partners of those with CF should be offered genetic testing.* As a group, individuals with a family history have relatively high

frequencies of mutations in the CFTR gene. Members of this group have increased awareness of their risk of being carriers, as well as increased familiarity with the disease and its impact on the family. Testing can be helpful with regard to reproductive decisionmaking and informative regarding family health.

2. *CF genetic testing should be offered to the prenatal population and couples currently planning a pregnancy, particularly those in high-risk populations.* Data indicate that a significant level of interest in CF testing exists in this group. Because this is a vulnerable population and because of the inherent time constraints, it is particularly important that they receive adequate and balanced information. The information includes, but is not limited to, sensitivity of the test, a description of the range of severity of the disease, and risks. The offer of testing should be made to enable couples who wish to avoid the birth of a child with CF to do so, without influencing those who do not. Care should be taken to ensure that the decision to have testing is completely voluntary.

3. *CF testing for the general population is not advocated.* Given the low incidence and prevalence of CF and the demonstrable lack of interest in the general population, there is little justification for testing.

   - *Routine genetic screening for CF in newborns is not advocated, based on available data.* Studies have not provided sufficient evidence that identifying CF patients earlier than the current average age of diagnosis improves outcomes. The panel recommends that studies of CFTR screening in newborns be developed to provide a foundation for assessment of benefits of early therapy.

   - *Education and informed consent.* Genetic testing for CF should begin with education concerning CF. It should be clear that the patient has received the material and has had an opportunity for questions to be answered before testing is undertaken. Development of model educational and consent forms for genetic testing, as well as education programs for providers, is encouraged. All persons undergoing genetic testing should give written informed consent for the test, receive culturally sensitive educational materials, and demonstrate an understanding of the test and test results.

     It is essential that the offering of CF carrier testing be phased in over a period of time to ensure that adequate education and appropriate genetic testing and counseling services are available to all persons being tested.

Genetic testing and counseling for CF in the populations identified by the panel's recommendations should be eligible for payment by insurers.

4. **<u>What Are the Optimal Practices for Cystic Fibrosis Genetic Testing (Setting, Timing, and the Practices of Education, Consent, and Counseling)?</u>**

The goal of genetic testing for CF is to provide individuals with information that will permit them to make informed reproductive and other decisions. Testing is of benefit only if there is access to the necessary comprehensive health services and resources that ensue from case/carrier detection. Components of a testing program should include education, counseling, and the use of medical facilities to improve health outcomes.

The setting must provide access for provision of comprehensive services. Whether it is based in a medical center or in a primary care setting, a professional interdisciplinary team should address the individual's genetic, medical, emotional, and reproductive health needs. The services should not be administered in isolation, but in association with tertiary care centers.

The complexity of DNA diagnostic data and the vast number of mutations in CF mandate sophisticated laboratory capability (or access to it) as an integral component. Laboratories providing molecular diagnostic capability should utilize tests that achieve a mutation detection rate of approximately 90 percent or better for Caucasians or a detection rate for African-Americans, Asian-Americans, Hispanics, Ashkenazi Jews, Native Americans, and others comparable to that available at present.

Timing for Testing Depends on Targeted Group

- In adults with a positive family history of CF, genetic testing should be provided at any time requested.

- Newborn siblings of patients with CF as well as other siblings who exhibit atypical symptoms should be tested. However, testing of minors for the purpose of identifying carrier status is not recommended.

- Carrier detection in pregnant couples with a family history of CF should be provided in an expeditious manner. Similarly, the request by a couple with known carrier status for prenatal diagnosis must be addressed promptly to facilitate access to all needed services so as to provide an optimal opportunity to make an informed decision.

- Couples in the prenatal population (i.e., those not in a high-risk group) should be offered the opportunity for carrier detection as early as possible to provide them time to consider the full range of informed reproductive decisions.

- The rationale for offering testing to couples currently planning a pregnancy is predicated on timely provision of balanced, accurate information about CF, including natural history of the disease, relative frequency in different ethnic and racial groups, variability of disease manifestation, and availability of highly sensitive and specific tests to determine carrier status.

- Although most males who have CF are sterile, partners of persons with CF should be tested on request for carrier status. The highest practical level of sensitivity of the DNA test should be used to maximize detection of at-risk couples.

Education

Genetic testing should be provided in response to the needs of patients. Thus, programs must provide information relating to genetics in general such as basic inheritance patterns, variable nature of disease expression, risk of occurrence, and diagnostic and therapeutic options. In the case of CF testing programs, balanced information should be presented and regularly updated. The elements that must be included are:

1. Natural history of the disease
2. Range of severity
3. Improvement in survival rates
4. Quality of life for patients and families
5. Full range of therapeutic modalities
6. Reproductive options, including adoption, use of artificial reproductive modalities, and continuation or termination of pregnancy

Educating patients and families can be accomplished by utilizing a wide variety of printed materials and media, including videos and interactive on-line systems. At present, information

content is presented in a variable manner. It is recommended that effort be directed to develop model information that highlights the positive as well as the negative aspects of living with CF, using input from people living with the disease, their families, and members from diverse racial/ethnic groups.

Every attempt should be made to ascertain the level of understanding and cultural background of the person being tested. Followup assessment to determine retention of knowledge is an essential ingredient of any educational program.

Informed Consent

To ensure informed choice, it is imperative that the informed consent process demonstrate that the individual has fully understood the multiple options and implications that ensue from genetic testing. It is also important to ensure that those who decline to be tested do so knowledgeably, although this is typically not documented. Informed consent must include a clear description of the disease, of the limitations of the genetic testing methods, and of the voluntary participation of the individual giving consent. Individuals must be assured that although every effort will be made to ensure the confidentiality of their medical and genetic data, absolute confidentiality cannot be guaranteed.

Counseling

Provision of accurate genetic counseling, particularly when the results are provided to the patient or when the intervention strategies are discussed, is essential. The implications of genetic testing, its limitations and strengths, and the risks of ensuing potential therapies and interventions mandate that individuals knowledgeable in genetics provide these services. The counseling skills required must combine respect for a patient's right to make an autonomous decision with an appropriate level of support to facilitate the decisionmaking process.

Any strategy attempting to provide these services to the public carries with it a responsibility to enhance the educational process for physicians and other health care providers. Rapid changes in the methodology of molecular diagnosis, and therapeutic options that result from them, mandate continuing education and involvement of genetic specialists in the process of translating these developments into practical and beneficial terms. CF centers should make counseling available to minor siblings who often have a need for information that goes unaddressed.

Nondiscrimination

Pivotal to individual autonomy is the guarantee that genetic data not be used for discrimination with reference to insurability, employment and educational opportunities, and social stigmatization.

Federal and State statutes currently in place to address nondiscriminatory practices against any carrier, person with a genetic disorder, or family member need to be enforced. However, these laws provide limited protection from discriminatory practices. Additional Federal and State statutes are needed to broaden protection from harm based on genetic status from educational, health care, and other organizations that may impact on and restrict immediate and long-term opportunities. Special attention to expand the understanding and awareness of the legal, insurance, health care, and educational professions about discriminatory practices should be undertaken.

In spite of laws that are put into place to protect people from external discrimination, less visible or more subtle harm may occur. For example, families may perceive differently a member found to be a carrier or found to be affected with a genetic disorder. These families may marginalize or ostracize the identified person. No laws can be passed to provide protection from this practice; however, future research is needed to understand the parameters of this problem and the moderating impact of education and counseling.

5. What Should Be the Future Directions for Research Relevant to Genetic Testing for Cystic Fibrosis and, More Broadly, for Research and Health Policies Related to Genetic Testing?

- As treatment options and screening technologies change, what are the impacts on medical costs, ancillary costs, and quality of life associated with CF? What are the cost-effective approaches to treatment and screening in different settings?
- What is the actual incidence of discrimination and stigmatization with respect to carriers, persons with genetic disorders, and their families? How does fear or anticipation of discrimination impact decisionmaking by some persons with identified genetic disorders?
- What is the most effective mechanism to educate health professionals about the current state of genetic disorders, genetic testing, and management of genetic disorders?
- What are effective educational strategies to educate the public and specific populations about genetics and genetic testing?
- What are patients' expectations of pretest education, genetic reproductive risk counseling, genetic evaluations, and transmittal of test results?
- Do early diagnosis and treatment of newborn infants with CF modify the morbidity as indicated by pulmonary function tests, maturation status, rates of infection, hospitalization, and mortality rates?
- A variety of screening strategies have been used in various studies (e.g., sequential versus couple screening). A systematic literature review should be undertaken, and, if warranted, a randomized controlled trial should be initiated to assess the relative merits of these strategies.
- Certain specific mutations appear to result in limited phenotypes, such as CBAVD. A goal of future research should be to continue to identify additional mutations, modifier genes, and environmental factors, and correlate these with the phenotype.
- Because CF is characterized by multiple mutations of the CFTR gene, this disease would be the prototype for the assessment of multiple methodologies to define numerous allelic mutations of a large gene.
- The optimal system for delivery of genetic services in rural and nonacademic settings should be studied.
- What are long-term effects of pregnancy termination or continuation on high-risk couples?

Conclusions and Recommendations

- Active research should continue on improved treatments for people with CF, enhanced molecular diagnosis of CF, and better understanding of the pathophysiology of CF.
- Over the past two decades, aggressive management of the pulmonary manifestations of CF and new treatment modalities have resulted in much longer survival.
- More than 90 percent of CF mutations can be identified in certain populations. Although generally good correlations exist between certain CF mutations and pancreatic status, it is known that CF mutations are not robust predictors of severity of disease and longevity.
- The goal of genetic testing is to provide individuals with information that will permit them to make informed decisions.
- CF genetic testing should be offered to adults with a positive family history of CF, to partners of people with CF, to couples currently planning a pregnancy, and to couples seeking prenatal testing.
- Comprehensive educational programs are recommended, utilizing a variety of media, for health care professionals and the public.
- Counseling services must be accurate and provide balanced information to afford individuals the opportunity to make autonomous decisions. Every attempt should be made to protect individual rights and genetic and medical privacy rights and to prevent discrimination and stigmatization.
- Access to genetic testing in the prenatal setting enhances the ability of couples to make reproductive choices, as shown by their interest in and use of the information they gain. The cost is reasonable in relation to the benefits obtained.
- Offering CF genetic testing to the general population or to newborn infants is not recommended.
- Genetic testing for many additional conditions will be available in the future. Some of the principles considered for CF genetic testing might well have broader application.
- It is essential that the offering of CF carrier testing be phased in over a period of time in order to ensure that adequate education and appropriate genetic testing and counseling services are available to all persons being tested.

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Setback in Screening For Cystic Fibrosis After Gene Discovery

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tion, "have been almost totally unsuccessful," said Dr. Barbara Handelin, a medical geneticist at Integrated Genetics in Framingham, Mass. "There are exceptions to almost every rule."

The cystic fibrosis story began in 1968, more than 20 years before the gene was found. At that time, Dr. Douglas S. Holsclaw, working at Children's Hospital in Boston, made an observation that turned out to be the first hint that a cystic fibrosis gene might cause more than the classic symptoms of the disease.

Cystic fibrosis, which affects an estimated 30,000 Americans, results in an accumulation of thick, sticky mucus in the pancreas and lungs. People with the disease eventually have pancreatic failure and recurrent bacterial infections of the lungs that lead, finally, to lung failure. But Dr. Holsclaw found another defect. When he did hernia repairs for boys with cystic fibrosis, or when he did autopsies on them, he noticed that they were missing the vas deferens, the tube that carries sperm to the penis.

No one had known about this defect because, until recently, boys with cystic fibrosis did not normally live to adulthood, when the infertility that would have been caused by a missing vas deferens might have become apparent. But with the administration of pancreatic enzymes and the development of improved treatments for the lung infections, people with cystic fibrosis now live into their 20's or 30's.

Dr. Holsclaw's observation "was opportunistic," noted Dr. Jean Amos, a geneticist at Boston University. "Who would have predicted that these boys would be infertile?"

Several other investigators took the next logical step. One, Dr. Robert Oates, co-director of the New England Male Reproductive Center at Boston University Medical Center, said his interest was piqued in 1990, when he started seeing relatively large numbers of men who were infertile because they had no vas deferens. A few years earlier, infertility specialists had discovered that men with this defect could father children if doctors aspirated sperm directly from their testicles and used them to fertilize a woman's eggs in a petri dish. Many men who were missing the vas deferens and had given up hope of being able to father children began flocking to fertility specialists.

Link to Various Illnesses

Dr. Oates said that the men he saw were "otherwise quite healthy," adding, "They had no lung problems, no pancreatic problems." But because he knew about the vas deferens defect in cystic fibrosis, he wondered whether the men might have mutations in their cystic fibrosis genes.

To his surprise, Dr. Oates said, his hunch was correct. He referred the men to Dr. Amos for genetic testing. So far, Dr. Amos said, she has seen 115 men, most of whom seem to have inherited mutations in their cystic fibrosis genes from both parents. She added that the men typically have one mutation that is severe. People who inherit this mutation from both parents seem to get cystic fibrosis. The other mutation most of these men inherited seems to be milder. Dr. Amos said it seems likely that the gene with the milder mutation functions well enough to prevent most manifestations of cystic fibrosis.

Independently, Dr. Handelin is finding the same thing. But she is seeing mutations that are even more puzzling. Some men have two mutations that are identical to those usually found in patients with cystic fibrosis, Dr. Handelin said. From looking at the men's genes, she said, "they should have cystic fibrosis, but they clearly don't." Ticking off the hallmarks of the disease, she said: "They have negative sweat tests, no history of pulmonary or G.I. disease or absorption problems. There are people out there with various separate manifestations of cystic fibrosis with incredibly mild disease. We haven't been able to say, 'Here are five mutations where you always find infertility and here are others where you always find C.F.'"

Dr. Handelin says that her favorite theory "for which I have no evidence" is that a third gene affects the expression of the mutations of the cystic fibrosis gene.

Dr. Kaback agreed that that explanation is possible. "Genes don't function in a vacuum," he said.

But infertility is not the only surprising manifestation of cystic fibrosis mutations. Dr. Gary Cutting, a molecular geneticist at Johns Hopkins University, is starting to find cystic fibrosis mutations in two groups of patients, those with a frequent complication of asthma known as allergic bronchopulmonary aspergillosis and those with a common manifestation of chronic bronchitis called chronic pseudomonas bronchitis. Researchers in France and Italy are also reporting cystic fibrosis mutations in patients with asthma and chronic bronchitis, Dr. Cutting said.

Highly Prevalent Mutation

In addition, said Dr. Handelin, cystic fibrosis mutations may turn out be much more common than anyone had expected. In collaboration with Dr. David Witt, assistant chief of the genetics department at Kaiser Permanente of Northern California in San Jose, she screened 5,000 healthy women coming in for routine prenatal care. The investigators were looking for a particular mutation of the cystic fibrosis gene, r117h, that was thought to occur in less than 1 percent of the population, an estimate derived from studies of people with cystic fibrosis. Dr. Handelin and her colleagues, however, found that 11 percent of the people they screened had the mutation, suggesting that cystic fibrosis is just the tip of the iceberg for the many mutations of the cystic fibrosis gene.

"It was a very surprising finding," Dr. Handelin said. "It tells you that this mutation is much more prevalent then you would expect. It is manifested in a disease that we didn't count as C.F."

Researchers are optimistic that the discoveries will lead to a new understanding of the spectrum of disorders caused by the cystic fibrosis gene and, possibly, to new treatments for more common diseases, like asthma. Dr. Cutting said that if some people with asthma and chronic bronchitis were really suffering from a genetic disorder, then gene therapy, which is being tested for cystic fibrosis, might benefit them.

Dr. Ronald Crystal of New York Hospital-Cornell Medical Center in New York said that the complex picture of the cystic fibrosis gene's manifestations should not affect attempts to treat cystic fibrosis with gene therapy. Studies indicate that people need only 5 to 10 percent of the protein made by the cystic fibrosis gene to be free of symptoms of cystic fibrosis, Dr. Crystal said, adding that "probably only one in five cells need it." That means that gene therapy does not have to accomplish a miracle and make every gene in every cell work perfectly. "That's very positive news," he said.

But, Dr. Handelin cautioned, the research will take time. And the complications that are emerging, "go against the idea that we will know everything we need to know in the next five years."

The findings, "complicate things terribly," said Dr. Cutting. If a man and his wife are screened and each is found to carry a different mutation of the cystic fibrosis gene, they will have one chance in four of having a child who inherits two mutated genes. Ordinarily, that would spell disease, but now it is not so certain.

"What do you tell them?" Dr. Cutting asked. "Do you say, 'Maybe your son will be infertile, or maybe your daughter will be healthy or maybe your child will have cystic fibrosis'?"

Molecular geneticists say that the story of cystic fibrosis is a cautionary tale. "The onus is on us not to sell this research in an oversimplified way," Dr. Handelin said.

Researchers added that such complications may turn out to be more the norm than the exception. Already, several other genes are starting to show their own confusing effects, making genetic counseling infinitely complicated.

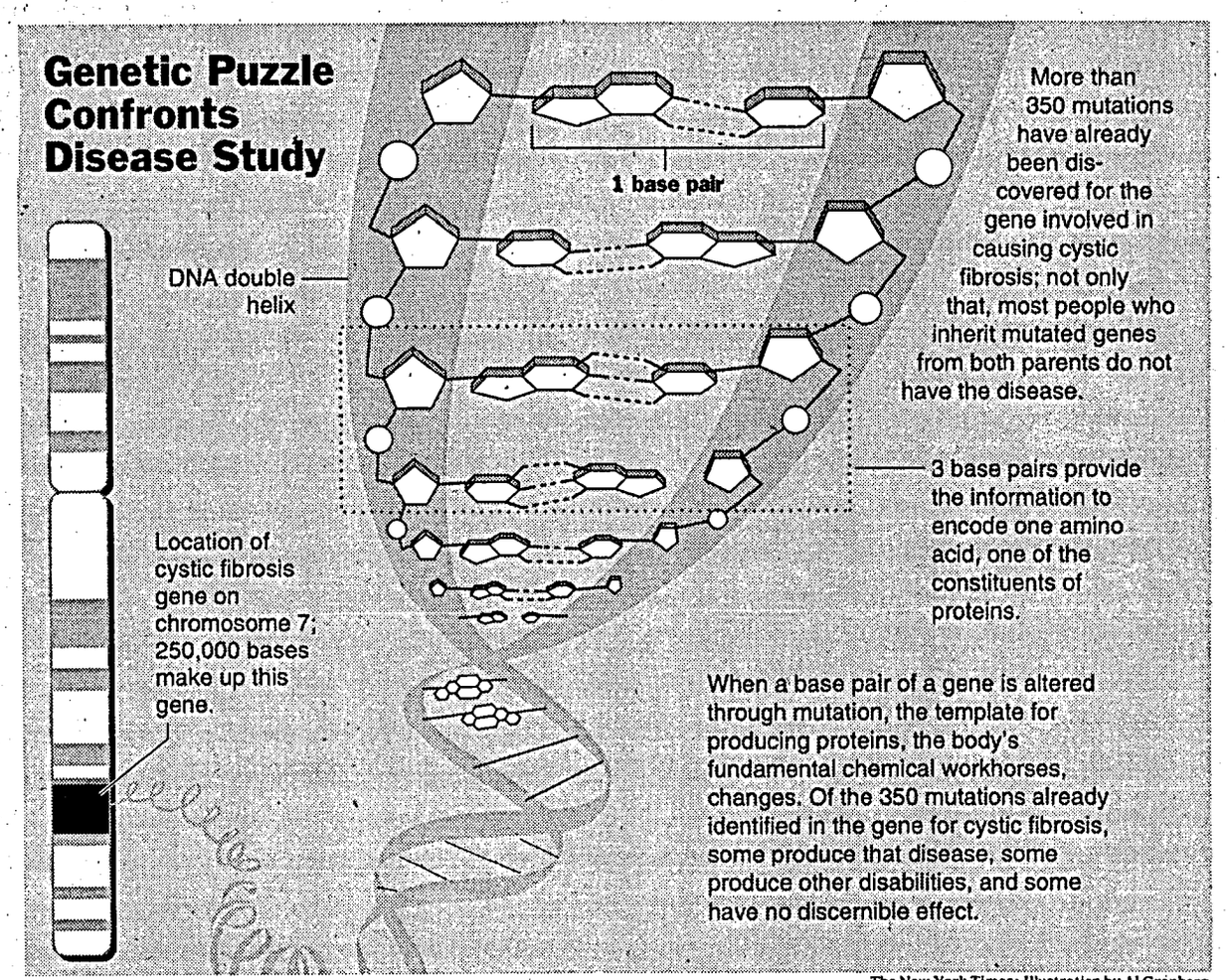
For example, said Dr. Kaback, the gene for Tay-Sachs disease also seems to have variable effects. This disease, most often found in Ashkenazi Jews, typically kills babies within a few years after they are born. But, Dr. Kaback said, researchers are finding some mutations in the Tay-Sachs gene that can result in "changes in the age of onset or severity and even some mutations that look like mutations but whose effects are benign."

The result, Dr. Kaback said, is that "it's not going to be simple: one gene, one effect," as researchers once thought it would be.

Dr. Handelin agreed. Whenever a new gene is cloned, she said, "people think, bingo, it's all solved," adding: "Everyone is tempted to say that this is the solution to our problems. But it may be the start of new problems."

Dr. Kaback said that the new wrinkles in molecular genetics were "a wonderful example of how, the smarter you get, the less you know."

But, the researchers emphasize, the complications do not mean that it is a mistake to search for genes. After all, Dr. Kaback said, finding a gene is a first step toward understanding what causes a disease and how to cure it.



The New York Times; Illustration by Al Granberg

With more than 350 mutations, the combinations are endless.

Different mutations produce different symptoms.

Rebuff for AIDS Vaccine

WASHINGTON, Nov. 15 (AP) — Congress is giving Government scientists six more months to make the case against testing an experimental AIDS vaccine, gp160, that got special treatment from lawmakers a year ago when Congress slipped $20 million into a military spending bill for clinical trials of the vaccine.

The company responsible for the developmental drug, Microgensys of Meriden, Conn., had been rebuffed by the National Institutes of Health when it sought special consideration of the drug.

"Congress should not be in the business of picking commercial products to test, especially in a situation as critical as the AIDS epidemic," said Representative Henry A. Waxman, Democrat of California, the chairman of the House Energy and Commerce subcommittee on health and the environment, who sponsored this year's measure. MicroGenSys had hired Russell Long, a former Senator from Louisiana, to lobby. He persuaded Senators Sam Nunn, a Georgia Democrat, and John Warner, a Virginia Republican, to add the money to last year's legislation.

Effort to Nurture Salmon in Thames Advances

The goal is to breed a strain of the species matched to the river.

By TERESA L. WAITE

LONDON

SCIENTISTS are a step closer to nurturing a self-sustaining strain of salmon in the Thames River, 160 years after the indigenous species were wiped out by pollution and impassable dams.

The scientists' efforts, a mixture of engineering and breeding, passed a crucial test this year when the first group of adult salmon of Thames parentage returned, swimming upstream past Big Ben and Parliament to complete their life cycle after feeding at sea.

While dams and altered river beds still prevent these second-generation fish from reaching spawning grounds in the Thames's tributaries, the returnees are the keystone in attempts to breed a strain of salmon whose genetic traits match the river's altered chemistry and terrain.

"These are very important fish to us," said Greg Armstrong, a fisheries scientist at the National Rivers Authority. "It's certainly an encouraging sign that our efforts are working."

Mr. Armstrong said that more than 300 salmon, including 30 bred from earlier Thames returnees, have returned so far this year. Fish counted at an upstream trap are identified by tags or the absence of the adipose fin, a small fleshy lump near the tail removed to mark stocks. Since not all returnees are caught, Mr. Armstrong said, the count is conservative.

Salmon face great pressure to survive, depending as they do on two fragile environments for the completion of their complex life cycle. They spawn and spend their youth in fresh water, then migrate to sea. Later they return to areas in which they hatched to spawn and die.

A Fastidious Fish

North Atlantic salmon have dwindled in this century because of overfishing, the depletion of species on which salmon depend and the destruction of salmon habitats in dozens of rivers in Europe and North America. Two hundred years ago the Thames teemed with salmon. By 1834 none remained.

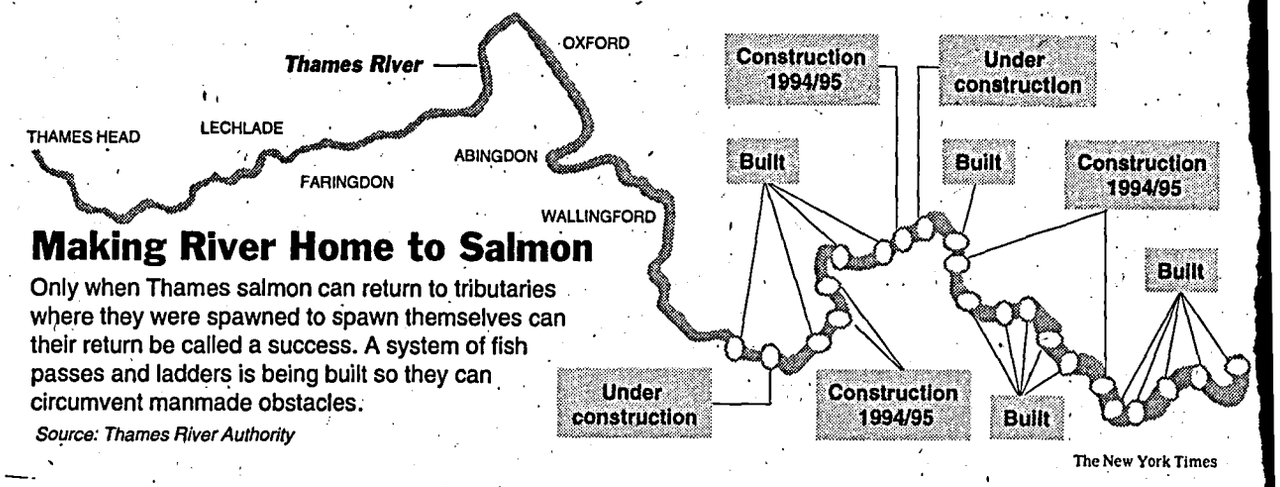
Salmon are fastidious fish, requiring clean, well-oxygenated water and easy access to shallow gravel breeding grounds. After the Industrial Revolution and the proliferation of indoor toilets turned the Thames into a sludge-filled sewer, the estuary remained uninhabitable to all species but eels until the 196[illegible] Government made a concerted effort to improve water quality.

More than 100 species of fish now live in the Thames, but man-made changes to the river have prevented the natural return of salmon. The deepening of the river for boat traffic destroyed shallow breeding areas, and the construction of locks and dams created insurmountable barriers to upstream migration.

The National Rivers Authority stocks the Thames with 200,000 young salmon each spring. As each generation of adults returns from the sea to spawn, scientists catch the most robust ones, perpetuating the genetic strains most compatible with the river and, in effect, breeding a new indigenous strain.

"It's natural selection with human help," Mr. Armstrong said.

About a third of the fish stocked in the Thames are bred from returnees; the rest come from other rivers and hatcheries in Britain. By 2000, scientists hope to stock only progeny from Thames-born returnees and to find some successful reproduction occur-

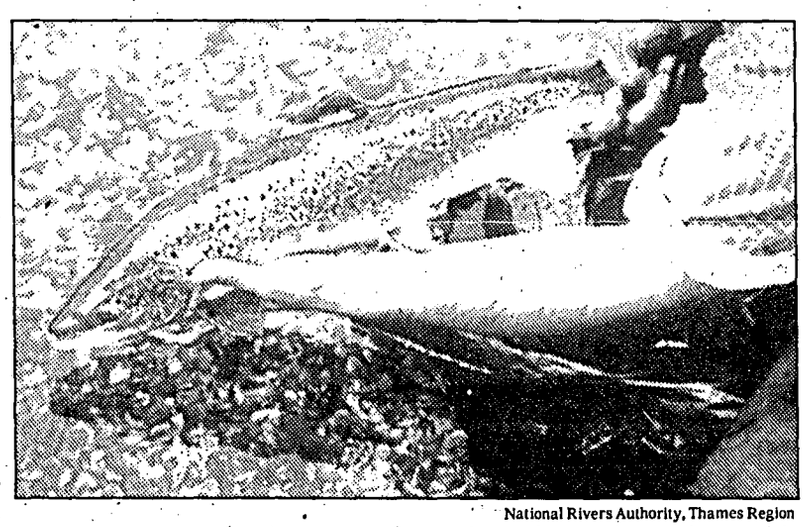


Making River Home to Salmon

Only when Thames salmon can return to tributaries where they were spawned to spawn themselves can their return be called a success. A system of fish passes and ladders is being built so they can circumvent manmade obstacles.

Source: Thames River Authority

The New York Times



National Rivers Authority, Thames Region

Thames River is starting to support salmon in small numbers with human help. This is a mature salmon being released near Molesey Pass.

Scientists started a small salmon stocking program in the Thames in the late 1970's, encouraged by the return of other species and the surprise finding of a stray salmon caught in a power station screen. It was the first salmon seen in the Thames in 140 years.

As adult stocked salmon started trickling back to spawn, a trust was formed to raise money to build ladders and fish passes at dams so salmon could get to breeding grounds. So far, 14 passes have been completed on the Thames. Three more are to open by the end of the year, and another five by March 1995. Others are being installed in tributaries as maintenance on dams is completed.

Once the chain of ladders is completed, the returning Atlantic salmon will be able to swim upstream unimpeded, make their way to the tributaries in which they were stocked and then spawn naturally. Only when this occurs can the project be deemed a success. Currently, the returning salmon are netted at the passes and e s ar breeding.

"We hope by end of the century a good percentage of the returning fish will spawn successfully on their own," Mr. Armstrong said. "A self-sustaining population should rapidly grow from there."

Dr. Geoffrey Tingley, a fisheries scientist at Imperial College in London, said that constructing passes is only half the battle. The quality of gravel beds in tributaries must be improved because in many areas, a deep blanket of silt now covers natural gravel beds.

"I can see no reason why the Thames can't become a salmon river again," Dr. Tingley said, "as long as salmon have easy access upstream to good spawning areas, and as long as the river downstream in the estuary remains clean."

If so, Britain's success will be counted as a milestone.

In the United States, three decades of efforts to restore salmon to rivers in the Northeast have not yet produced the hoped-for success, said Larry Stolte, a coordinator with the Fish and Wildlife Service in New Hampshire. Only an effort on the Penobscot River in Maine has produced a handful of salmon that continue to spawn in the wild.

In American rivers hydroelectric dams as high as 80 feet present returning salmon with a herculean challenge. Mr. Stolte said that because most dams on the Thames are not more than nine feet high, it might be easier to make the river completely passable for salmon again.

He said that efforts to breed the salmon that return offer the best chance for success, but added, "We've learned that it takes a lot less time to destroy a wild resource than to bring it back."

Mr. Armstrong said, "Restoring salmon is not just a grand conservation exercise." In the long run, the survival of the whole struggling stock of North Atlantic salmon is at stake. "The more rivers that are made hospitable again, the greater the chances that North Atlantic salmon will sur-

Cystic Fibrosis Surprise: Genetic Screening Falters

Gene mutation pattern turns out to be more complex than suspected.

By GINA KOLATA

FOUR years ago, when molecular geneticists isolated the gene for cystic fibrosis, some scientists were ecstatic. This was one of the first fruits of the avid search for the genes that cause various diseases. Screening for the gene would provide the prototype, some thought, for national screening programs for other dread diseases and the basis for offering prenatal diagnosis to couples who carry the gene.

Now, however, the story is taking an unexpected twist. Human genetics, at least in this case, turns out to be far more complicated than expected. Biologists have found more than 350 points at which the gene can be mutated, and more are appearing almost weekly. At the same time, scientists are finding that many people who inherit mutated genes from both parents do not have cystic fibrosis.

With so many possible mutations, the potential combinations in a person who inherits one gene from each parent are endless. And the researchers are finding that combinations of different mutations produce different effects. Some may cause crippling and usually fatal cystic fibrosis and others may cause less serious disorders, like infertility, asthma or chronic bronchitis.

The picture could be even more complicated if, as some researchers suspect, other genes come into play by altering the way different mutations of the cystic fibrosis gene are expressed. That would mean that a pair of mutations inherited by one person might behave differently from that same pair inherited by another person, depending on the state of a third, regulatory gene.

Dr. Norman Fost, a pediatrician and ethicist at the University of Wisconsin, said that as the evidence from the cystic fibrosis research points out, "there is, in fact, no such thing as a single-gene genetic disorder," adding: "One of the worst things that Mendel ever did was work with this plant that was either tall or short. Not a single gene in human biology works that way."

Dr. Michael Kaback, a professor of pediatrics and reproductive medicine at the University of California at San Diego, said geneticists can make good predictions when they counsel individuals whose family members have had cystic fibrosis. They can pinpoint the combination of mutations in those family members and can tell if a fetus is carrying it. "For family members where C.F. patients have been identified, testing is certainly relevant," Dr. Kaback said.

But in those with no family history of the disease, or who have inherited either different mutations from each parent or a combination of unfamiliar mutations, making any prediction is risky. Attempts to associate particular combinations of mutations with particular outcomes in the general popula-

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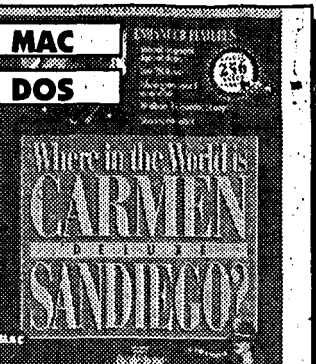

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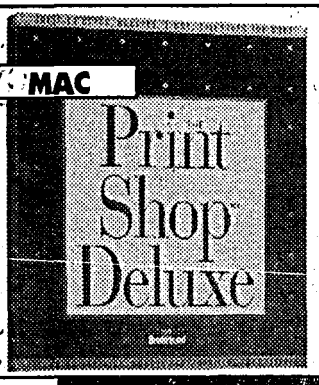

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Make medical research a key national priority

By TIMOTHY F. MURPHY, M.D.

MY VIEW

Words from Western New York

I was dismayed to read about the disappearance of Mars Observer, the billion-dollar spacecraft that is now lost in space. Ironically, on the same day its fate was reported, I received my box of 70 grant applications to review for the National Institutes of Health. I knew as I looked at this pile of requests for medical research money that only a few would be funded.

For the past four years I have been a member of an NIH study section, a group of outside scientific consultants. We review grant applications from scientists around the country, prioritizing their proposals based on scientific merit. Our work helps guide the government in assigning federal funding.

Approximately 55 of the 70 applications I received that day will be rated as "outstanding" or "excellent" by highly critical reviewers. These are projects that could advance medical care in this country. Unfortunately, fewer than 10 of the 70 will receive funding. There just isn't enough money in the NIH budget.

Medical research should be a national priority — especially now. There has been a virtual explosion in the understanding of molecules, cells and organisms in the past decades. This progress has the potential to revolutionize health care. Yet the money isn't there.

About 2,000 average-size NIH grants could be funded with the money spent on the Mars Observer. It is difficult for me to understand how our leaders have decided the relative importance of space exploration as opposed to the health of our people. I agree that the space program is important. However, an adjustment of our national priorities is in order. We could be doing much more in prevention, diagnosis and treatment of illness.

Take one example. Approximately three-fourths of all children will have at least one ear infection by the age of 6. Many children have repeated episodes. They are painful and lead to temporary hearing loss at a time when speech and language are developing. This can lead to problems in language development, which lead in turn to difficulties in school.

Any parent of a child with ear infections can describe the torment of sleepless nights, innumerable visits to the doctor, weeks of medications and the anxiety of wondering about the effects of repeated infections on the child's development.

The best solution is to develop vaccines to prevent these infections before they occur. Many excellent research projects studying this important problem are conceived but not carried out — because researchers don't have enough money to do the work.

In addition to the obvious benefits in improving health, increased support of medical research has clear economic benefits. There are numerous examples to illustrate this. Inexpensive viral vaccines currently save billions of dollars annually in the United States. Antibody testing has had an enormous economic impact by eliminating the cost of medical care for many people with diseases from blood transfusions.

When I return from NIH study section meetings, I worry about how many careers of promising researchers have been snuffed out by the lack of funds to support medical research. It is crucial that our nation attract the brightest students into this area. I have always encouraged talented young people to pursue careers in medical research. However, it will be difficult to persuade them if there is no economic future for them.

Proponents of putting more resources into the space program argue that it will lead to new technologies and more jobs. But the same benefits will result from devoting more resources to medical research. The additional benefit is that the new technology will lead directly to improving health, prolonging life and improving the quality of life.

I am not suggesting that the space program be eliminated. I am suggesting that we carefully evaluate the focus of our national research and development efforts. When I think of the Mars Observer floating uselessly in space, I know that my NIH study section could have distributed that $1 billion to much greater benefit for Americans.

TIMOTHY F. MURPHY, M.D., is chief of the Division of Infectious Diseases at the University at Buffalo School of Medicine.

Send submissions for this column to My View, The Buffalo News, Box 100, Buffalo, N.Y. 14240.

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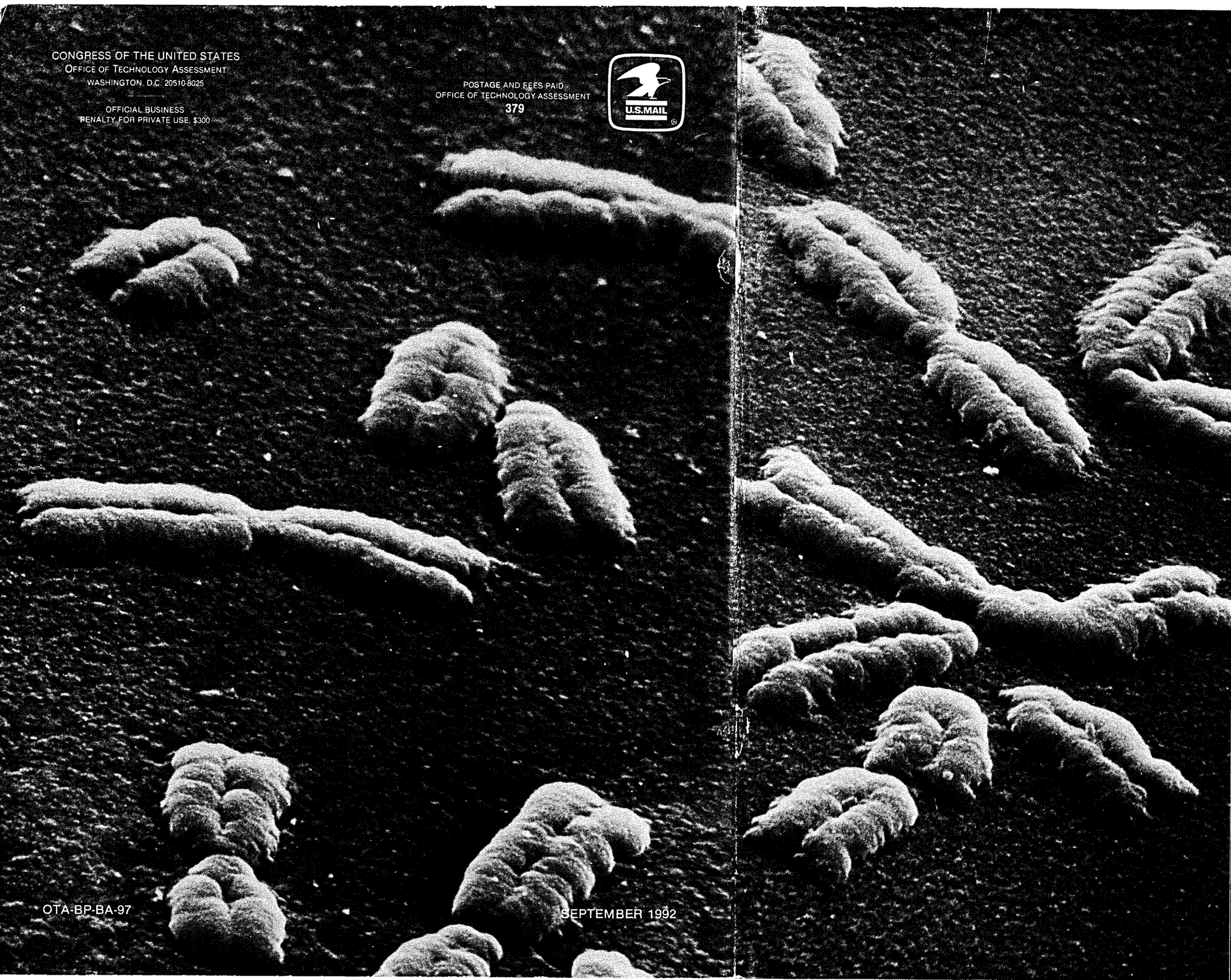

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The Office of Technology Assessment (OTA) was created in 1972 as an analytical arm of Congress. OTA's basic function is to help legislative policymakers anticipate and plan for the consequences of technological changes and to examine the many ways, expected and unexpected, in which technology affects people's lives. The assessment of technology calls for exploration of the physical, biological, economic, social, and political impacts that can result from applications of scientific knowledge. OTA provides Congress with independent and timely information about the potential effects—both beneficial and harmful—of technological applications.

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Genetic Counseling and Cystic Fibrosis Carrier Screening: Results of a Survey

Background Paper

Congress of the United States
Office of Technology Assessment

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Foreword

For years, experts have theorized about the consequences of increased knowledge of human genetics. In the early 1990s, development of a DNA-based test to identify carriers of cystic fibrosis (CF) moved the debate from the theoretical to the practical. The CF carrier assay is but one of many tests to come that will place genetic counselors and nurses working in genetics at the front line on the issues raised by assimilation of DNA tests into clinical practice.

This OTA Background Paper presents results from a 1991 OTA survey of 431 genetic counselors and nurse geneticists. It was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening. The survey supports OTA's August 1992 assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*; the full assessment was requested by the House Committee on Science, Space, and Technology, the House Committee on Energy and Commerce, and Representative David R. Obey.

The survey data collected by OTA reflect the tensions and concerns surrounding the widespread implementation of CF carrier screening. Those who currently oppose routine carrier screening for CF raise concerns about the sensitivity of the test, the numbers of individuals that would be potentially screened—and the subsequent effect on the clinical genetics infrastructure—and the possibilities of stigma, discrimination, and poor quality in services. Those who think CF carrier screening should be widely available believe the information provided by the test increases patient autonomy and lowers uncertainty regarding reproductive futures.

OTA was assisted in preparing the survey instrument and Background Paper by a panel of advisors, contractors, workshop participants, and reviewers selected for their expertise and diverse points of view. We gratefully acknowledge the contribution of each of these individuals. OTA, however, remains solely responsible for the contents of this Background Paper.

JOHN H. GIBBONS
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NOTE: OTA is grateful for the valuable assistance and thoughtful critiques provided by the advisory panel members. The panel does not, however, necessarily approve, disapprove, or endorse this report. OTA assumes full responsibility for the report and the accuracy of its contents.

Discrimination: Differential treatment or favor with a prejudiced outlook or action.
Dominant: An allele that exerts its phenotypic effect when present either in homozygous or heterozygous form.
DNA: See *deoxyribonucleic acid.*
DNA analysis: A direct examination of the genetic material, DNA, to reveal whether a individual has mutation(s) for CF or other disorders.
DNA probe: Short segment of DNA labeled with a radioactive or other chemical tag and then used to detect the presence of a particular DNA sequence through hybridization to its complementary sequence.
Gene: The fundamental physical and functional unit of heredity. A gene is an ordered sequence of nucleotide base pairs to which a specific product or function can be assigned.
Gene therapy: The deliberate administration of genetic material into the cells of a patient with the intent of correcting a specific genetic defect.
Genetic counseling: A clinical service involving educational, informational, and psychosocial elements to provide an individual (and sometimes his or her family) with information about heritable conditions. Genetic counseling is performed by genetics specialists, including physicians, Ph.D. clinical geneticists, genetic counselors, nurses, and social workers.
Genetic screening: The analysis of samples from asymptomatic individuals with no family history of a disorder, groups of such individuals, or populations.
Genetic testing: The use of specific assays to determine the genetic status of individuals already suspected to be at high risk (e.g., family history or symptoms) for a particular inherited condition.
Genetics: The study of the patterns of inheritance of specific traits.
Genome: All the genetic material in the chromosomes of a particular organism; its size is generally given as its total number of base pairs. The human genome is 3.3 billion base pairs.
Heterozygote: A heterozygous individual, such as a CF carrier.
Heterozygous: Having two different alleles at a particular locus.
Homozygote: A homozygous individual.
Homozygous: Having the same alleles at a particular locus.
Immunoreactive trypsin (IRT) test: An assay that measures levels of pancreatic trypsin, a digestive enzyme. As a protocol for newborn CF screening, a drop of blood is isolated on a card, dried, and chemically analyzed to detect elevated levels of the enzyme. It is not intended to be a diagnostic test.
Mutation: Changes in the composition of DNA.
Nucleotide: The unit of DNA consisting of one of four bases—adenine, guanine, cytosine, or thymine—attached to a phosphate-sugar group. The sugar group is deoxyribose in DNA. In RNA, the sugar group is ribose, and the base uracil substitutes for thymine.
Probe: A short segment of DNA tagged with a reporter molecule, such as radioactive phosphorus (^{32}P), used to detect the presence of that particular complementary DNA sequence.
Protein: A biological molecule whose structure is determined by the sequence of nucleotides in DNA. Proteins are required for the structure, function, and regulation of cells, tissues, and organs in the body.
Recessive: An allele that exerts its phenotypic effect only when present in homozygous form, otherwise being masked by the dominant allele.
Sensitivity: The ability of a test to identify correctly those who have a disease.
Sickle cell anemia: An autosomal recessive disorder affecting red blood cell flow through the circulatory system, causing complications in numerous organ systems. Sickle cell anemia predominantly occurs in individuals of African descent.
Sickle cell trait: The heterozygous state of sickle cell anemia; sickle cell carrier status.
Single-gene disorder: Hereditary disorder caused by a single gene (e.g., cystic fibrosis, Tay-Sachs disease, sickle cell anemia).
Specificity: The ability of a test to identify correctly those who do not have the characteristic which is being tested.
Stigmatization: Branding, marking, or discrediting because of a particular characteristic.
Sweat test: An assay used to confirm CF that measures levels of sodium (Na^+) and chloride (Cl^-) ions. These ions appear in high concentrations in patients with CF. Sweating is induced by running a low electric current through a pilocarpine-soaked gauze pad on the individual's arm or back. The amounts of Na^+ and Cl^- in the sweat can then be determined to confirm or question a diagnosis of CF.
Tay-Sachs disease: A lethal autosomal recessive disorder affecting the central nervous system which results in mental retardation and early death. Tay-Sachs disease predominantly occurs among Jews of Eastern and Central European descent and populations in the United States and Canada descended from French Canadian ancestors.

Appendix C

Acronyms and Glossary

Acronyms

-/- —negative CF carrier/negative CF carrier (couple)
+/- —positive CF carrier/negative CF carrier (couple)
+/+ —positive CF carrier/positive CF carrier (couple)
ABMG —American Board of Medical Genetics
ASHG —American Society of Human Genetics
BC/BS —Blue Cross and Blue Shield
CF —cystic fibrosis
CFTR —cystic fibrosis transmembrane conductance regulator
ΔF508 —delta F508 (most prevalent CF mutation)
ΔF508+6-12 —delta F508 plus 6 to 12 additional CF mutations
DNA —deoxyribonucleic acid
G542X —a CF mutation
G551D —a CF mutation
HMO —health maintenance organization
ISONG —International Society of Nurses in Genetics
MSAFP —maternal serum alpha-fetoprotein
N1303K —a CF mutation
NIH —National Institutes of Health (NIH)
NSGC —National Society of Genetic Counselors
OTA —Office of Technology Assessment
R553X —a CF mutation
W1282X —a CF mutation

Glossary of Terms

Allele: Alternative form of a genetic locus (e.g., at a locus for eye color there might be alleles resulting in blue or brown eyes); alleles are inherited separately from each parent.

β-thalassemia: An autosomal recessive disorder affecting the red blood cells, resulting in anemia, infections, growth retardation, and other complications. β-thalassemia predominantly occurs among individuals of Mediterranean, Middle Eastern, Asian Indian, Chinese, Southeast Asian, and African descent.

Buccal: Relating to the inside of the cheek. A buccal swab collects cells that can be analyzed for CF mutations.

Carrier: An individual apparently normal, but possessing a single copy of a recessive gene obscured by a dominant allele; a heterozygote.

Chest physical therapy (chest PT): A cornerstone of CF therapy that moves the mucus blocking major air passages out of the lungs. A specific form of chest PT is bronchial drainage during which an individual claps on the chest or back of the patient who is usually lying on a table.

Chromosome: A threadlike structure that carries genetic information arranged in a linear sequence. In humans, it consists of a complex of nucleic acids and proteins.

Confidentiality: A fundamental component of the health care provider-patient relationship in which the professional has the duty to keep private all that is disclosed by the patient.

Consanguineous: Related by blood or origin, rather than by marriage.

Cystic fibrosis (CF): A life-shortening, autosomal recessive disorder affecting the respiratory, gastrointestinal, reproductive, and skeletal systems, as well as the sweat glands. CF is caused by mutations in the CF gene that affect the CF gene product, cystic fibrosis transmembrane conductance regulator (CFTR). Individuals with CF possess two mutant CF genes.

Cystic fibrosis carrier: An individual who possesses one CF mutation and one normal CF gene. CF carriers manifest no symptoms of the disorder. See *carrier.*

Cystic fibrosis carrier screening: The performance of tests on persons for whom no family history of CF exists to determine whether they have one aberrant CF gene and one normal CF gene. See *cystic fibrosis screening.*

Cystic fibrosis screening: The performance of tests 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. This type of diagnostic screening usually involves newborns, but rarely for CF, except in Colorado and Wisconsin. See *cystic fibrosis carrier screening.*

Cystic fibrosis transmembrane conductance regulator (CFTR): The CF gene product, which regulates chloride (Cl^-) conductance and might be a Cl^- ion channel, the structure that governs Cl^- entry and exit in the cell. CFTR produced by a mutant CF gene is frequently impaired, resulting in the medical manifestations of CF in affected individuals.

ΔF508: A three base pair deletion in the CF gene that results in a faulty CF gene product (i.e., a flawed CFTR). This mutation results in the deletion of one amino acid, phenylalanine, at position number 508 in CFTR. ΔF508 is the most common mutant allele among the greater than 170 identified in the CF gene.

Deoxyribonucleic acid (DNA): The molecule that encodes genetic information. DNA is a double-stranded helix held together by weak bonds between base pairs of nucleotides.

Genetic Counseling and Cystic Fibrosis Carrier Screening: Results of a Survey

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[1] Through December 1991

Contents

Figures

59. Where should CF population screening programs be provided? (check all that apply)

a. ___ in public schools
b. ___ in public health departments
c. ___ in organized, community-wide programs
d. ___ in the primary care setting i.e., physicians
e. ___ in genetic centers/programs
f. ___ in the workplace
g. ___ other (specify): _____

60. Who should pay for screening? (Please rank, but be realistic.)

a. ___ self pay by patient
b. ___ third party payment
c. ___ employers
d. ___ State/city or county
e. ___ Federal government
f. ___ other (specify): _____

61. Do you agree or disagree with the following statements?
1=strongly agree; 2=agree; 3=undecided; 4=disagree; 5=strongly disagree)

a. ___ genetic counseling should precede DNA testing for CF when there is a positive family history.
b. ___ genetic counseling should precede DNA testing for CF when there is a negative family history.
c. ___ educational materials (culturally sensitive and understandable) can provide adequate information about CF screening.
d. ___ a need for more genetic counselors exists.
e. ___ informed consent prior to CF screening is a necessity.

62. In your opinion, what are the important issues that need to be addressed by pilot programs in CF screening? List in order of priority:

1.
2.
3.
4.

63. What strategies have you considered implementing if widespread screening for CF becomes a reality?

64. What do you feel the minimum criteria for CF carrier screening should be (protocol)?

Thank you very much for your cooperation in answering our questions! On the back of this survey, please feel free to give us as any other options, concerns, or suggestions that you feel our questions did not address. These comments will be anonymous, but may be incorporated in our report to Congress.

53. How was your test covered?

a. ___ by my insurance
b. ___ professional courtesy
c. ___ self pay
d. ___ research subject

54. To what extent, if at all, should each of the following groups be involved with educating the public about DNA testing for CF, if it becomes standard practice?

1=to little or no extent; 2=to some extent; 3=to a moderate extent; 4=to a great extent; 5=to a very great extent; 6=no opinion

a. ___ primary care providers
b. ___ public health departments
c. ___ genetic counselors
d. ___ genetics programs
e. ___ nurses
f. ___ family planning clinics
g. ___ voluntary support groups
h. ___ schools
i. ___ lay press
j. ___ television
k. ___ other: _____

55. If widespread CF carrier screening begins, it should be:

a. ___ mandatory b. ___ voluntary

56. If widespread CF carrier screening begins, what target populations should be screened? (check all that apply)

a. ___ prenatal
b. ___ newborns
c. ___ children ages 2-12
d. ___ children ages 13-18
e. ___ adults in reproductive years
f. ___ adults post reproductive years
g. ___ pregnant women or "couples"

57. If CF carrier screening is voluntary, who should organize the screening programs? (check all that apply)

a. ___ voluntary health organizations
b. ___ State or local health department
c. ___ Federal Government
d. ___ medical societies
e. ___ the human genetics community
f. ___ primary care givers
g. ___ others (specify): _____

58. If CF carrier screening is mandatory, who should organize the screening programs? (check all that apply)

a. ___ voluntary health organizations
b. ___ State or local health department
c. ___ Federal Government
d. ___ medical societies
e. ___ the human genetics community
f. ___ primary care givers
g. ___ others (specify): _____

Tables

44. **If you are—or have been—involved with CF testing, does the laboratory you use provide (check all that apply):**
    a. ___ direct mutation analysis
    b. ___ DNA linkage analysis
    c. ___ DNA haplotyping
    d. ___ staging of studies depending on case
    e. ___ prenatal DNA analysis
    f. ___ fetal intestinal enzyme analysis
    g. ___ DNA banking

45. **For direct mutation analysis of CF, what mutations does the laboratory you use include? (Please list or give number):**

THE FOLLOWING QUESTIONS ARE TO BE ANSWERED BY ALL RESPONDENTS

46. **Are you familiar with the following statements concerning CF screening published by:**

    a. 1990 ASHG ad hoc CF Screening Committee: ___ no ___ yes
    b. 1990 NIH panel: ___ no ___ yes

    If yes to either one of the above, how have you incorporated this into clinical practice?

47. **At this time do you think it is appropriate to provide CF screening in cases where family history is negative?**
    a. ___ no b. ___ yes c. ___ uncertain

    If yes, why?

48. **Do you feel there is a optimum rate of detection at which widespread CF carrier screening should proceed?**
    a. ___ yes, specify: _____ % rate of detection
    b. ___ no
    c. ___ no opinion

49. **Are you familiar with the NSGC brochure "Genetic Testing for Cystic Fibrosis: A Handbook for Professionals"?**
    a. ___ no b. ___ yes

50. **Have you developed any educational materials relevant to DNA testing specifically for CF?**
    a. ___ no b. ___ yes (Please send a copy.)

51. **Have you been tested for CF carrier status?**
    a. ___ no b. ___ yes

52. **If you have been tested for CF carrier status, why were you tested?**
    a. ___ research subject
    b. ___ wanted to know
    c. ___ positive family history
    d. ___ family planning
    e. ___ other:_____

39. For each of the following patient groups, indicate how often, if at all, you introduce the topic of DNA testing for CF.

1=seldom if ever; 2=sometimes; 3=often; 4=very often; 5=almost always

a. ___ all patients/families
b. ___ pregnant women seeking prenatal diagnosis
c. ___ couples/individuals with a positive family history for CF
d. ___ Caucasian couples/individuals with negative family history for CF
f. ___ individual/families who inquire about CF
e. ___ selected couples/individuals; how selected:

40. Have you made an effort to contact old genetics families as appropriate regarding the availability of CF testing?

a. ___ yes, by (check all that apply):
1) ___ telephone
2) ___ letters/mass mailing
3) ___ at future visits
4) ___ other: _____

b. ___ no, because (check all that apply):
1) ___ not enough time; too busy
2) ___ no mechanism for rapid chart retrieval
3) ___ requires chart by chart analysis
4) ___ plan to do so in future, as time permits
5) ___ other: _____

41. During the last 12 months:

a. Have you referred any patients for DNA testing for CF?
1) ___ no
2) ___ yes: how many individuals: _____ # samples _____

b. Have you referred any patients/families for DNA testing for other disorders?
1) ___ no
2) ___ yes: how many individuals: _____ # samples _____

If yes, for which conditions:

42. At your institution, is DNA testing for CF:
a. ___ performed at onsite/inhouse lab
b. ___ sent offsite to lab less than or equal to 50 miles away
c. ___ sent offsite to lab between 50 miles and 150 miles away
d. ___ sent offsite to lab greater than 150 miles away

43. Type of laboratory used for CF testing:
a. ___ private/commercial
b. ___ private hospital
c. ___ university hospital
d. ___ regional laboratory
e. ___ other: _____

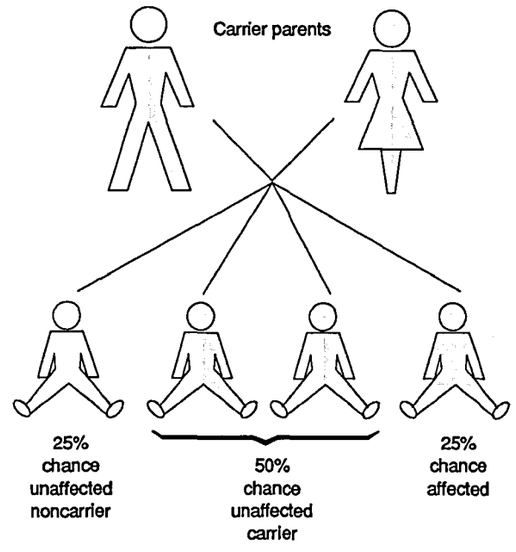
Chapter 1
Introduction and Background

Cystic fibrosis (CF) is the most common, life-shortening, recessive genetic disorder affecting Caucasians of European descent. From 1,700 to 2,000 babies with CF are born annually in the United States. The diagnosis of an infant with CF often reveals the first and only clue that the genetic trait exists in the family.

Parents of a child with CF are, by definition, obligate CF carriers. They have no symptoms of CF, but with each pregnancy are at 1 in 4 risk of having a child with CF and 1 in 2 risk of having a child who is a carrier (figure 1-1). Such couples are sometimes referred to as carrier couples, or couples who are positive/positive (+/+). If a couple is positive/negative (+/-)—the father is a carrier, but the mother is not, or vice versa—their offspring can be CF carriers, but cannot have CF. Couples are not at risk of having a child with CF if only one or neither partner is a carrier.

Four of five individuals with CF are born to families with no previous history of the illness. Beyond the approximately 30,000 Americans who have CF, as many as 8 million individuals could be CF carriers. With no knowledge of a family history of CF, American Caucasians have about a 1 in 25 risk of being a CF carrier. The risk of carrier status increases when an individual in a family is diagnosed with CF, with risks calculated by relationship to the affected individual (table 1-1).

Figure 1-1—Inheritance of Cystic Fibrosis



SOURCE: Office of Technology Assessment, 1992.

Prior to 1989, the absence or presence of CF in one's family, as well as ethnic and racial background, were the only indicators available to determine risk of carrier status. In 1989, however, scientists identified the most common change, or mutation, in the genetic material—deoxyribonucleic acid (DNA)—that causes CF. Following this discovery came tests to detect mutations in the specific area of DNA—the CF gene—that is responsible for the disease.

The Office of Technology Assessment (OTA) report *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (1) focuses on using these DNA tests to screen and identify CF carriers among the general population before they have a child with CF. This background paper, conducted in support of the OTA assessment, reports the results of an OTA survey of 431 members of either the National Society of Genetic Counselors (NSGC) or the International Society of Nurses in Genetics (ISONG). Conducted in summer 1991, the survey was designed to evaluate genetic counseling attitudes and practices regarding widespread CF carrier screening, a prospect that has been viewed with mixed feelings.

Table 1-1—A Priori Carrier Risks for Cystic Fibrosis

Negative family history	
Caucasian	1 in 25 (4%)
African American	1 in 60 to 65 (1.5 to 1.7%)
Asian American	1 in 150 (0.7%)
Hispanic American	1 in 40 to 50 (2 to 2.5%)
Positive family history	
Parent of child with CF	1 in 1 (100%)
Sibling with CF	2 in 3 (67%)
Aunt or uncle with CF[a]	1 in 3 (33%)
First cousin with CF	1 in 4 (25%)
Niece/nephew with CF[a]	1 in 2 (50%)

[a] Consanguineous.

SOURCE: Office of Technology Assessment, 1992.

Consensus exists that individuals who have relatives with CF should be told about the availability of CF carrier tests; the disagreement is whether *everyone* should be informed about the assays, since 80 percent of babies with CF are born to couples with no previous family history of the condition. Concern about the scientific, legal, economic, ethical, and social implications of the prospect that large numbers of people might be screened for their CF carrier status led the House Committee on Science, Space, and Technology, the House Committee on Energy and Commerce, and Representative David R. Obey to request the OTA assessment.

WHAT IS CYSTIC FIBROSIS?

CF is not a new disease. First described in 17th century folklore, medical literature has long documented that CF compromises many functions throughout the body—chiefly the respiratory, gastrointestinal, and reproductive systems and the sweat glands.

Many affected babies are not immediately diagnosed as having CF. Although the disease is always present at birth in affected individuals, the onset of recognizable clinical symptoms varies widely. Physicians diagnose CF using a combination of clinical criteria and diagnostic laboratory tests. Although an assay called the sweat test remains the primary diagnostic test for CF, DNA mutation analysis can diagnose more than 70 percent of cases.

CF exerts its greatest toll on the respiratory and digestive systems, and the severity of respiratory problems often determines the quality of life and survival. There is no cure for CF. Treatment focuses on managing the respiratory and digestive symptoms to maintain a stable condition and lengthen lifespan. Because of CF's varied progression, the regimen and level of therapy depends on the individual. Most therapy involves home treatment (e.g., chest physical therapy to clear mucus from the lungs), outpatient care at one of more than 110 clinics devoted specifically to CF health care, and occasional hospital stays. Today, physicians can look to an ever-expanding array of new pharmaceutical options to manage the care of CF patients; on the horizon are hopes for gene therapy.

Over the last half-century, treatment of CF has evolved so that an illness nearly always fatal in early childhood is now one where life expectancy into adulthood is common. Fifty years ago, most infants born with CF died in the first 2 years of life. In 1990, median survival was 28 years—i.e., of the individuals born with CF in 1962, half were alive in 1990.

THE CYSTIC FIBROSIS GENE

CF is a genetic illness transmitted from parents to their children via genetic directions stored in DNA. In humans, these directions, including those responsible for CF, are stored among genes arrayed on 46 structures called chromosomes. The gene responsible for CF lies on chromosome 7 and results in a product called the cystic fibrosis transmembrane conductance regulator (CFTR). In most people with CF, a three-base pair deletion in both of their CF alleles results in a faulty CFTR, which leads to CF pathology. This three-base pair mutation occurs at position number 508 in the CFTR and is abbreviated as delta F508 (ΔF508). More than 170 additional mutations in the CF gene also lead to faulty CFTRs. Individuals with CF have two of the same, or two different, mutations. CF carriers have only one mutation; their second CF allele produces normal CFTR.

About 70 percent of CF carriers have the ΔF508 mutation.[1] International studies demonstrate ethnic and regional variation in the frequency distribution of this mutation; as expected, the multicultural nature of the United States reflects this variation. Most of the other 170+ mutations appear in a small fraction of individuals or families, although a few occur at a frequency as great as 1 to 3 percent. Some symptoms (or their lack of severity) correlate with particular mutations. Digestive difficulties from pancreatic insufficiency, for example, generally associate with ΔF508.

CYSTIC FIBROSIS MUTATION ANALYSIS

With localization of the CF gene, ΔF508, and other CF mutations, it is now possible to directly analyze DNA from any individual for the presence

[1] Quoted mutation frequencies for ΔF508 and other CF mutations always depend on racial and ethnic background. Throughout this background paper, OTA presents current expert estimates of appropriate ranges of detection frequencies or sometimes uses a specific figure with qualification (e.g., about 90 percent; approximately 95 percent). OTA adopts such language to avoid restating each time that a frequency depends on racial and ethnic background, not to underemphasize the importance in the distribution variation of CF mutations. In some cases—made clear within the text—a specific frequency is chosen for illustrative or hypothetical purposes.

33. How frequently do you use each of the following formats to provide genetic counseling?

1=seldom if ever; 2=sometimes; 3=often; 4=very often; 5=almost always

a. ___ individual counseling session(s)
b. ___ group counseling
c. ___ videotape alone
d. ___ videotape with counseling
e. ___ written educational materials
f. ___ slide-tape
g. ___ interactive computer

34. Where is the closest CF treatment center to your institution?

a. ___ at my institution
b. ___ less than or equal to 50 miles
c. ___ greater than 50 miles
d. ___ not aware of one

35. Do you personally provide genetic counseling through the CF treatment center in your area?

a. ___ no b. ___ yes

If yes, please provide the following information for 1990.

1) total # new patients seen by the CF center _____
2) total # return patients seen by the CF center _____
3) # referrals for genetic counseling _____
4) # requests for information on DNA testing _____
5) # undergoing actual DNA testing _____ individuals _____ families

36. Do you or your group/unit have a specific policy regarding DNA testing for CF?

a. ___ no, we do not. b. ___ yes; if yes, what is it?

37. Are individuals/families seeking DNA testing for CF asked to sign an informed consent?

a. ___ no b. ___ yes

38. Do you or your group/unit have official policies and procedures for other issues in genetics? (check all that apply)

a. ___ DNA storage
b. ___ prenatal diagnosis for sex selection
c. ___ non-paternity
d. ___ confidentiality and Huntington's disease testing
e. ___ other: _____

28. **Have you had any experience with a patient's insurance claims for DNA testing being rejected?**
    a. ___ no experience b. ___ yes. Please provide details:

29. **Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing?**
    a. ___ no experience b. ___ yes. Please provide details:

30. **Consider the following reasons for referral for genetic counseling. Please estimate to the best of your ability, the average NUMBER of patients you see per month, total amount of direct COUNSELOR TIME spent (in minutes), and the average number of VISITS needed to provide genetic counseling to individuals and/or families for each of the following scenarios. (Answer for cases appropriate to your practice.)**

	AVG # Pts	Time/ visit	AVG # visits
a. prenatal counseling for advanced maternal age	____	____	____
b. positive family history for neural tube defects concerns for current pregnancy	____	____	____
c. Elevated MSAFP screen	____	____	____
d. Couple with newly diagnosed (Tri 21) Down's Syndrome child	____	____	____
e. Couple with 14/21 translocation Down's Syndrome child	____	____	____
f. Carrier testing for DMD	____	____	____
g. Newly diagnosed case of neurofibromatosis	____	____	____
h. Newly diagnosed CF family	____	____	____
i. Carrier testing for CF, with a positive family history	____	____	____
j. Carrier testing for CF, with a negative family history	____	____	____

31. **If you have not been involved with counseling for CF, based on your experience, how much direct counselor time (minutes) would you estimate would be needed to:**
    a. obtain 3 generational family pedigree: _____ (minutes)
    b. discuss carrier testing and recurrence risks: _____ (minutes)

32. **How would this estimate compare to the direct patient time spent with your typical patient load?**
    a. ___ more time b. ___ less time c. ___ about the same

of CF mutations. Using today's technologies, CF mutation analysis is usually a one-time test that can inform an individual whether he or she carries any of the CF mutations for which tests are conducted. Carrier *screening* for CF (or CF carrier screening) refers to performing CF mutation analysis on DNA from an individual who has no family history of CF.

Current technology, however, can leave ambiguity, but not because the tests per se are imprecise. Properly performed, DNA-based tests for CF mutations are accurate and specific—meaning if the ΔF508 mutation (or another CF mutation) is present in the individual's genome and an assay is performed to search for that mutation, the test will detect it more than 99 percent of the time, absent laboratory error. Instead, ambiguity stems from the intrinsic nature of the cause of the disease: Besides ΔF508, more than 170 mutations in the CF gene also cause CF.

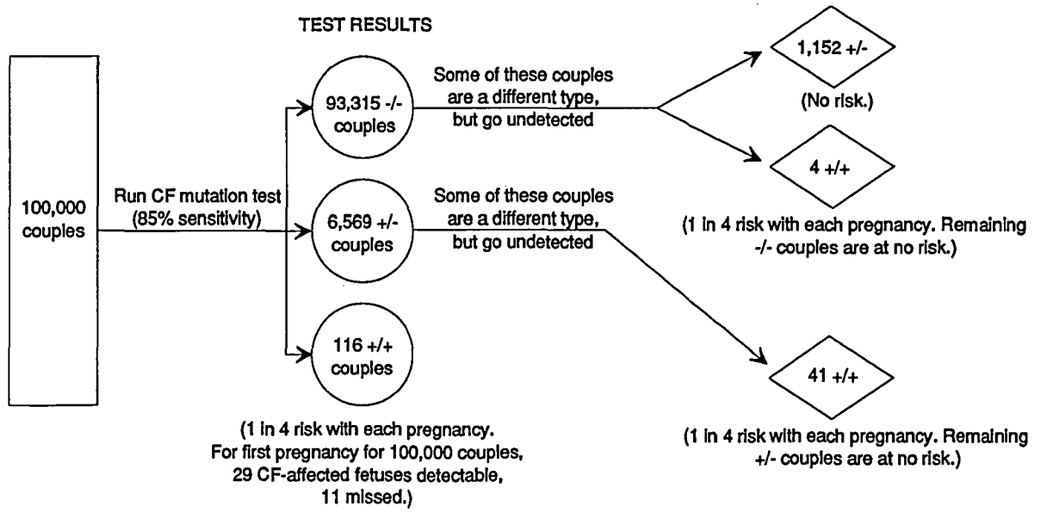
In the United States, about 1 in 25 Caucasians carries one CF mutation. Current assays use ΔF508 plus 6 to 12 other CF mutations (ΔF508+6-12) and identify about 85 percent of CF carriers (in Ashkenazic Jews, ΔF508+6 identifies about 95 percent of carriers). Thus, using ΔF508+6-12 means 10 to 15 percent of actual carriers go undetected. In other words, since tests to detect 170+ mutations are impractical, a negative test result does not guarantee that a person is not a carrier.

Using ΔF508+6-12 means that some couples receive test results that indicate one partner is a carrier and one is not, when in fact the negative partner carries one of the rare CF mutations that is not assayed. Thus, while most couples whose test results are +/- are at zero risk of having a child with CF, some couples with a +/- test result actually are couples whose genetic status is +/+ (but goes undetected) and who are at 1 in 4 risk of a child with CF for each pregnancy. Couples with a +/- test result, then, might misunderstand that their reduced risk of bearing a child with CF is not zero risk (figure 1-2).

CONTROVERSY ABOUT CYSTIC FIBROSIS CARRIER SCREENING

Prospects of routine CF carrier screening polarize people. No mandatory genetic screening programs of adult populations exist in the United States. OTA has found it highly unlikely that CF carrier screening will set a precedent in this regard (1). People agree that persons with a family history of CF should have the opportunity to avail themselves of CF mutation analysis, yet controversy swirls around using the same tests in the general population.

Figure 1-2—Cystic Fibrosis Mutation Test Results at 85 Percent Sensitivity



SOURCE: Office of Technology Assessment, 1992.

Proponents of a measured approach to CF carrier screening express concern about several issues that might be raised if use of CF carrier tests becomes routine. Invariably, discussions about CF carrier screening raise concerns about the use of genetic information by insurance companies (2) and become linked broader social concerns about health care reform in the United States. Related to this are concerns about commercialization of genetic research, i.e., 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. Also expressed are questions about the adequacy of quality assurance for DNA diagnostic facilities, personnel, and the tests themselves. Others also wonder whether the current number of genetic specialists can handle a swell of CF carrier screening cases, let alone cases from tests for other genetic conditions expected to arise from the Human Genome Project. Finally, the extraordinary tensions in the United States about abortion affect discussions about CF carrier testing and screening.

Those who advocate CF carrier tests for use beyond affected families are equally concerned about these issues. They assert, however, that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. Proponents of providing such information 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.

SCOPE AND ORGANIZATION OF THIS BACKGROUND PAPER

One of the tasks of genetic specialists is to provide the educational and counseling services necessary to successful implementation of new technologies. Increasingly, genetic counselors and nurses working in genetics will be at the front line on the issues raised by DNA technologies' assimilation into practice.

The OTA survey was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening. The results of the survey are reported in chapters 2 and 3. A summary appears in chapter 4. A description of the survey methodology is in appendix A, and the survey instrument is reproduced in appendix B.

CHAPTER 1 REFERENCES

1. U.S. Congress, Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA-BA-532 (Washington, DC: U.S. Government Printing Office, August 1992).
2. U.S. Congress, Office of Technology Assessment, *Genetic Tests and Health Insurance—Results of a Survey*, OTA-BP-BA-98 (Washington, DC: U.S. Government Printing Office, October 1992).

24. (cont.) With respect to your clinical practice, estimate the percent (%) of your patients who are:

C. LANGUAGE	Percent (%)
n. English speaking	_____
o. Non-English speaking	_____
p. unable to estimate	_____

25. Do your patients have health care coverage?

a. ___ seldom if ever (0-15% of patients seen)
b. ___ sometimes (about 16-50% of patients)
c. ___ often (about 51-74% of patients)
d. ___ very often (about 75-89% of patients)
e. ___ always or almost always (90-100% of patients)

26. Please estimate the percent of patients by category of coverage.

	Coverage Category	Percent(%)
a.	commercial insurance	_____
b.	Blue Cross/Blue Shield	_____
c.	HMO or managed care plan	_____
d.	Medicaid	_____
e.	Medicare	_____
f.	CHAMPUS	_____
g.	self pay	_____
h.	no insurance	_____
i.	indigent	_____
j.	unknown	_____

27. For individuals with insurance coverage, what has been your experience with reimbursement of fees for service in each of the following areas? Also, please indicate the average fee amount charged for each service.

1=seldom if ever covered; 2=sometimes covered; 3=often covered; 4=very often covered; 5=almost always covered; 6=uncertain

a. ___ general genetic counseling: Fee $_____
b. ___ genetic counseling for cystic fibrosis with positive family history: Fee $_____
c. ___ genetic counseling for cystic fibrosis with negative family history: Fee $_____
d. ___ routine metabolic screen: Fee $_____
e. ___ routine cytogenetic analysis: Fee $_____
f. ___ DNA analysis for cystic fibrosis: Fee $_____

21. Indicate the frequency of patients seen by you for each major area of clinical practice.

1=seldom if ever; 2=sometimes; 3=often (i.e., majority); 4=very often; 5=all or almost all

a. ___ prenatal genetics
b. ___ pediatric genetics
c. ___ adult genetics
d. ___ teratogen exposure
e. ___ reproductive loss
f. ___ specialty disease(s) clinics (please specify): _____
g. ___ newborn screening
h. ___ MSAFP screening follow-up
i. ___ carrier screening (specify disease): _____

22. Does your institution participate in collecting the CORN data set?
a. ___ yes b. ___ no c. ___ don't know

23. For each of the following categories, indicate the number (or best estimate) of genetics clients/patients served in 1990, either DIRECTLY (i.e., counselor to client relationship; one-on-one genetic counseling) or INDIRECTLY (i.e., involvement such as consultant to primary care physician regarding a patient, telephone consultation).

	TYPE OF PATIENT CONTACT		
	Direct	**Indirect**	**Total**
All patients seen in 1990			
a. by your unit:	_____	_____	_____
b. by you individually:	_____	_____	_____
CF patients/families seen in 1990			
c. by your institution:	_____	_____	_____
d. by you individually:	_____	_____	_____

24. With respect to your clinical practice, estimate the percent (%) of your patients who are:

	Percent (%)
A. RACE/ETHNICITY	
a. Asian/Pacific Islander	_____
b. Black	_____
c. Caucasian	_____
d. Native American	_____
e. Spanish surname	_____
f. unable to estimate	_____
B. AGE DISTRIBUTION	
g. neonatal	_____
h. infants	_____
i. children	_____
j. adolescents	_____
k. adults - reproductive age	_____
l. adults - post reproductive age	_____
m. unable to estimate	_____

Chapter 2
Providers, Clientele, and Genetic Services

The purpose of the OTA survey was to evaluate the extent to which genetic counselors and nurses in genetics are routinely offering carrier screening for cystic fibrosis (CF) to their clientele, to assess their attitudes and beliefs about the appropriateness of such screening, and to obtain a sense of the environment in which they work. While members of the National Society of Genetic Counselors (NSGC) and the International Society of Nurses in Genetics (ISONG) are by no means the only health professionals providing genetic counseling, they comprise a professional segment devoted explicitly to that end. Physicians, social workers, public health workers, and research scientists also provide genetic services. Those groups were not included in this survey.

To better understand the setting in which routine carrier screening for CF might take place, OTA gathered data regarding not only counselors' attitudes and practices regarding CF carrier screening (ch. 3), but also the settings in which they work, the numbers and types of clients they serve, clinical practices, work routines, fees charged, and third-party payment options available to their clientele. Understanding the environment in which CF carrier screening takes place was a critical part of the analysis reported in *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (10).

THE SURVEY POPULATION

Of the 703 members of the NSGC who received questionnaires, 351—or 50 percent—responded. Of the 110 members of ISONG who received the questionnaire, 80—or 73 percent—responded. Thus, 80 percent of the respondent group are members of NSGC and 20 percent are members of ISONG.[1]

As preliminary analysis revealed no significant difference in question response between the two populations, all data were combined for the final analysis. The combined response rate is 53 percent.

Genetic Counselors

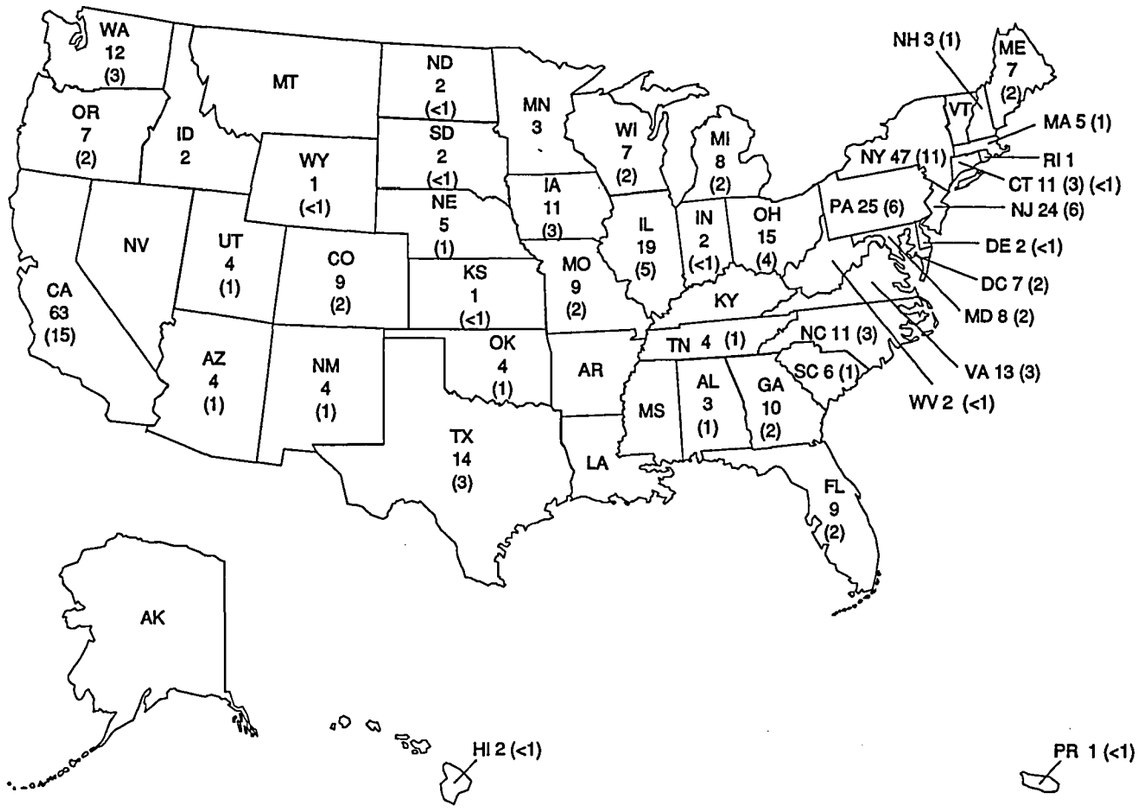
The master's-level genetic counselor is a relatively new addition to the health care system. In 1971, 10 graduates of the first such program entered the workforce; in 1979, the NSGC was incorporated as a professional organization. Today, there are approximately 1,000 master's-level genetic counselors practicing in the United States.

Master's-level genetic counselors receive specialized multidisciplinary training and experience to prepare them for counseling related to a wide variety of genetic disorders and birth defects. They are typically graduates from a 2-year master's degree program, during which time they receive didactic course work in the principles and application of human genetics, clinical and medical genetics, genetic laboratory methods, and interviewing and counseling. Genetic counselors are also trained in social, ethical, legal, and cultural issues relating to genetic diseases, principles of public health and health care delivery systems, and education for the lay and professional community (12). Over the past 20 years, master's-level graduate programs in genetic counseling have increased to 15, and combined, they produce approximately 75 graduates each year (7). At the time of the OTA survey, there were 703 genetic counselors who were full members of NSGC (associate, student, and foreign members were not surveyed). Of all respondents to the survey, 70 percent had a master's degree in genetic counseling. An additional 10 percent held a master's degree in another area, and 8 percent had a Ph.D.

Genetic counselors receive a minimum of 400 hours of supervised clinical training in at least three clinical settings, including a general genetics clinic, a prenatal diagnosis clinic, and a speciality disease clinic. Until 1992, graduates were eligible to sit for the certification examination in genetic counseling by the American Board of Medical Genetics (ABMG), but continuing certification of these individuals by this body is uncertain. In the past, counselors were required to submit their credentials and a logbook of 50 cases obtained in a clinically accredited training

[1] These response rates are typical of other mail surveys reported in the literature (1,6). One review found response rates for a two wave survey (initial mailing and one followup) ranged from 37 to 58.4 percent (6). OTA's aggregate response rate clearly falls within this range, as does the response rate of the genetic counselors; the response rate of the nurses in genetics exceeds it.

Figure 2-1—Geographic Distribution of Survey Respondents[a]



[a]Actual number of respondents from a State is listed, with the percentage the number represents in parentheses.
SOURCE: Office of Technology Assessment, 1992.

site before taking the exam (7). Most survey respondents survey were board certified (65 percent) or board eligible (19 percent).

Nurses in Genetics

There are nearly 2 million registered professional nurses in the United States, many involved in maternal and child health nursing. These professionals provide a unique potential to contribute to the effective delivery of genetic services. Efforts are under way to encourage the incorporation of clinical genetics into the curricula of schools of nursing at both the graduate and undergraduate level (4). The need for better genetics education in nursing stems from the recognition that genetics generally has been within the realm of tertiary care; thus, genetics specialists are not always in the position to screen every individual needing genetics referral (4). That is, individuals in need of genetic services must first be identified by the primary health care professional, and in some settings—such as community, occupational, or school health—nurses are the only link with the health care system (3). Thus, nurses can assist in the identification, education and counseling, and followup of patients (2,4). Though nurses can be a valuable part of genetics services, to date they are a largely untapped resource (3).

Opportunities for clinical genetics experience in nursing programs vary. Genetics is generally a part of the nursing school curriculum, but variability exists among programs (3). Four of the 200 universities in the United States that offer graduate degrees

15. **If you were asked about DNA testing/screening for CF, please estimate the number of requests per month (January - June, 1991)?** _____ (per month)

16. **Compared to 2 years ago, would you say the number of requests made between January - June, 1991 represents:**
    a. ___ a large decrease
    b. ___ a small decrease
    c. ___ no change
    d. ___ a small increase
    e. ___ a large increase

17. **If you noted an increase, when did you note this? (month/year)** _____

18. **In your current position are you engaged in providing genetic counseling?**
    a. ___ yes b. ___ no

If NO, skip the CLINICAL PRACTICE QUESTIONS and GO TO QUESTION #46

THE NEXT SERIES OF QUESTIONS ARE TO BE ANSWERED BY THOSE INDIVIDUALS WHO CURRENTLY PROVIDE GENETIC COUNSELING SERVICES
(All others please skip to question #46.)

19. **Which best describes the primary service area in which you work?**
    a. ___ rural
    b. ___ suburban
    c. ___ metropolitan/urban
    d. ___ statewide
    e. ___ regional (more than one State)
    f. ___ national
    g. ___ other: _____

20. **Current level of staffing (including yourself) in your counseling unit/program (please indicate number).**

	#
a. M.D. geneticists	____
b. Ph.D. geneticists	____
c. M.D./Ph.D. geneticists	____
d. genetic counselors	____
e. secretaries	____
f. other: _____	____

11. **Which best describes your work setting(s)? Designate a primary (1) and secondary (2) setting, if applicable.**
    - a. ___ private hospital/medical facility
    - b. ___ university medical center
    - c. ___ free standing clinic
    - d. ___ Health Maintenance Organization (HMO)
    - e. ___ private group practice
    - f. ___ solo private practice
    - g. ___ private industry (specify type): _____
    - h. ___ State laboratory (specify type): _____
    - i. ___ regional laboratory (specify type): _____
    - j. ___ commercial laboratory
    - k. ___ Public Health department (State, county, or city)
    - l. ___ State government agency
    - m. ___ Federal government agency
    - n. ___ voluntary health organization
    - o. ___ educational institution (K-12)
    - p. ___ higher educational institution (undergraduate or graduate)
    - q. ___ other: _____

12. **On average, how many hours a week are you involved in:**
    - a. ___ direct patient contact (counseling patients)
    - b. ___ indirect patient activities (review of literature or records, coordinating referrals)
    - c. ___ performing administrative/managerial tasks
    - d. ___ educating health professionals, medical students, GC trainees
    - e. ___ educating the general public, schools, undergraduates
    - f. ___ performing laboratory work
    - g. ___ research
    - h. ___ marketing/business
    - i. ___ other: _____

13. **What sources of information about new advances in the field of human genetics do you rely on? (check all that apply)**
    - a. ___ professional colleagues
    - b. ___ medical journals
    - c. ___ grand rounds
    - d. ___ State or regional conferences
    - e. ___ national conferences
    - f. ___ American Society of Human Genetics
    - g. ___ National Society of Genetic Counselors
    - h. ___ continuing education courses
    - i. ___ literature from biotechnology/commercial firms
    - j. ___ lay press
    - k. ___ other: _____

14. **In your current position, how frequently were you asked about DNA testing/screening for CF during the 6-month period from January - June, 1991? Please consider this in the context of your total clinical practice.**
    - a. ___ never
    - b. ___ rarely
    - c. ___ occasionally
    - d. ___ frequently
    - e. ___ very frequently

in nursing have established programs providing a master's-level genetics major (3). A small number of nurses, particularly those in maternal and child health nursing, have focused on genetics in order to sit for the genetic counseling examination given by the American Board of Medical Genetics (ABMG) (3,5). There are over 100 nurses employed in genetics who also belong to ISONG and therefore received OTA's questionnaire. It is likely that many more nurses deliver genetic services but are unidentifiable through current databases. Of the total survey respondents, 12 percent reported having either an R.N. or B.S.N. degree. Nurses might also have a master's degree or Ph.D. and could be included in the 80 percent of respondents who reported having a master's degree or the 8 percent who reported having a Ph.D.

Demographic Profile of Survey Respondents

The typical individual working as a genetic counselor or nurse in genetics is likely to be female (92 percent), in her mid-30s (mean age of 37), Caucasian (96 percent; 2 percent are Hispanic, 1 percent African American, 1 percent Asian American), and married (70 percent). On average, she is likely to have been in practice for 6 to 7 years, having received her degree in 1985. Eight-seven percent of these individuals speak only English; 5 percent also speak Spanish, and 8 percent speak English and a language other than Spanish.

Respondents represented every State except Arkansas, Louisiana, Kentucky, Mississippi, Montana, and Nevada (figure 2-1). There is a heavy concentration of counselors in five States, with 43 percent of respondents located in California, Illinois, New Jersey, New York, and Pennsylvania, and 23 percent located in three northeastern States, New Jersey, New York, and Pennsylvania (table 2-1). California had the highest representation at 15 percent. These data are consistent with those collected and biannually reported by the NSGC (8). Hence, OTA's survey respondent pool is representative of the NSGC membership and no sample weighting was necessary.

WORK ENVIRONMENTS

The majority of respondents (83 percent) are currently engaged in providing genetic counseling. Seventeen percent work in an environment where they are not encountering direct patient contact, perhaps serving as administrators, educators, or researchers. The primary work settings for all respondents are presented in table 2-2. Most counselors and nurses are employed in a university medical center (36 percent) or a private hospital or medical facility (36 percent). The remainder work in a variety of settings, such as public health departments, health maintenance organizations, colleges or universities, private group practices, free standing clinics, or commercial laboratories. Again, these data are consistent with the data collected by NSGC on a biennial basis for its professional status survey (8).

Table 2-1—Geographic Concentration of Survey Respondents

State	Number (percent)
California	63 (15)
New York	47 (11)
Pennsylvania	25 (6)
New Jersey	24 (6)
Illinois	19 (5)
Total	178 (43)

SOURCE: Office of Technology Assessment, 1992.

Table 2-2—Primary Work Setting

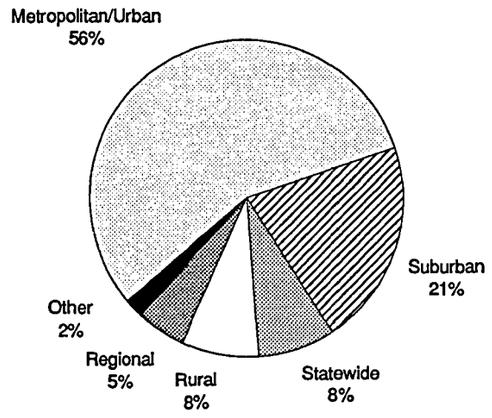
	Number (percent)
University medical center	151 (36)
Private hospital or medical facility	150 (36)
Public health department	22 (5)
Health maintenance organization	15 (4)
College or university	14 (3)
Private group practice	11 (3)
Free-standing clinic	10 (2)
Commercial laboratory	9 (2)
Other	31 (7)

SOURCE: Office of Technology Assessment, 1992.

Centers of expertise in clinical genetics tend to be located at large urban medical centers, often with a teaching mission. The work location and setting of the survey population reflect that tendency. Respondents are most likely to work in a metropolitan or urban setting (58 percent) (figure 2-2). Counselors and nurses in genetics are less likely to be found working in rural settings. Counselors tend to work with M.D. geneticists, Ph.D. geneticists, other genetic counselors, and a variety of support staff. Most rural centers are unable to support this level of professional personnel and often rely on regional service areas. Five percent of respondents reported working in a regional genetics area.

Respondents spend nearly two-thirds (65 percent) of their work week—about 26 hours per week—on patient activities, whether direct patient contact

Figure 2-2—Primary Service Areas of Respondents



SOURCE: Office of Technology Assessment, 1992.

(e.g., intake or counseling) or indirect (e.g., written communication, scheduling, and management of referrals) (table 2-3). An additional day is spent on administrative procedures. This leaves little time for other activities such as educating other health professionals or the general public. On average, counselors and nurses in genetics spend little time on public education. Fifty percent report spending no time on this activity, while 26 percent report spending, on average, an hour a week on public education (figure 2-3). Individual counseling sessions are time and labor intensive and are the primary format for delivering genetic information (table 2-4). Respondents report that they seldom if ever rely on group counseling (67 percent) or videotape with counseling (76 percent).

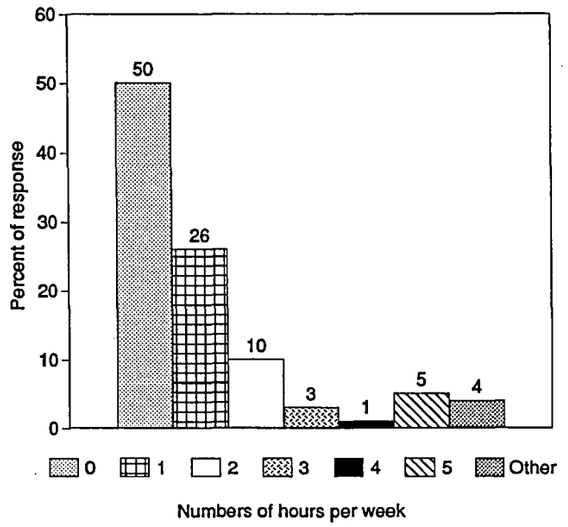
On average, each genetic counselor and nurse in genetics saw 482 patients in 1990. Averages do not, however, speak to the great variability among practices. Responses ranged from 10 to 2,300 clients. Counselors and nurses providing prenatal

Table 2-3—Average Weekly Schedule of Genetic Counselor or Nurse in Genetics

Activity	Hours per week
Direct patient contact	15
Indirect patient activities	11
Administration/management	7
Educating health professionals	3
Research	2
Educating the general public	1
Marketing/business	1

SOURCE: Office of Technology Assessment, 1992.

Figure 2-3—Average Hours Spent Per Week on Public Education



SOURCE: Office of Technology Assessment, 1992.

diagnosis and followup for elevated maternal serum alpha-fetoprotein (MSAFP) screening tend to have more clients.

In routine genetic counseling, the genetics specialist elicits the reasons for testing or screening and discusses the implications of possible outcomes. The counselor prepares the individual for both positive and negative test results. A genetic counseling session is also the time to discuss risk reduction strategies, if relevant, and the nature and severity of the disorder for which the test is being done. One task of the genetics professional is to communicate risks to the client—a job not easily performed. The more complex the information, or the more emotionally laden, the more time might be required. Survey respondents estimate that the time needed to conduct routine prenatal counseling is 1 hour. Counseling for

Table 2-4—Formats for Genetic Counseling

	Predominant response (%)
Individual counseling sessions	Almost always (84)
Group counseling	Seldom if ever (67)
Videotape alone	Seldom if ever (98)
Videotape with counseling	Seldom if ever (76)
Written educational materials	Very often (24)
Slide-tape	Seldom if ever (88)
Interactive computer	Seldom if ever (97)

SOURCE: Office of Technology Assessment, 1992.

Office of Technology Assessment
United States Congress
Washington, D.C. 20510-8025

SURVEY OF GENETIC COUNSELING ATTITUDES AND PRACTICES REGARDING CYSTIC FIBROSIS SCREENING

Genetic Counselor Demographics

1. **Sex:** a. ___ female b. ___ male

2. **Age:** ___ years

3. **Race:** a. ___ Asian d. ___ Hispanic
   b. ___ Black e. ___ Native American
   c. ___ Caucasian f. ___ Other: _____

4. **Marital status:**
   a. ___ married c. ___ never married
   b. ___ widowed d. ___ divorced/separated

5. **In what State do you work?** State a._____ ZIP code b. _____

6. **Degrees held:** Year granted:
   a. ___ MA/MS - Genetic counseling _____
   b. ___ RN/BSN _____
   c. ___ MSN _____
   d. ___ MPH _____
   e. ___ MSW _____
   f. ___ Ph.D.: _____ _____
   g. ___ M.D. _____
   h. ___ J.D. _____
   i. ___ currently in degree program: _____ (type)

7. **How many years of clinical practice as a genetic counselor do you have?** _____

8. **Certification status (American Board of Medical Genetics)**
   a. ___ Board certified (CIRCLE Year): 1982, 1984, 1987, 1990
   b. ___ Board eligible
   c. ___ not necessary for position
   d. ___ none

9. **Are you fluent in any language other than English?**
   a. ___ no b. ___ yes, I speak English and (specify other): _____

10. **Present employment status:**
    a. ___ full time
    b. ___ part time: _____ hours/week
    c. ___ not working

Appendix B

Survey Instrument

As part of the 1992 assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA surveyed the summer 1991 memberships of the International Society of Nurses in Genetics and the National Society of Genetic Counselors. The items for the two questionnaires were identical, and the following is a reproduction of the survey instrument.

newly diagnosed genetic disorders in newborns, children, or adults takes more time and more visits. Carrier testing for families with a positive family history for CF was estimated to take, on average, two visits involving more than 1 hour each. Counseling for CF carrier screening, with no family history, however, was estimated to take one visit of less than an hour. The need for sufficient and appropriate pretest education and post-test counseling is discussed in depth in the full OTA report (10).

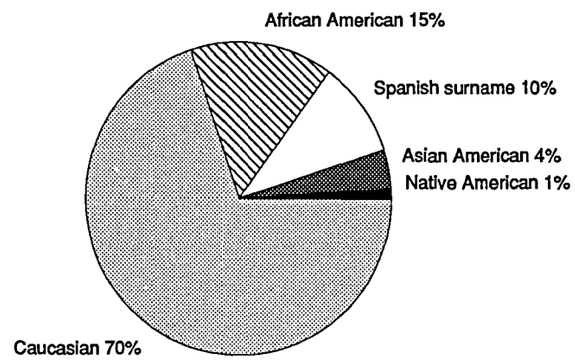
GENETICS CLIENTELE

Genetic counselors and nurses in genetics work in a variety of settings and often the setting in which they work dictates the types of clients they encounter. For example, working in a department of obstetrics and gynecology is likely to mean that the majority of one's clients are pregnant or undergoing family planning prior to pregnancy. Employment in a department of pediatrics or a children's hospital means that most clients are likely to be children and their families. Some counselors work in specialty clinics, such as cranio-facial clinics or sickle cell screening centers. Thus, their clientele are more likely to be adult or African American, respectively. The OTA survey results are reported in the aggregate and fail to illustrate that some practitioners work in specialized settings, often with one type of clientele.

The majority of individuals seen by genetic counselors and nurses in genetics are Caucasian (70 percent) (figure 2-4). Respondents report an ethnic and racial breakdown that is reflective of national population averages. For example, approximately 15 percent of genetics clientele are reported as African American; this minority group represents 12 percent of the U.S. population. These data do not provide information, however, about equitable allocation of genetic services locally or regionally. African Americans or Asian Americans might find genetic services accessible in one city or one region but not in another. Genetics services in cities with large minority populations might be more likely to hire health care providers with language or cultural skills suitable to certain populations.

Ninety-two percent of genetics clientele are English speaking. As mentioned earlier, 13 percent of genetic counselors and nurses reported fluency in a language other than English, but no effort was made by OTA to correlate provider fluency with clientele needs.

Figure 2-4—Racial/Ethnic Background of Clinical Genetics Clientele

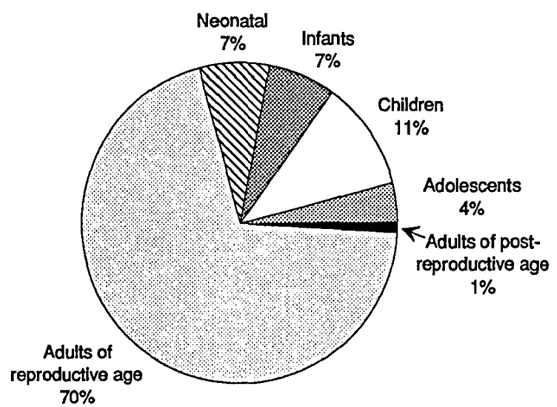


SOURCE: Office of Technology Assessment, 1992.

A variety of age groups are seen, but adults of reproductive age comprise 70 percent of the average clinic clientele. The second largest group of individuals seen are children (11 percent). Infants and neonates collectively comprise 14 percent of genetics clientele (figure 2-5).

Most of the adults of reproductive age are seen for prenatal diagnosis (figure 2-6), most likely for advanced maternal age. Prenatal genetics patients were reported as being seen very often or almost always by nearly two-thirds of respondents (figure 2-6). Clearly, prenatal diagnosis is a primary reason for individuals to have contact with the clinical genetics setting. Respondents also reported that

Figure 2-5—Age Distribution of Genetics Clientele



SOURCE: Office of Technology Assessment, 1992.

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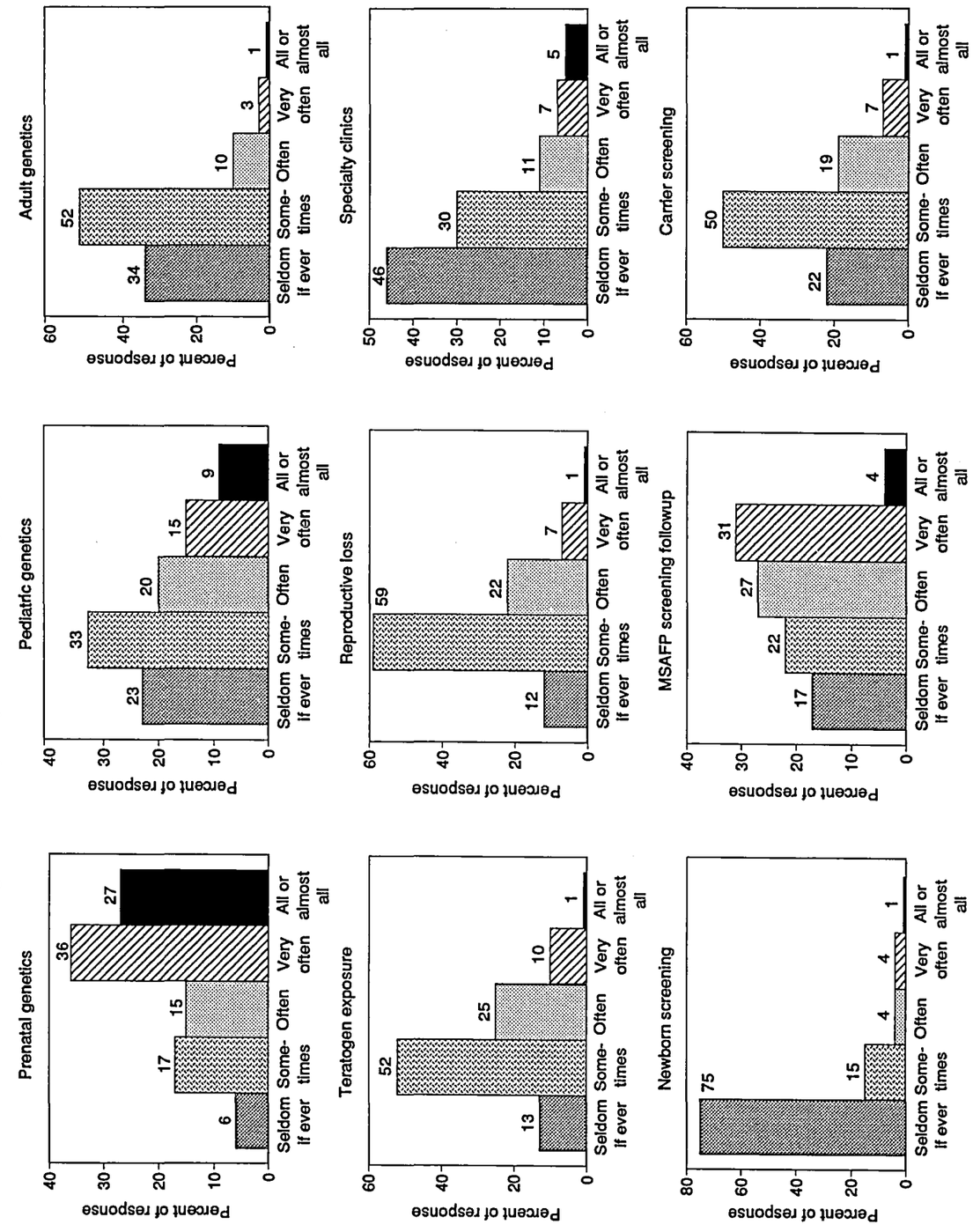


Figure 2-6—Frequency of Patients Seen by Major Areas of Clinical Practice

SOURCE: Office of Technology Assessment, 1992.

Appendix A
Survey Method

Data for this survey were collected from 431 survey questionnaires mailed to 813 individuals in June and July of 1991. The sample was drawn from the membership list of the National Society of Genetic Counselors (NSGC) and the mailing list of the International Society of Nurses in Genetics (ISONG). Only full members (excluding student, associate, and foreign memberships) of the NSGC were surveyed. The initial mailing list provided by ISONG was screened to remove individuals who were not practicing nurses from the sample (e.g., journalists, vendors).

Questionnaires were not numerically or otherwise coded, and hence were completely anonymous. Respondents were asked to return their questionnaire in a post-paid envelope provided by OTA. Approximately 2 weeks after the initial mailing, a followup letter was sent to all survey respondents. The second wave improved the response rate by about 15 percent.

The content of the instruments was identical for the two populations, but the questionnaires were reproduced on different colored stock for easier tracking. Preliminary analysis revealed no significant difference in question response between the NSGC and ISONG samples, and so all data were combined into one set for the final analyses.

Surveys returned after September 30, 1991 were not included in the final data analyses. A statistical software package was used to provide frequency distributions and cross-tabulations of the data. No weighting was done of the sample, as OTA believes that the sample closely represents the entire population.

pregnant women receiving followup counseling for abnormal MSAFP results often (27 percent) or very often (31 percent) are a part of their clientele (figure 2-6). Individuals seeking carrier screening for a variety of genetic disorders, such as those described in table 2-5, seldom (22 percent) or sometimes (50 percent) comprise the clientele in genetics clinics (figure 2-6). Cystic fibrosis was reported most frequently as the disease for which carrier screening or testing is offered (table 2-5), and a majority of respondents (62 percent) report they have seen more than 100 clients for CF-related reasons in 1990 (figure 2-7).

FEES AND THIRD-PARTY COVERAGE

How expensive are genetic services and will insurers pay for them? How do third-party payors decide what is medically indicated and, therefore, should be covered? Many of these issues are addressed in the full OTA report (10) as well as the Background Paper, *Genetic Tests and Health Insurance—Results of a Survey* (11). In this survey of genetic counselors and nurses, OTA obtained information about the fees charged by providers for a variety of genetic services, including those related to CF, and their experiences with third-party coverage. Costs of services and the availability of third-party coverage will be crucial to the rate and magnitude at which services will be used. This is particularly relevant to the debate about CF carrier screening as the procedure is relatively new, is counter to most insurers' policies against paying for screening, and could involve potentially large numbers of people.

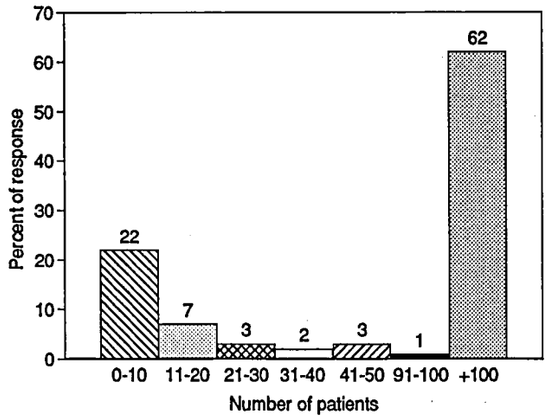
For many years, genetic counselors have faced the problem that few third-party insurers will reimburse for counseling services unless performed by a physician. The costs of counseling are reimbursed as general medical consultation fees or absorbed as part of costs on research grants (9).

Table 2-5—Most Common Diseases for Which Carrier Screening/Testing Is Offered

(Ranked by frequency of response)
1. Cystic fibrosis
2. Tay Sachs disease
3. Sickle cell anemia
4. Duchenne muscular dystrophy
5. Thalassemia
6. Hemophilia
7. Hemoglobinopathies
8. Fragile X syndrome

SOURCE: Office of Technology Assessment, 1992.

Figure 2-7—Number of Cystic Fibrosis Patients or Families Seen in Genetics Units in 1990



SOURCE: Office of Technology Assessment, 1992.

Fees for Genetic Services

Genetic counseling can be provided alone or in conjunction with diagnostic procedures. Most survey respondents work in large university or private medical centers where billing departments are often quite separate and distinct from the various clinical departments. Fees are coded and processed independently. This might explain why a majority of respondents did not know whether certain genetic services were reimbursable and, in some cases, did not even know the fee schedule for basic genetic services (table 2-6). For those who knew the fee schedule for genetic services, general genetic counseling averaged $80 per session. The range was $0

Table 2-6—Average Fees and Knowledge of Fees for Genetic Services

Service	Fee	Percent respondents uncertain of fee
General genetic counseling	$ 80	45
Genetic counseling for CF with a positive family history	$112	54
Genetic counseling for CF with a negative family history	$105	68
Routine metabolic screen	$157	70
Routine cytogenetic analysis	$425	50
DNA analysis for CF	$235	66

SOURCE: Office of Technology Assessment, 1992.

Table 2-7—Fees for General Counseling

Fee	Percent response
$0 to 50	2
$51 to 100	31
$101 to 150	25
$151 to 200	2
$201 to 250	7
$251 to 300	5
$301 to 350	38

SOURCE: Office of Technology Assessment, 1992.

to $350 (table 2-7). The fee for genetic counseling for individuals with a family history of CF was not significantly different from the fee that would be charged to individuals requesting the same services with a negative history for CF ($112 versus $105). In the summer of 1991, the average fee for DNA analysis for CF was $235 although spring 1992 data collected separately by OTA found an average cost of $170 per sample.

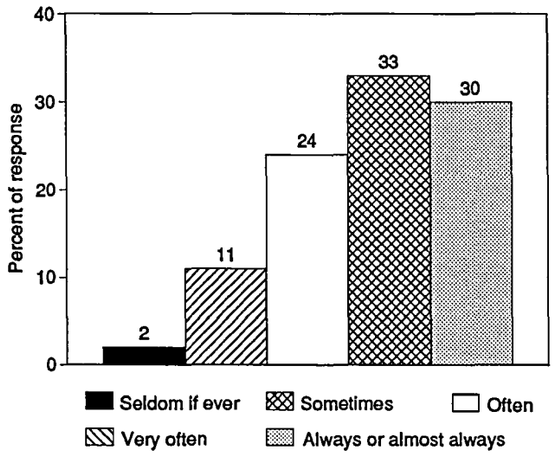
Third-Party Coverage

Respondents reported that most of their clients are covered by some type of health insurance. Two percent said that their patients seldom if ever have health care coverage, whereas 63 percent reported that their clients very often or always have coverage (figure 2-8). Commercial insurance, health maintenance organizations, or managed care programs comprise over half of the coverage (figure 2-9). Medicaid (21 percent) and Blue Cross/Blue Shield plans (17 percent) also cover genetics clients. Four percent of clients have no insurance and 3 percent are indigent.

With regard to coverage of genetic counseling services accompanying DNA-based tests to determine CF carrier status, respondents reported a higher likelihood of coverage if there is a family history of CF than if there is no family history (figure 2-10). This result was confirmed by OTA's survey of health insurers, which found health insurers rarely reimburse individuals for CF carrier tests in the absence of a family history (11).

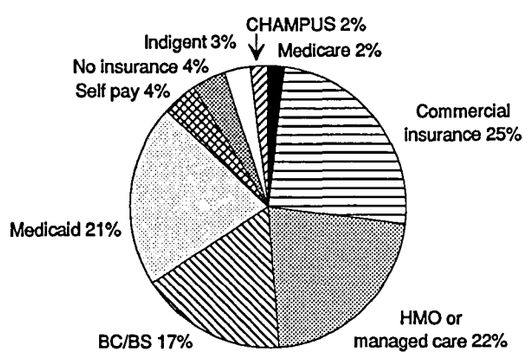
OTA attempted to ascertain whether individuals who avail themselves of genetic tests subsequently have difficulty obtaining or retaining health insurance. The survey asked for reported occurrences for genetic tests, generally, not just carrier tests for CF or other disorders.[2] OTA asked:

Figure 2-8—Health Care Coverage for Genetics Clientele



SOURCE: Office of Technology Assessment, 1992.

Figure 2-9—General Types of Health Care Coverage for Genetics Clientele



SOURCE: Office of Technology Assessment, 1992.

> Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing? If yes, please provide details.

Approximately four-fifths (347) of the 431 respondents to OTA's inquiry currently perform genetic counseling. Fifty respondents (14 percent) reported they had clients who had experienced difficulties obtaining or retaining health care coverage.

[2] In a separate survey of health insurers, OTA asked respondents to speculate about accepting applicants with certain genetic conditions (11).

creased genetics education for all health care professionals is desirable. Routine carrier screening for CF—and tests yet to be developed for other genetic conditions—will require adequate training and education of individuals in the broader health care delivery system. Some survey respondents recognize the critical role other health care professionals will play in pretest education and indicated that should the momentum toward CF carrier screening accelerate, they would make efforts to increase their public and professional education activities.

Although genetic counselors and nurses in genetics work in a variety of settings, they are concentrated in metropolitan medical centers on the West coast or in the Northeast. States with large rural populations are less likely to be served. The clientele served, in the aggregate, tend to be representative of the national averages for racial and ethnic populations, although no effort was made by OTA to match racial and ethnic data with regions, cities, or localities. This diversity presents great opportunity in terms of professional and public education, yet few counselors report an emphasis on these activities in their weekly routine because patient services comprise two-thirds of their time.

One of the tasks of genetic specialists, however, is to provide the educational and counseling services necessary to successful implementation of new technologies. Diagnostic tools, such as DNA tests, can provide powerful information. Increasingly, genetic counselors and nurses working in genetics will be at the front line on the issues raised by assimilating DNA technologies into clinical practice.

informed consent and quality of services. Proponents argue that the tests are sensitive enough for current use and that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. 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. In this survey population, however, advocates of routine CF carrier screening were in the minority.

Perhaps the point on which there was greatest consensus among respondents is on the issue of autonomy and choice in screening. There are no mandatory genetic screening programs of adult populations in the United States. Ninety-nine percent of survey participants responded that CF carrier screening should be voluntary and never mandatory.

Given the existing tensions surrounding CF mutation analysis in the general population, who should serve as gatekeeper of this new technology? Survey respondents strongly believe that CF carrier screening should be organized by and provided by the human genetics community. This assumes, however, that large numbers of Americans will learn of their CF carrier status through interaction with the genetic services system.

Based on the client populations reported in this survey, routine CF carrier screening will likely integrate into medicine in the reproductive context first. The prenatal population has been the traditional entry point into genetic services for many people; OTA's survey found 70 percent of the genetics clientele are adults of reproductive age, reinforcing the notion of prenatal diagnosis as an entry point for primary genetics service.

Preconceptional individuals are the ideal population for CF carrier screening, according to survey respondents, but for most individuals the first real opportunity for carrier screening takes place post-conception. Thus, despite survey respondents' desire that information about the availability of assays such as CF mutation analysis should come from genetic specialists, the primary responsibility for providing CF carrier screening is likely to reside with obstetricians, at least initially, and especially if reimbursement for CF mutation analysis and its attendant counseling become part of routine obstetric care. Such a scenario would mirror that which has occurred with maternal serum alpha-fetoprotein screening to detect fetuses with neural tube or abdominal wall defects or Down syndrome—a prospect that concerns some, but not others.

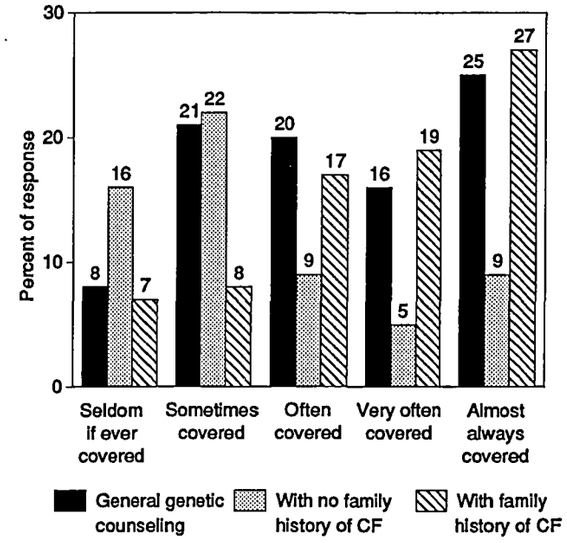
OTA's survey of genetic counselors and nurses also reports some consumers experience difficulties in obtaining or retaining health care coverage after genetic tests, though the large majority were not for carrier status, but were for genetic illness. Nevertheless, because genetic-based predictive testing promises to have a profound impact on clinical medicine—and because access to medical care is inextricably linked to private health insurance in this country—such cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

Critics of widespread CF carrier screening question whether the present genetic counseling system in the United States can handle the swell of cases if CF carrier screening becomes routine. Currently, about 1,000 master's-level genetic counselors practice in the United States, and an additional 100 nurses in genetics provide similar services. OTA's survey of genetic counselors and nurses in genetics indicates that respondents believe routine CF carrier screening will strain the present genetic services delivery system. Respondents estimated that, on average, 1 hour would be needed to obtain a three-generational family history and to discuss CF carrier screening and genetic risks.

Skeptics of a personnel shortage assert that counseling about CF carrier assays is likely to take place in the general obstetric/prenatal context, however, and believe 1 hour exaggerates the amount of time that suffices for all prenatal tests, let alone only CF carrier screening. Furthermore, counseling related to CF carrier screening is likely to extend beyond genetics professionals to include other physicians and allied health professionals. For example, an unknown number of social workers, psychologists, and other public health professionals perform genetic counseling, often to minority and underserved populations.

Ultimately, the issue of adequate services and professional capacity could turn on the extent to which patients receive genetic services through specialized clinical settings, as they largely do now, versus access through primary care, community health, and public health settings. Overall, OTA cannot conclude whether increased numbers of genetic specialists are necessary, but clearly in-

Figure 2-10—Third-Party Reimbursement for General Genetic Counseling and Counseling Specifically for Cystic Fibrosis



SOURCE: Office of Technology Assessment, 1992.

Table 2-8—Difficulties in Obtaining or Retaining Health Insurance After Genetic Tests

Question: Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing?

	Number	(percent)
No	281	81
Yes	50	14
No answer	16	5

SOURCE: Office of Technology Assessment, 1992.

age as a result of genetic testing (table 2-8). Because some respondents described more than one case, the number of affirmative answers understates the actual number of cases. Examination of the qualitative responses, some of which are presented in table 2-9, reveals affirmative responses represent, at minimum, 68 individual cases. (Where the term "patients" was used with specifics not described, a single event was recorded.)

It is important to emphasize that most of the cases revealed through the OTA survey do not involve recessive disorders and carrier screening for conditions like CF. And while one assumption might have been that health care coverage for CF carriers would not be an issue because the individuals have no symptoms of the disorder, OTA's survey of health insurers reveals that a few respondents would require a waiting period or deny coverage for CF carriers (10,11).

Test results for some conditions where positive results led to reported difficulties—such as for Huntington disease, adult polycystic kidney disease, and Marfan syndrome—were cited by more than one respondent. In addition to affirmative answers, several respondents reported that although they had no direct experience with a patient's difficulty in obtaining or retaining health care coverage, they had clients who feared their coverage would be dropped if they requested payment for tests from insurers. One respondent commented that greater than 80 percent of her clients who test for Huntington disease self-pay. Similarly, others with no direct experience said they often advise patients not to request reimbursement for a test so that an insurer would not learn that testing had occurred. One counselor offered the information that a patient had refused testing for adult polycystic kidney disease because of concern over health insurance. Another respondent reported that a patient with a CF-affected child had been dropped by one insurance company and would not consider prenatal testing in the future for fear her current insurer would not cover the child should she decide to continue the pregnancy.

The data collected through this question permit neither extrapolation about the total number of cases that have occurred in the United States nor speculation about any trends. OTA also did not attempt to ascertain whether patients had challenged—or were challenging—insurers' rulings. Thus, OTA cannot determine whether some of the disputes reported in table 2-9 were resolved fully in favor of the consumer because the initial judgment was deemed improper or illegal. Some cases, for example, reported a fetus or newborn had tested positive and the policy cancelled. In all 50 States and the District of Columbia, insurers must cover (or offer the option to include) a newborn child if a valid insurance contract for the parent exists. However, whether the insurance company can deny specific benefits for the newborn by evoking the preexisting condition clause generally contained in all insurance contracts is unclear.

In presenting table 2-9, OTA does not judge the validity—positively or negatively—of the claim. Some cases might have been settled in favor of the individual. Others might have been cases where an

Table 2-9—Case Descriptions of Genetic Testing and Health Insurance Problems[a]

Positive test for adult polycystic kidney disease resulted in canceled policy or increased rate for company of newly diagnosed individual.
Positive test for Huntington disease resulted in canceled policy or being denied coverage through a health maintenance organization.
Positive test for neurofibromatosis resulted in canceled policy.
Positive test for Marfan syndrome resulted in canceled policy.
Positive test for Down syndrome resulted in canceled policy or increased rate.
Positive test for alpha-1-antitrypsin defined as preexisting condition; therapy related to condition not covered.
Positive test for Fabry disease resulted in canceled policy.
Woman with balanced translocation excluded from future maternity coverage.
Positive Fragile X carrier status and subsequent job change resulted in no coverage.
After prenatal diagnosis of hemophilia-affected fetus, coverage denied due to preexisting condition clause.
Denied coverage or encountered difficulty retaining coverage after birth of infant with phenylketonuria.
Woman diagnosed with Turner's syndrome denied coverage for cardiac status based on karyotype. Normal electrocardiogram failed to satisfy company.
Family with previous Meckel-Gruber fetus denied coverage in subsequent applications despite using prenatal diagnosis and therapeutic abortion.
Mother tested positive as carrier for severe hemophilia A. Prenatal diagnosis revealed affected boy; not covered as preexisting condition when pregnancy carried to term.
After a test revealed that a woman was a balanced translocation carrier, she was initially denied coverage under spouse's insurance because of risk of unbalanced conception. Subsequently overturned.
Woman without prior knowledge that she was an obligate carrier for X-linked adrenoleukodystrophy found out she was a carrier. She had two sons, both of whom were healthy, but each at 50 percent risk. Testing was done so they could be put on an experimental diet to prevent problems that can arise from mid- to late childhood or early adulthood. One boy tested positive. The family's private pay policy (Blue Cross/Blue Shield) is attempting to disqualify the family for failing to report the family history under preexisting conditions.
After birth of child with CF, unable to insure unaffected siblings or themselves.

[a]1991 OTA survey of genetic counselors and nurses in genetics. Not all cases, or multiple cases involving same disorder, listed.

SOURCE: Office of Technology Assessment, 1992.

applicant attempted to select against an insurer by misrepresenting his or her health history, which would have been resolved against the individual.

In 1991, at least 50 genetic counselors or nurses in clinical practice knew of at least 68 actual incidents where their own patients reported difficulties with health insurance due to genetic tests. OTA estimates, based on the average number of patients directly counseled, that genetic counselors and nurses responding to the survey collectively saw about 110,600 individuals in 1990. However, OTA did not advise respondents to limit descriptions of clients' insurance difficulty to 1990. Thus, it is unlikely that all reported cases occurred in 1990; assuming all cases occurred in 1990 means the 68 cases represent 0.06 percent of patients seen by respondents.

Critics question whether the data—especially the qualitative descriptions—merely represent more anecdotal stories that unfairly present one side of the story and for which no response can be developed. Skeptics point out that some of the cases might fall into the gray area of whether exclusion or increased rates resulted because an adverse medical condition was revealed through a diagnostic test that just happened to be genetic. The border between what conditions are genetic or not is blurred, however, and will become increasingly diffuse. Because genetic-based predictive testing promises to have a profound impact on clinical medicine—and because access to medical care is inextricably linked to private health insurance in this country—these cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

SUMMARY

Although genetic counselors and nurses in genetics work in a variety of settings, they are concentrated in metropolitan medical centers on the West coast or Northeast region. States with a large proportion of rural residents are less likely to be served. The clientele served, in the aggregate, tend to be representative of the national averages for majority and minority groups, although no effort was made by OTA to match racial and ethnic data with regions, cities, or localities.

Most genetic counselors have a master's degree and are either certified or eligible for professional

Chapter 4
Summary

For years, experts theorized about confronting the potential consequences of increased knowledge of human genetics. In the early 1990s, the cystic fibrosis (CF) mutation test moved the debate from the theoretical to the practical. OTA concludes that the value of the CF carrier test is the information it provides. No one can estimate in common terms what it means to an individual to possess information about his or her genetic status, especially when the value concerns reproductive decisionmaking. On a larger scale, the potential for widespread CF carrier screening raises legal, ethical, economic, and political considerations.

This survey of genetic counselors and nurses working in genetics, conducted in the summer of 1991, reflects the tensions and concerns surrounding dissemination of CF mutation analysis. The survey was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening.

In summer 1991, most genetic counselors and nurses in genetics did not offer unsolicited CF carrier screening and expressed concerns about access to health insurance, quality control, public education, discrimination, stigmatization, and the adequacy of trained personnel as reasons why they did not. They are also unlikely to be providing genetic counseling and DNA tests to families followed in CF clinics and have not yet made efforts to contact CF families seen previously to offer carrier testing to family members, although agreement exists that such individuals should be offered CF mutation analysis.

Reasons why survey respondents do not offer CF mutation analysis are varied, but professional guidelines exert some influence. The 1990 policy statement of the American Society of Human Genetics (ASHG) stated that CF carrier screening is "*NOT* yet the standard of care," and a majority of survey respondents were aware of that statement. Several stated that it alone was the reason for their refusal to offer CF carrier screening. In mid-1992, after extended discussion, ASHG's leadership approved a revised statement that CF mutation analysis "is not recommended" for those without a family history of CF. Some argue that the subtle change in language of the new statement reflects an evolution of debate within the society—that some believe CF carrier screening *may now be offered* to individuals without a family history of CF, although it might not be the "standard of care." Others argue that ASHG's position is unchanged. The effect of the new statement remains to be seen.

Concern about test sensitivity was another barrier that respondents said should be addressed before routine CF carrier screening. Two-thirds of participants felt that an optimum frequency of detection should be reached before they would feel comfortable offering CF carrier screening to the general population, although nearly a quarter of respondents were uncertain about whether an optimum was necessary. Of those who felt there is an optimal frequency of detection, nearly half felt that 95 percent test sensitivity should be required before proceeding with widespread CF carrier screening. Twenty-five percent believed test sensitivity should be greater than 95 percent, with 4 percent stating that it should be 100 percent. At the time this survey was conducted, test sensitivity was approximately 80 percent. It has increased to 85 to 90 percent as of summer 1992, so opinions might have changed.

Two other factors ranked slightly more important than test sensitivity as criteria to consider before implementing routine CF carrier screening: the availability of adequate counseling and an adequate system of referral for individuals who test positive. Genetic counseling can be labor intensive. Survey respondents indicated that they spend most of their work week seeing or talking with clients; patient loads are frequently heavy. Respondents said that, given the potentially complex or emotional nature of some genetic information, professionals trained in human genetics are essential to insure high quality care and informed consent. Guarantee of informed consent also was mentioned as necessary for implementation of large-scale carrier screening.

Those who advocate CF carrier tests for use beyond affected families are no less concerned about

certification. They spend most of their work week seeing or talking with clients. Less time is spent on administration and research, and even less on professional and public education. Seventy percent of the genetics clientele is comprised of adults of reproductive age suggesting the strong influence of prenatal diagnosis as a primary genetics service. Respondents report that their counseling services are frequently not covered by third parties, even when "medically indicated."

OTA's survey reports consumers can experience difficulties in obtaining or retaining health care coverage after genetic tests. Because genetic-based predictive testing promises to have a profound impact on clinical medicine—and because access to medical care is inextricably linked to private health insurance in this country—these cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

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Table 3-15—Issues that Need to be Addressed by Pilot Programs in Cystic Fibrosis Carrier Screening

Rank order
1. Access to genetic counseling
2. Education of the public
3. Payment/cost
4. Sensitivity of the test
5. Protection of confidentiality
6. Quality control and assurance
7. Identification of a target group
8. Availability of reproductive options

SOURCE: Office of Technology Assessment, 1992.

ents what issues they viewed as important before widespread screening is embraced. Specifically, survey participants were asked at the conclusion of the questionnaire to list by priority the important issues to be addressed by pilot studies in CF carrier screening.

Interestingly, the sensitivity of the test, which was often cited as the reason not to proceed with screening, was ranked fourth (table 3-15). Access to genetic counseling was listed as the most important issue to be addressed. But with vast geographic inequities in availability of genetic services it is not clear how access could be considered as anything other than a variable in following pretest and post-test consumer behavior. Education of the public was ranked as second in level of importance for evaluation by pilot programs. Payment and cost issues were ranked third.

SUMMARY

A majority (53 percent) of genetic counselors and nurses in genetics do not offer unsolicited CF carrier screening. They are also unlikely to be providing genetic counseling and DNA tests to families followed in CF clinics and have not yet made efforts to contact CF families seen previously to offer carrier testing to family members. Those who advocate CF carrier tests for use beyond affected families argue that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. This population was a minority (21 percent) of respondents.

If carrier screening is to become routine, 99 percent of respondents believe it should be voluntary, and a majority prefer it be offered to preconceptional adults. Given the clientele found in most clinical genetics settings, it is likely that CF carrier screening will be offered as part of family planning or reproductive health, and the medical specialty most likely to offer the test will be obstetrics. This perceived tension over the technology's control likely contributes to the opinions of some in the clinical genetics community that widespread CF carrier screening is premature until greater genetics education of professionals is in place. With regard to CF carrier screening, concern exists that layers of uncertainty will inhibit informed consent, adequate pretest education, and post-test counseling and that, ultimately, more harm than good might be done. Yet respondents recognize the critical role that could be played in pretest education by other health care professionals and some indicated that should the momentum toward CF carrier screening accelerate, they would make efforts to increase their public and professional education activities.

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Chapter 3
Cystic Fibrosis Carrier Screening: Policies and Practices

Prospects of routine cystic fibrosis (CF) carrier screening polarize people. Everyone agrees that persons with a family history of CF should have the opportunity to avail themselves of CF mutation analysis, yet controversy swirls around using the same test in the general population. This polarization is illustrated in the written comments of two survey participants.

> *NO* to widespread screening! Must be close to 100 percent detection for all CF mutations before it can even be considered.
>
> Let's go with screening! I can't believe we are not halfway through a pilot program by mid 1991.

As described in the full OTA report (18), proponents of a measured approach to CF carrier screening express concern about several issues that might be raised if CF carrier screening becomes routine, such as the use of genetic information by insurance companies to set rates or deny coverage, and concerns that market pressures will drive widespread use of tests before the potential for discrimination or stigmatization by other individuals or institutions is assessed. Also expressed are questions about the adequacy of quality assurance for DNA diagnostic facilities, personnel, and the tests themselves. Still others also wonder whether the current number of health care professionals in genetics can handle a swell of CF carrier screening cases, let alone cases of other genetic conditions arising from increased knowledge from the Human Genome Project. Finally, the extraordinary tensions in the United States about abortion affect discussions about CF carrier testing and screening.

In summer 1991, OTA asked genetic counselors and nurses in genetics to provide data regarding their experiences concerning CF carrier screening as a means to judge the validity of these concerns. The questionnaire was designed to gather data on the frequency of DNA analysis for CF carrier status and trends over time, clinic policies regarding CF carrier screening, counseling and clinical practices regarding CF carrier testing and screening, and sources influencing the development of, and policies and procedures related to, CF mutation analysis. Survey participants were also asked their opinions about who should conduct carrier screening, in what settings, and on what target population(s). Respondents were encouraged to rank the most important issues to be addressed before embarking on a large-scale screening program.

The data in this chapter are specific to CF carrier screening. Data regarding third-party reimbursement for DNA-based tests are presented in chapter 2, along with general demographic data concerning the survey respondents and their clientele and clinical settings.

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Survey participants were asked to consider three issues. First, what is their opinion or the policy of their institution about the appropriateness of CF carrier screening at this time? Second, what are the current logistics of providing DNA-based tests for CF carrier status—i.e., once a decision had been made to offer CF mutation analysis, which mutations are analyzed, and how are those individuals to be tested identified or contacted? Third, survey participants were asked to estimate whether requests for DNA-based tests for CF had changed since the tests' development in 1989.

Policies on Cystic Fibrosis Carrier Screening

Currently, it is standard practice to offer CF carrier tests to individuals who have a positive family history of CF (6,16,18). An unaffected sibling of an individual with CF has a 2 in 3 likelihood of being a CF carrier. A consanguineous uncle or aunt of an individual with CF has a 1 in 2 likelihood of being a carrier. A first cousin of an individual with CF has a 1 in 4 likelihood of being a carrier (table 3-1).

As of the summer of 1991, most genetic counselors and nurses in genetics did not offer unsolicited CF mutation assays to individuals with a negative family history. A large majority of survey respondents use medical journals and other professional sources to obtain information regarding new advances in human genetics (table 3-2), and the American Society of Human Genetics (ASHG) and the National Institutes of Health (NIH) published policy documents in 1990 discouraging CF carrier

Table 3-1—A Priori Carrier Risks for Cystic Fibrosis

Negative family history	
Caucasian	1 in 25 (4%)
African American	1 in 60 to 65 (1.5 to 1.7%)
Asian American	1 in 150 (0.7%)
Hispanic American	1 in 46 (2.2%)
Positive family history	
Parent of child with CF	1 in 1 (100%)
Sibling with CF	2 in 3 (67%)
Aunt or uncle with CF[a]	1 in 3 (33%)
First cousin with CF	1 in 4 (25%)
Niece/nephew with CF[a]	1 in 2 (50%)

[a] Consanguineous.

SOURCE: Office of Technology Assessment, 1992.

Table 3-2—Sources of Information About New Advances in Human Genetics

Human genetics	Percent indicating yes
Medical journals	96
Professional colleagues	94
National conferences	83
American Society of Human Genetics	82
National Society of Genetic Counselors	80
State or regional conferences	71
Grand rounds	44
Lay press	37
Continuing education courses	35
Literature from biotechnology companies or commercial firms	35
Other	8

SOURCE: Office of Technology Assessment, 1992.

screening (6,16).[1] Seventy-six percent of respondents stated that they were familiar with the 1990 ASHG statement. Thirty-five percent were familiar with the NIH statement.

OTA's survey of genetic counselors and nurses revealed that 53 percent of respondents believe that CF carrier tests should only be offered to individuals with a positive family history of CF and not to those with a negative family history. Twenty-one percent felt that CF carrier tests should be offered to individuals with no family history. The most frequently cited reasons for making tests available to individuals regardless of family history were to reduce anxiety or increase patient autonomy. In the words of one counselor, "DNA screening is a personal issue, different in every case. What one person or family feels may be quite different from that of another person or family in any given genetic disorder with any given family history." Twenty-six percent of respondents were uncertain as to whether they should provide CF carrier screening where family history is negative.

When asked about their likelihood of introducing the topic of CF carrier tests during a counseling session, 82 percent of respondents stated that they would seldom, if ever, do so to all patients or families (table 3-3). Seventy-three percent would seldom, if ever, discuss it with pregnant women seeking prenatal diagnosis unless there was a family history of CF, in which case, 90 percent would almost always bring it up during counseling.

When asked whether their institution or clinic had a specific policy regarding CF carrier screening, 33 percent of genetic counselors and nurses responded in the affirmative. Of those responses, 70 percent stated that it is the policy of their clinic or organization to offer CF carrier tests only to those with a positive family history (table 3-4).

The overall lack of policies for CF carrier screening apparently stems from the fact that, in general, explicit and official policies for clinical practices were not routine at the majority of facilities. When asked whether their group or unit had

Table 3-3—Likelihood of Introducing the Topic of DNA Testing for Cystic Fibrosis

Patient population	Predominant response	(Percent)
All patients/families	Seldom if ever	(82)
Pregnant women seeking prenatal diagnosis	Seldom if ever	(73)
Couples/individuals with a family history of CF	Almost always	(90)
Caucasian couples/individuals with a negative history of CF	Seldom if ever	(65)
Individuals/families who inquire about CF	Almost always	(80)
Selected couples/individuals	Seldom if ever	(72)

SOURCE: Office of Technology Assessment, 1992.

Table 3-4—Specific Policies Regarding DNA Testing for Cystic Fibrosis

Policy	Percent
Offer to all regardless of family history	14
Offer only to those with a positive family history	70
Provide to those with no family history upon request if informed consent is obtained	16

SOURCE: Office of Technology Assessment, 1992.

[1] In 1992, ASHG's leadership issued a revised statement that CF mutation analysis "is not recommended" for those without a family history of CF, but it has not yet been published (1,18).

Table 3-13—Time Required for Genetic Counseling for Various Conditions

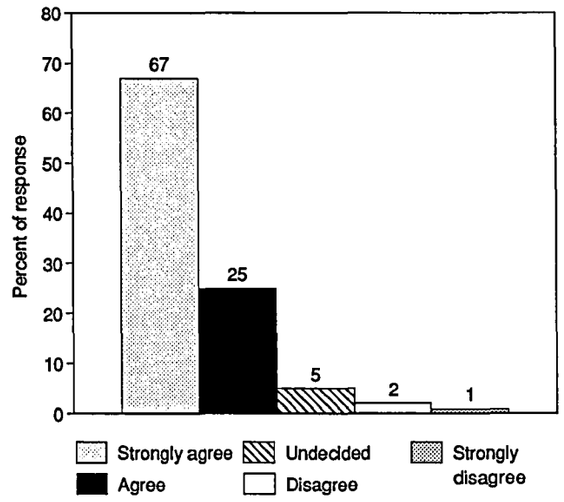
Condition	Time (minutes/visit)	Number visits
Prenatal counseling for advanced maternal age	54	1
Positive family history for neural tube defects	57	1
Elevated MSAFP screen	55	1
Couple with newly diagnosed (Tri21) Down syndrome child	78	2
Couple with 14/21 translocation Down syndrome child	73	2
Carrier testing for Duchenne muscular dystrophy	75	2
Newly diagnosed case of neurofibromatosis	70	2
Newly diagnosed CF family	59	2
Carrier testing for CF, with a positive family history	70	2
Carrier testing for CF, with a negative family history	44	1

SOURCE: Office of Technology Assessment, 1992.

Two-thirds of respondents strongly agreed that a need for more genetic counselors exists (figure 3-9). A few respondents raised the possibility of training "single-gene" counselors to assist in the increased workload, although others expressed concern about this prospect, as taking a family history can reveal other genetic conditions that might not be detected by an individual trained to handle one genetic disorder (18). Still other respondents mentioned the need for more professional education of health care providers who might be in the position of administering such tests, and many survey participants noted that all groups of health care providers should be involved after appropriate training and education. Noted one genetic counselor, "Once screening is close to 100 percent sensitive, doctors and nurses could easily be trained to provide the necessary counseling."

When asked what strategies would be considered to alleviate the projected increase in workload should widespread CF carrier screening occur, 55 percent gave either no response or reported that they had not yet developed any. Of those who had considered or developed strategies, 40 percent said they would plan professional education activities to educate other health professionals, 21 percent would develop videotapes for patient education, 15 percent said they would conduct public education, and 14 percent reported they would arrange for group counseling sessions (table 3-14).

Figure 3-9—Opinions Regarding the Need for More Genetic Counselors



A need for more genetic counselors exists.

SOURCE: Office of Technology Assessment, 1992.

Table 3-14—Strategies for Implementation of Widespread Cystic Fibrosis Carrier Screening

Question: What strategies have you considered implementing if widespread screening for CF becomes a reality?[a]

Strategy	Percent
Plan professional education activities	40
Develop videotapes for patient education	21
Conduct public education	15
Arrange for group counseling sessions	14
Administrative changes in clinics to handle patient load	13

[a] 237 of the 431 respondents gave no response.

SOURCE: Office of Technology Assessment, 1992.

ISSUES TO BE ADDRESSED BEFORE IMPLEMENTATION

When OTA undertook this survey, privately funded pilot projects were under way, but federally funded pilot studies to evaluate CF mutation analysis in the general population had not yet begun, although NIH had begun a grant competition for such projects (18).[3] Thus, OTA asked survey respond-

[3] In October 1991, NIH launched a 3-year research initiative on clinical assessments of alternative approaches to genetic education, testing, and counseling related to CF mutation analysis (18).

Table 3-10—Who Should Pay for Cystic Fibrosis Carrier Screening?

Rank order
1. Third parties
2. Self pay
3. State, city, or county
4. Federal Government
5. Employers

SOURCE: Office of Technology Assessment, 1992.

Table 3-11—Target Populations for Cystic Fibrosis Carrier Screening

Population	Yes	No[a]
	(percent)	
Adults in reproductive years	88	8
Prenatal	75	22
Pregnant women or "couples"	66	31
Newborns	33	63
Children ages 13 to 18	19	78
Children ages 2 to 12	6	91
Adults in post reproductive years	3	94

[a]3 percent had no response in each category.

SOURCE: Office of Technology Assessment, 1992.

individuals to know their risks before getting pregnant (12). Others argue that individuals not facing a pregnancy are not motivated to seek or use information on their carrier status, but will wait until they are either planning a family or starting a family before viewing such information as useful (5).

CF carrier screening offered as part of primary health care rather than prenatal care is likely to encourage preconceptional CF carrier screening. For most individuals, however, the first real opportunity for carrier screening takes place postconception (8). In the future, the primary responsibility for providing CF carrier screening might reside with the obstetrician, as has happened with MSAFP screening. Sixty-six percent of respondents to OTA's survey identified pregnant women or couples as the appropriate target population for CF carrier screening, yet 88 percent more generally identified adults in their reproductive years as the appropriate target group (table 3-11). While most respondents state that the *ideal* target population for carrier screening is the preconceptional adult, in reality, the first target population is likely to be the prenatal population because it has been the traditional entry point into genetic services for many people and comprises the largest population served by genetics centers (table 3-12).

Table 3-12—Frequency of Patients Seen by Major Areas of Clinical Practice

Area	Predominant response
Prenatal genetics	Very often
Pediatric genetics	Sometimes
Adult genetics	Sometimes
Teratogen exposure	Sometimes
Reproductive loss	Sometimes
Specialty disease(s) clinics	Sometimes
Newborn screening	Seldom if ever
MSAFP screening followup	Often
Carrier screening	Sometimes

SOURCE: Office of Technology Assessment, 1992.

PROFESSIONAL CAPACITY

Another issue in considering widespread carrier screening for CF is whether there are enough adequately trained health professionals to handle the volume of tests. One study estimated that a minimum of 651,000 counseling hours would be required annually if the maximum estimate of 6 to 8 million preconceptional couples are screened for CF carrier status (19). Considering the current number of practicing genetic counselors in the United States today, this translates to 17 weeks per year from each genetic counselor to serve solely CF-related clients. On the other hand, another estimate suggests the supply of genetic specialists could absorb routine carrier screening for CF, sickle cell anemia, hemophilia, and Duchenne muscular dystrophy, assuming that obstetricians or other primary care physicians perform the screening on pregnant women, with referral of those with positive results to genetics professionals (10).

The counselors and nurses surveyed by OTA estimate pretest counseling time for CF carrier status would range from about 45 minutes to over 1 hour, depending on family history (table 3-13). It is unclear to what extent increased demand for CF carrier screening would strain the current system. Current estimates undercount the number of health care professionals who practice genetic counseling and assume that counseling would always be provided in a clinical genetics setting by board-certified or board-eligible counselors. Such estimates also ignore the role that aggressive public education can play in improving pretest knowledge. Improvements in public education could result in dramatically less time required in formal counseling, as could reliance on health professionals not formally trained in genetics.

official policies and procedures for other issues in genetics, 21 percent reported they have policies regarding DNA storage, 42 percent have policies in place concerning prenatal diagnosis for sex selection, 37 percent have policies regarding cases of nonpaternity, and 28 percent adhere to policies regarding confidentiality and Huntington disease testing.

Criteria for Cystic Fibrosis Carrier Screening

Sixty-five percent of survey participants felt strongly that there is an optimum rate of detection that should be reached before they would feel comfortable offering CF carrier screening, as compared to 14 percent who felt there is not and 21 percent who were uncertain. Of those who felt there is an optimum rate of detection, nearly half (46 percent) said that 95 percent test sensitivity should be required before proceeding with widespread screening. Twenty-five percent believe test sensitivity should be even higher, with 4 percent stating that it should be 100 percent (figure 3-1).

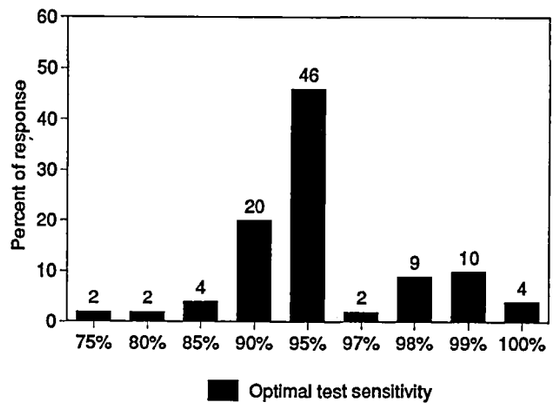
However, survey respondents ranked the availability of adequate counseling and an adequate system of referral for individuals who test positive as slightly more important criteria for CF carrier screening than test sensitivity (table 3-5). Guarantee of informed consent also was mentioned as necessary for implementation of large-scale CF carrier screening.

Perhaps the point on which there was greatest consensus among the respondents is on the issue of autonomy and choice in screening. There are no mandatory genetic screening programs of adult populations in the United States. Ninety-nine percent of survey participants responded that CF carrier screening should be voluntary and never mandatory.

Practices Regarding DNA-Based Cystic Fibrosis Carrier Tests

When asked about the frequency of requests for DNA testing or screening for CF carrier status during the 6-month period from January to June 1991, most respondents reported occasional requests (figure 3-2). When asked to compare this time period with the previous 2 years, nearly half indicated a small increase in the number of requests and a quarter noted a large increase in requests (figure 3-3). The survey did not distinguish whether the requests were carrier tests for individuals known to

Figure 3-1—Opinions on Optimal Rate of Detection



SOURCE: Office of Technology Assessment, 1992.

Table 3-5—Minimal Criteria for Cystic Fibrosis Carrier Screening Protocol

Question: What do you feel should be the minimum criteria for CF carrier screening (protocol)?

Criteria	Percent[a]
Provision of adequate counseling	40
Adequate system of referral in place	37
Improved test sensitivity	35
Guarantee of informed consent	32
Availability of educational materials	18
Only offer to families with a positive history of CF	15
Must be voluntary	14
Reasonable cost or payment	12
Protection of confidentiality	12

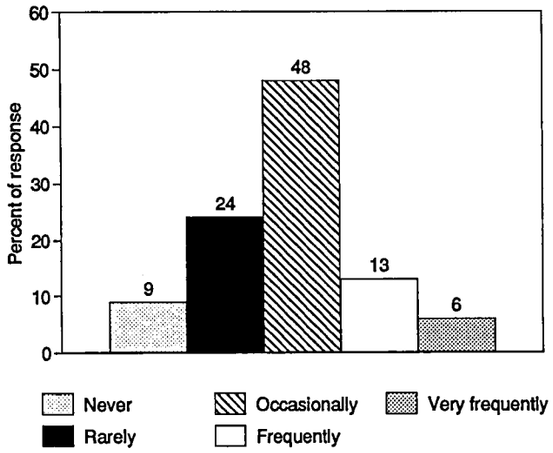
[a]Percentages do not add to 100; respondents could reply with multiple answers.

SOURCE: Office of Technology Assessment, 1992.

be at risk by virtue of family history or carrier screens for individuals with no known family history of CF.

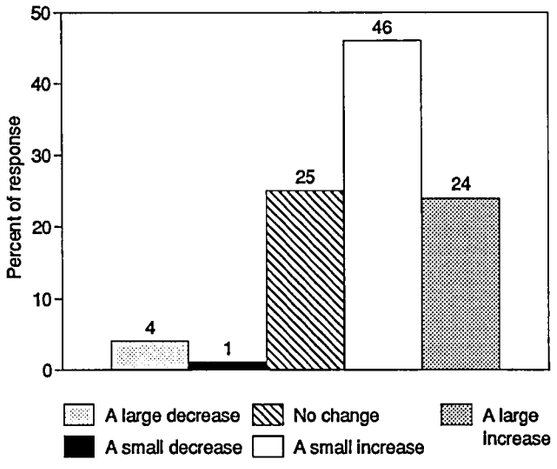
Although 55 percent of survey participants responded that a CF treatment center exists at their institution, 86 percent reported that they do not provide genetic counseling through that facility. Several respondents noted that this is the choice of the CF treatment provider, not necessarily the genetics unit. Because OTA did not survey CF treatment centers, it is not known to what extent CF families are informed of, offered, or request carrier testing. The data do show, however, that most families who have a child with CF are not routinely

Figure 3-2—Frequency of Requests for Cystic Fibrosis Carrier Screening/Testing, January-June 1991



SOURCE: Office of Technology Assessment, 1992.

Figure 3-3—Comparison of Requests for Cystic Fibrosis Carrier Screening/Testing Between January-June 1991 and Past 2 Years



SOURCE: Office of Technology Assessment, 1992.

seen in genetics service settings, and few counselors have routine contact with CF families.

Encouraging known carriers to notify consanguineous relatives (e.g., siblings and first cousins) provides economic and pragmatic benefits because it can detect a larger percentage of at-risk couples (18); testing those known to be at higher risk because of family history is more effective than screening those with unknown risk. In reality, complex psychological factors enter when family members of individuals with CF contemplate screening, and it cannot be assumed that all will want to be tested.

For this type of carrier identification to work, those providing health care and counseling to CF families will have to actively participate in referrals of relatives to genetics centers, an uncommon practice, according to OTA's data. Fewer than 10 percent of respondents reported contacting previously identified CF families with whom they had had contact about the availability of CF mutation analysis.

For those respondents whose institutions are engaged in CF carrier testing or screening, direct DNA mutation analysis is the most common approach (table 3-6). In the recent past, the sensitivity of the carrier test was limited to the ΔF508 mutation. All respondents involved in analyzing CF carrier status assay for the ΔF508 mutation. But roughly 74 percent indicated that they also test for at least one other mutation, most commonly four others, G551D, R553X, G542X, and N1303K (table 3-7). At the time the survey was done, the mutation that accounts for 60 percent of CF mutations in Jewish persons of

Table 3-6—Types of Genetic Analyses Provided for Cystic Fibrosis Screening/Testing

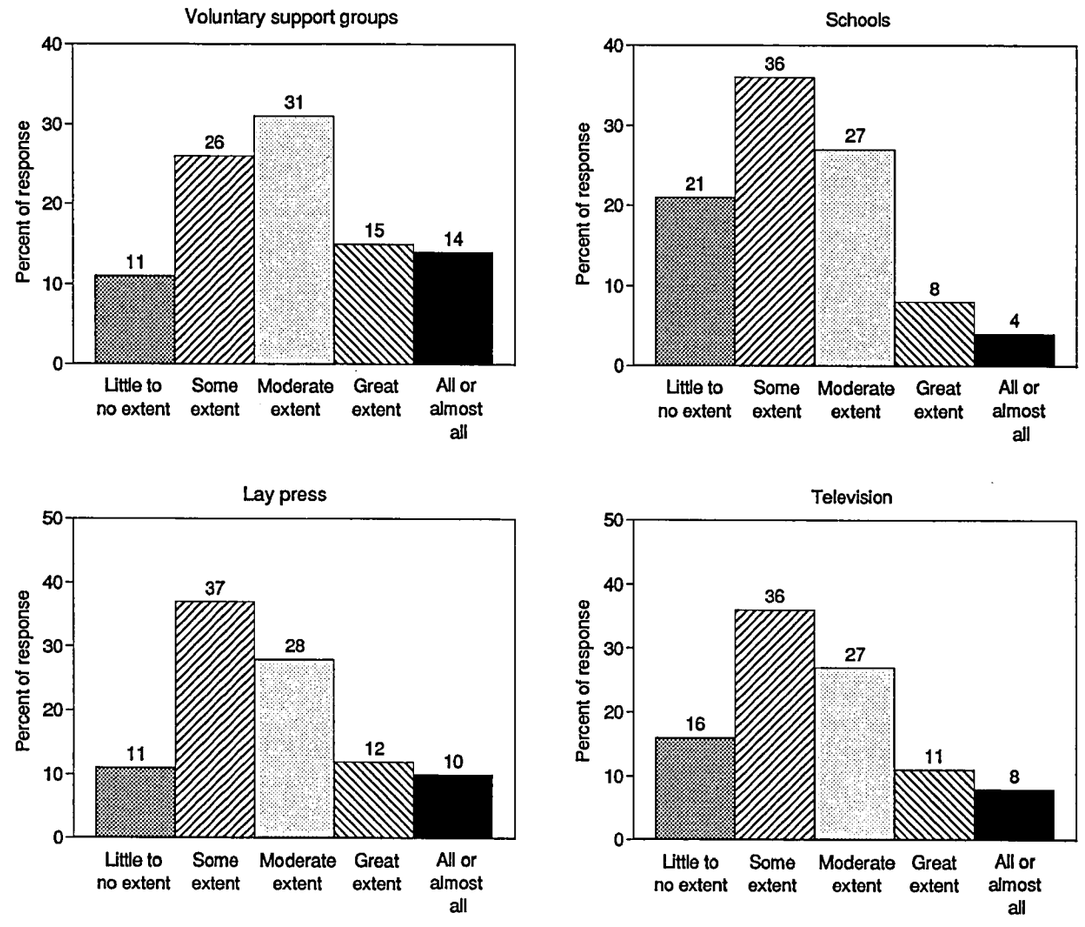
Procedure	Percent response
Direct mutation analysis	67
Prenatal DNA analysis	63
DNA linkage analysis	61
DNA haplotyping	56
Staging of studies	37
DNA banking	31
Fetal intestinal enzyme analysis	28

SOURCE: Office of Technology Assessment, 1992.

Table 3-7—Cystic Fibrosis Mutations Routinely Analyzed

Mutation	Percent response
ΔF508	100
G551D	77
R553X	76
G542X	71
N1303K	70
Other	79

SOURCE: Office of Technology Assessment, 1992.



SOURCE: Office of Technology Assessment, 1992.

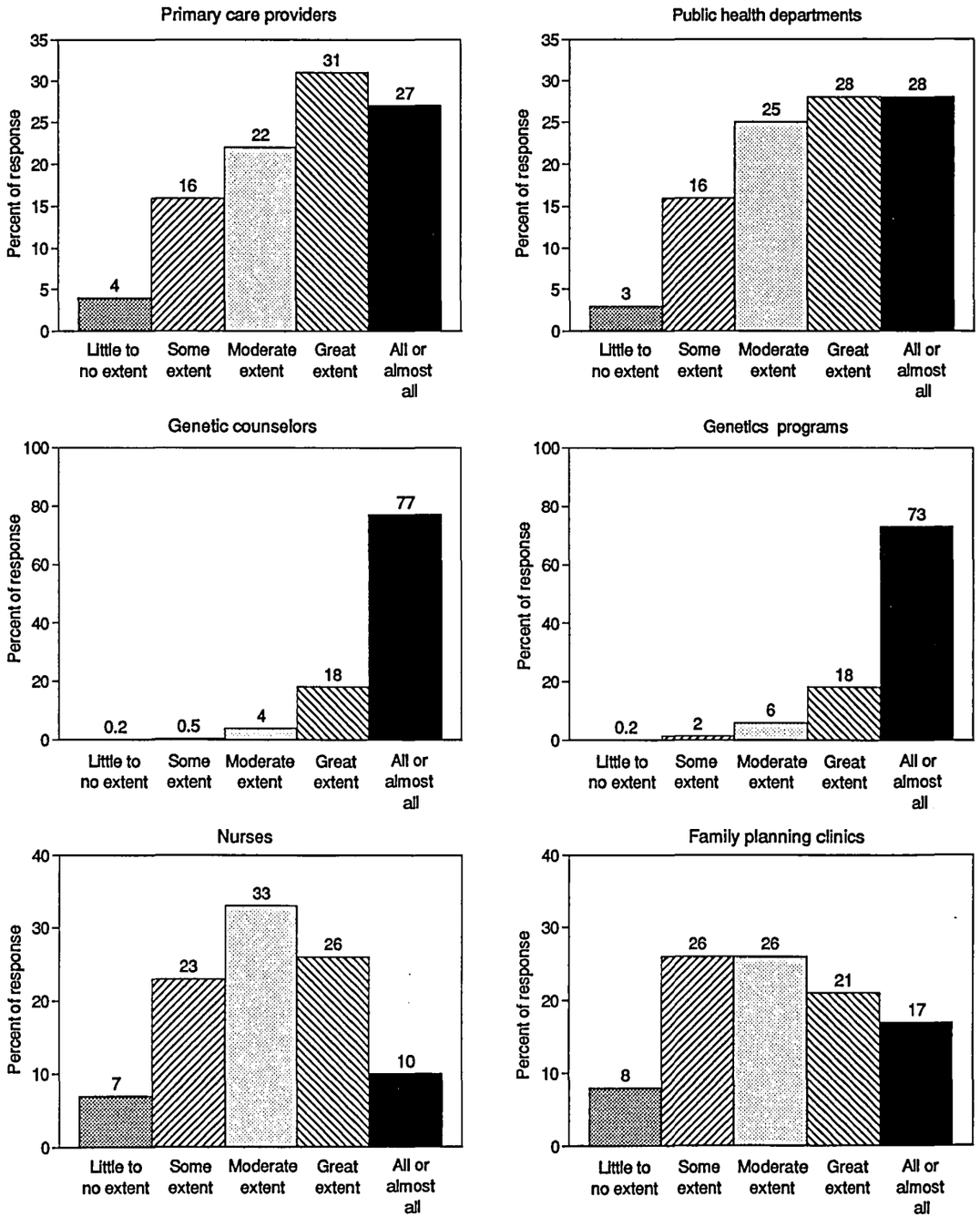
high-school screening programs have been conducted in Montreal, Canada for some time. For any disease where screening is done in childhood or adolescence, however, the benefits of such screening, including savings in resources or anxiety, must be balanced against the potential problems, such as the possibility that an adolescent will be falsely assigned to a low-risk group because of poor test sensitivity (thereby obviating further screening), or the possibility of psychosocial harm to the child as a result of identified carrier status (9).

Adolescents were not considered an appropriate target by the genetic counselors and nurses surveyed by OTA (table 3-11). Less than one-fifth felt individuals ages 13 to 18 years should be screened; only 6 percent responded that children ages 2 through 12 years should be screened.

Adults—Preconceptional or Prenatal?

One debate surrounding CF carrier screening focuses on whether the goals are best accomplished by targeting preconceptional adults or pregnant women. These approaches are not necessarily mutually exclusive. Many believe, however, that the receipt of troubling information during pregnancy is not desirable, and that it would be better for

Figure 3-8—Extent to Which Various Groups Should Be Involved with Cystic Fibrosis Pretest Education

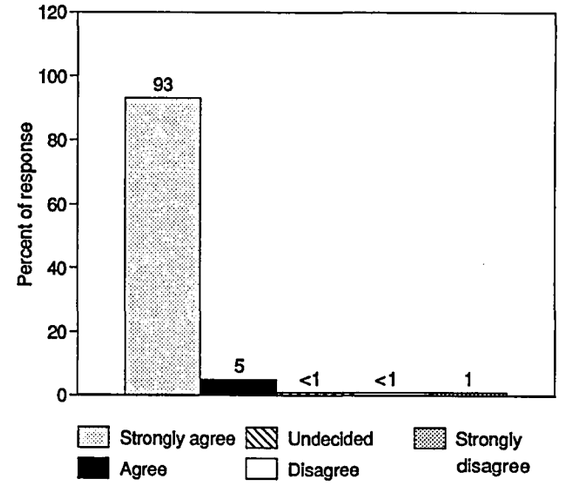


Central and Eastern European descent (Ashkenazic Jews), W1282X, had not been found.[2]

Respondents report an almost even split between commercial and university-based laboratories as the facility performing their CF mutation assays (45 percent and 48 percent, respectively). Most centers send the sample offsite (76 percent), frequently to a laboratory greater than 150 miles away.

Finally, although the need for professional and public education was cited as critical for the implementation of widespread carrier screening, few genetic counselors and nurses in genetics reported spending professional time engaged in either activity. For those respondents who do, an average of 3 hours per week devoted to educating health professionals and 1 hour per week on educating the general public was reported (ch. 2). For CF carrier screening, specifically, 8 percent of genetic counselors and nurses had developed, or were in the process of developing, educational materials relevant to DNA tests for CF mutation.

Figure 3-4—Opinions Regarding Genetic Counseling of Individuals with a Positive Family History



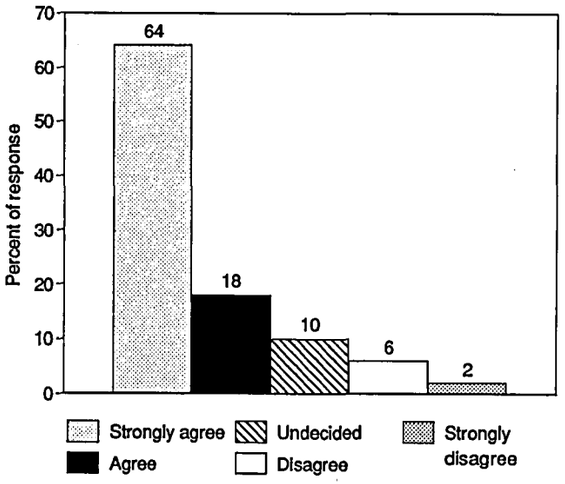
Genetic counseling should precede DNA testing for CF when there is a positive family history.

SOURCE: Office of Technology Assessment, 1992.

PREFERRED STRATEGIES AND PROTOCOLS

The importance of informed consent, careful presentation of counseling, and confidentiality have long been recognized as essential components of genetic testing and screening (9). Respondents strongly agreed that genetic counseling should precede DNA tests for CF carrier status regardless of family history (figures 3-4 and 3-5). Geneticists, perhaps more than any other medical specialty, have advocated a nondirective approach to counseling and have a strong commitment to patient autonomy (3). Further, a history of concern exists about the delivery of genetic information by health professionals used to a more directive approach (7). This concern has been played out in the debate over maternal serum alpha-fetoprotein (MSAFP) screening and is a factor in the reluctance of the clinical genetics community to rush toward widespread screening for any disease (18). For example, as part of the debates surrounding MSAFP and CF carrier screening, concern has been voiced about informed consent—in particular, that tests would be available to primary care practitioners who might incorporate

Figure 3-5—Opinions Regarding Genetic Counseling of Individuals with a Negative Family History



Genetic counseling should precede DNA testing for CF when there is a negative family history.

SOURCE: Office of Technology Assessment, 1992.

[2] When the survey was fielded, test sensitivity was 75 to 85 percent, depending on race and ethnicity. Today, most commercial and university laboratories examine ΔF508 and 6 to 12 additional mutations, and taken together these mutations comprise 85 to 90 percent of CF mutations in U.S. Caucasians (95 percent in Ashkenazic Jews).

297-911 O - 92 - 3

the assay into their practice without considering the informed consent requirements usually adhered to in genetics practices. Seventy-nine percent strongly agree that informed consent prior to CF carrier screening is a necessity (figure 3-6).

In addition to informed consent, prescreening education for clients is imperative. Information regarding an individual's a priori risk, types of tests available, and uncertainties in risk assessment based on screening results are important for potential screenees to understand. When asked if educational materials can provide adequate information about CF carrier screening, 44 percent disagreed or strongly disagreed with that concept (figure 3-7).

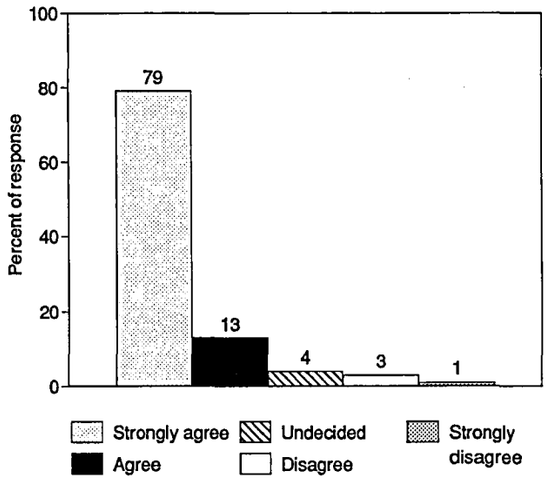
Who Should Provide Cystic Fibrosis Carrier Screening?

Concern about the complex nature of some genetic information and the need in some cases for post-test counseling leads many human genetics professionals to advocate restricting CF carrier screening primarily to the human genetics community. Pretest education, felt many respondents, can be offered by a wide range of professionals (figure 3-8), but organizing CF carrier screening should be provided by genetic specialists (table 3-8). Nearly 82 percent of the respondents surveyed by OTA said the human genetics community should be the primary organizer of CF carrier screening programs (table 3-8). Also mentioned were State or local health departments (59 percent) and primary caregivers (27 percent). Over 89 percent believed CF population screening should be provided in genetics centers, but 59 percent thought CF carrier screening could also be provided in the primary care setting or organized, community-wide programs (53 percent) (table 3-9). Concern about the sometimes difficult nature of communicating risk information regarding CF—even for experienced genetic centers—has led some in the clinical genetics community to caution against rapid movement to routine CF carrier screening (2). In the words of one respondent:

> Counseling should not be left to hurried family practitioners or OB's [obstetrician/gynecologists], who routinely spend less than 15 minutes with each patient.

As noted in chapter 2, most counselors and nurses spend little to no time on professional education or general public education in schools and communities. Thus, the majority of people will rely on their primary care provider for preliminary, if not most,

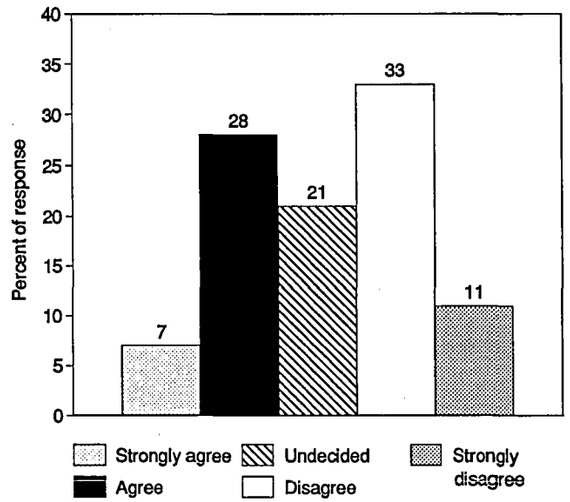
Figure 3-6—Opinions Regarding the Need for Informed Consent Prior to Cystic Fibrosis Carrier Screening



Informed consent prior to CF carrier screening is a necessity.

SOURCE: Office of Technology Assessment, 1992.

Figure 3-7—Opinions Regarding the Use of Educational Materials as a Source of Information About Cystic Fibrosis Carrier Screening



Educational materials (culturally sensitive and understandable) can provide adequate information about CF carrier screening.

SOURCE: Office of Technology Assessment, 1992.

Table 3-8—Preferred Organizations for Implementation of Voluntary Cystic Fibrosis Carrier Screening

Organization	Yes	No[a]
	(percent)	
Human genetics community	82	15
State or local health department	59	39
Voluntary health organizations	30	67
Primary caregivers	27	71
Medical societies	17	81
Federal Government	15	82

[a]3 percent gave no response

SOURCE: Office of Technology Assessment, 1992.

Table 3-9—Preferred Sites for Cystic Fibrosis Carrier Screening Programs

Site	Yes	No[a]
	(percent)	
Genetics centers	89	7
Primary care setting	59	37
Community-wide	53	43
Public health department	48	49
Public schools	14	83
Workplace	9	87

[a]3.5 percent gave no response

SOURCE: Office of Technology Assessment, 1992.

genetic information (18), and many survey respondents said primary care providers and public health departments should play an active role in educating the public about DNA tests for CF carrier status (figure 3-8). Health care provider and community-wide genetics education will become increasingly important, as will the interaction of genetic specialists with other health professionals and the public.

Who Should Pay for Cystic Fibrosis Carrier Screening?

When asked who should pay for screening, 80 percent of respondents ranked third parties as the primary source of payment (table 3-10). Self pay was ranked second, and employers ranked last. Additionally, some participants noted that if screening ever became mandatory, as in many State newborn screening programs, the State or Federal Government should be responsible for payment.

Strategies for Screening Various Populations

Two key considerations in deciding how routine CF carrier screening is best implemented are the clinical settings in which it will take place and the target populations. Delineation of a target group (or groups) determines other elements such as location, educational approach and tools, time, format, types of counseling, facilities, and publicity.

The NIH statement on CF carrier screening emphasized the importance of preconceptional screening (16). Most pilot projects in the United Kingdom are directed at preconceptional populations (18). One program in Canada targets high school students (11).

Newborn Screening

Numerous newborn screening programs exist for genetic disorders such as sickle cell anemia and phenylketonuria. These are programs intended to screen for the presence of disease, although some can also detect the carrier status of the newborn. Using the immunoreactive trypsin assay, Wisconsin has performed statewide neonatal screening for CF disease since 1985, and primary care physicians have been cooperative in referring screened patients to designated CF centers for followup (14). But even newborn screening for CF disease is not without controversy. Evidence of heightened anxiety and disrupted maternal-infant bonding have been reported in cases of false-positive diagnoses (4).

For at least two reasons, many believe that newborn screening is an inappropriate and inefficient mechanism for carrier detection. First, newborns determined to be carriers must be tracked through their reproductive years to ensure they are aware of their carrier status. Second, detection of newborn carriers might unnecessarily raise the anxiety level of parents. Thus, newborn screening for CF carrier status is not generally viewed as acceptable (15). This survey revealed that 33 percent of genetic counselors and nurses in genetics believed the newborn population would be an appropriate target group for widespread CF carrier screening (table 3-11).

Adolescent Preconceptional Screening

Some geneticists advocate carrier screening at the high-school level (11). A recent nationwide survey of American attitudes about, and knowledge of, genetic tests showed better knowledge and more positive attitudes in younger populations (17). Studies of pregnant women known to be carriers of a hemoglobinopathy gene have shown that age is a predictor of postcounseling knowledge—younger women (and adolescents as young as 12 years old) are more likely to understand genetic information (13). While not routinely done in the United States,

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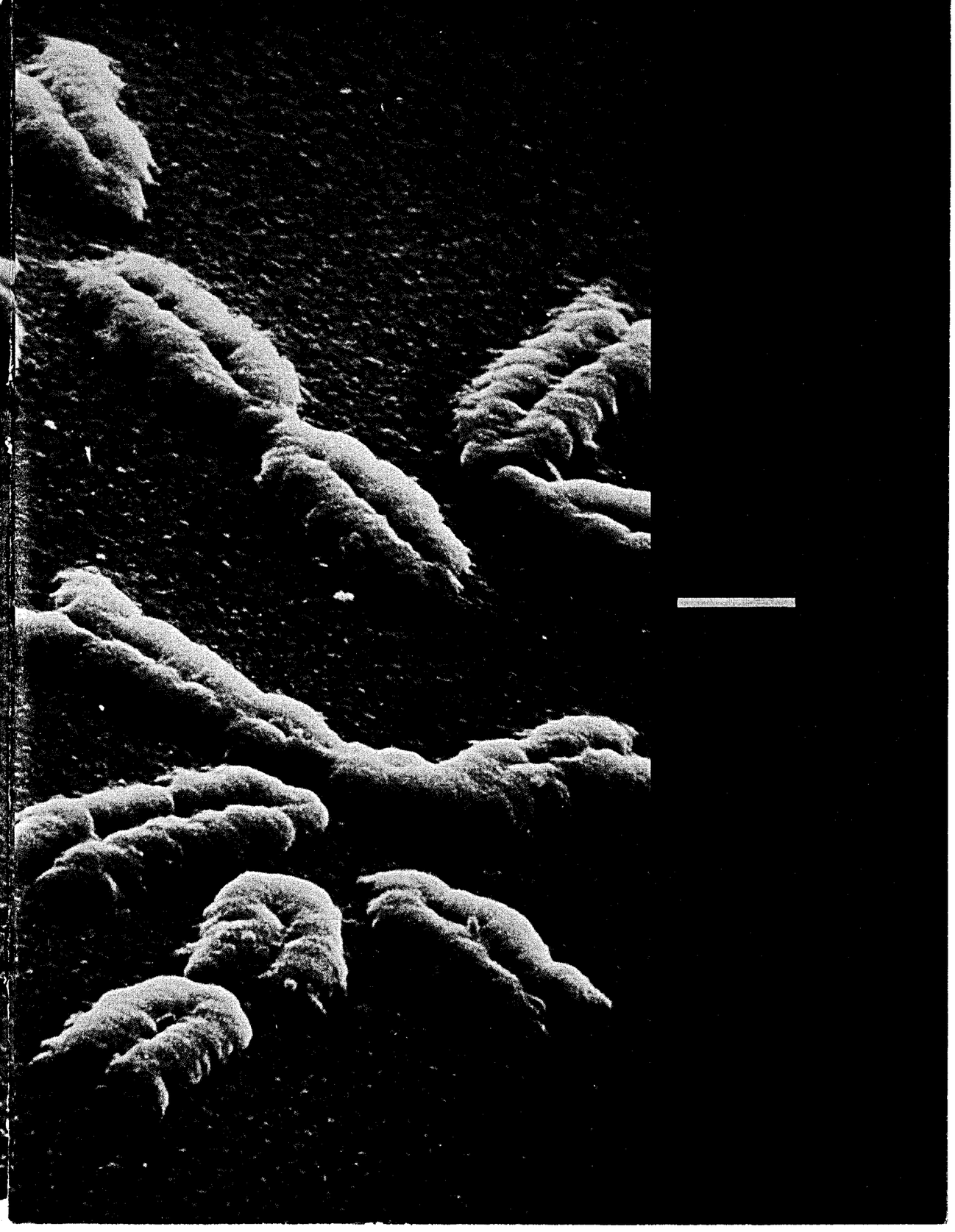

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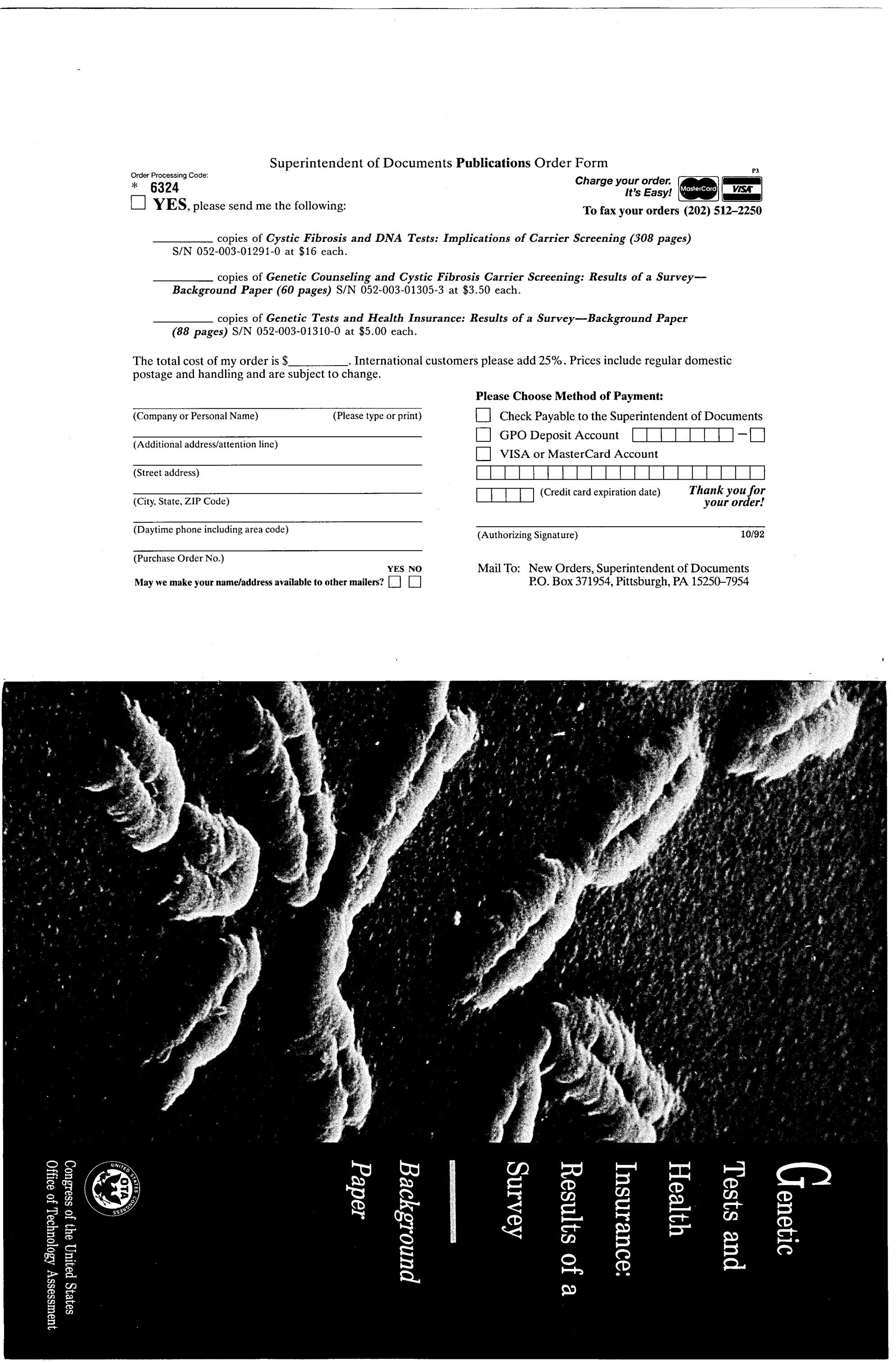

Genetic Tests and Health Insurance: Results of a Survey

Background Paper

Congress of the United States
Office of Technology Assessment

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Sickle cell trait: Sickle cell carrier status.
Single-gene disorder: Hereditary disorder caused by a single gene (e.g., CF, Huntington disease, Tay-Sachs disease, sickle cell anemia).
Tay-Sachs disease: A lethal, recessive disorder affecting the central nervous system which results in mental retardation and early death. Tay-Sachs disease predominantly occurs among Jews of Eastern and Central European descent and populations in the United States and Canada descended from French Canadian ancestors.
Underwrite: The process by which an insurer determines whether and on what basis it will accept an application for insurance.

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Foreword

As we increase our knowledge of human genetic diseases and improve our ability to diagnose and predict them, concern about denial or restriction of health care insurance is often raised. Yet little is known about either health insurers' attitudes toward reimbursement for genetic tests or policies for using test results in underwriting. To assess these views and practices, OTA surveyed commercial insurers, Blue Cross and Blue Shield plans, and health maintenance organizations that offer individual or medically underwritten group policies.

OTA undertook the survey in support of its assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, which was published in August 1992. That report—requested by the House Committee on Science, Space, and Technology, the House Committee on Energy and Commerce, and Representative David R. Obey—focuses on survey results specific to cystic fibrosis carrier screening. This background paper summarizes information about cystic fibrosis and presents additional results that pertain to the broader topic of health insurers' practices and attitudes toward genetic information and genetic tests for diseases other than cystic fibrosis. It presents survey findings related to:

- how health insurers view information from various sources—e.g., genetic tests, other medical tests, or family histories—in underwriting decisions;
- current and future policies toward reimbursing consumers for the costs of genetic tests; and
- expectations about the impact and use of genetic tests and genetic information on health insurance.

OTA was assisted in preparing the survey instrument and background paper by a panel of advisors, contractors, workshop participants, and reviewers selected for their expertise and diverse points of view. We gratefully acknowledge the contribution of each of these individuals. OTA, however, remains solely responsible for the contents of this background paper.

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Director

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NOTE: OTA is grateful for the valuable assistance and thoughtful critiques provided by the advisory panel members. The panel does not, however, necessarily approve, disapprove, or endorse this report. OTA assumes full responsibility for the report and the accuracy of its contents.

Appendix E
Acronyms and Glossary

Acronyms

APS	—attending physician statement
BC/BS	—Blue Cross and Blue Shield
DNA	—deoxyribonucleic acid
GHAA	—Group Health Association of America
HIAA	—Health Insurance Association of America
OTA	—Office of Technology Assessment
MIB	—Medical Information Bureau, Inc.

Glossary of Terms

Adverse selection: The tendency of persons with poorer than average health expectations to apply for or continue insurance to a greater extent than persons with average or better health expectations. Also known as "antiselection."

Allele: Alternative variants of a gene that occur at a given site (e.g., at a site for eye color there might be alleles resulting in blue or brown eyes); alleles are inherited separately from each parent.

Carrier: An apparently unaffected individual who possesses a single copy of a recessive gene obscured by a dominant allele; a heterozygote.

Community rating: A method of determining premium rates based on the allocation of total costs without regard to past group experience. Community rating is required of federally qualified health maintenance organizations.

Cystic fibrosis (CF): A life-shortening, recessive disorder affecting the respiratory, gastrointestinal, reproductive, and skeletal systems, as well as the sweat glands. CF is caused by mutations in the CF gene that affect the CF gene product, cystic fibrosis transmembrane conductance regulator (CFTR). Individuals with CF possess two mutant CF genes.

Cystic fibrosis carrier: An individual who possesses one CF mutation and one normal CF gene. CF carriers manifest no symptoms of the disorder. See *carrier.*

Cystic fibrosis carrier screening: The performance of tests on persons for whom no family history of CF exists to determine whether they have one aberrant CF gene and one normal CF gene. See *cystic fibrosis screening.*

Cystic fibrosis screening: The performance of tests 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. Many States screen newborns for genetic disease, but only Colorado and Wisconsin routinely screen for CF. See *cystic fibrosis carrier screening.*

Deoxyribonucleic acid (DNA): The molecule that encodes genetic information. DNA is a double-stranded helix held together by weak bonds between base pairs of nucleotides.

DNA: See *deoxyribonucleic acid.*

Dominant: In genetics, referring to a situation where only one copy of an allele is necessary for the effect (e.g., disease) to be expressed.

Genetic counseling: A clinical service involving educational, informational, and psychosocial element to provide an individual (and sometimes his or her family) with information about heritable conditions. Genetic counseling is performed by genetics specialists, including physicians, Ph.D. clinical geneticists, genetic counselors, nurses, and social workers.

Genetic test: An assay to reveal whether an individual has an inherited disorder, predisposition to such a disorder, or is a carrier for one.

Health maintenance organization (HMO): A health care organization that serves as both payer and provider of comprehensive medical services, provided by a defined group of physicians to an enrolled, fee-paying population.

Huntington disease: A chronic, dominant inherited disorder characterized by involuntary movements of the extremities and progressive dementia; age of onset is usually between 40 and 50 years of age.

Open enrollment: A health insurance enrollment period during which coverage is offered regardless of health status and without medical screening. Open enrollment periods are characteristic of some Blue Cross and Blue Shield plans and health maintenance organizations.

Preexisting condition: A condition existing before an insurance policy goes into effect and commonly defined as one which would cause an ordinarily prudent person to seek diagnosis, care, or treatment.

Prenatal testing: Assay performed after conception but before birth—usually via amniocentesis or chorionic villus sampling—to assess the status of the fetus.

Rated premium: A premium with an added surcharge that is required by insurers to cover the additional risk associated with certain medical conditions. Rated premiums usually range from 25 to 100 percent of the standard premium.

Recessive: In genetics, referring to a situation where two copies of an allele are necessary for the effect (e.g., disease) to be expressed.

Sickle cell anemia: A recessive disorder affecting red blood cell flow through the circulatory system, causing complications in numerous organ systems. Sickle cell anemia predominantly occurs in individuals of African descent.

Appendix D

Acknowledgments

OTA would like to thank the members of the advisory panel and external reviewers for their review of draft materials related to this background paper during the course of the assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*. In addition, OTA acknowledges the following additional reviewers and workshop participants for their assistance in developing and reviewing drafts of the survey instrument:

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Genetic Tests and Health Insurance—Results of a Survey
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[1] Through December 1991

Contents

Tables

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us as any other opinions, concerns, or suggestions related to genetic testing and insurance that you feel our questions did not address. These comments will be strictly anonymous but may be incorporated in our report to Congress. Please write these comments below.

We have attached a peel-off identification number on the questionnaire. This is the only link between the companies who were sampled and the questionnaires returned. We would prefer that you leave the identification number on the questionnaire when you return it. Our staff will remove the label upon receipt, making the questionnaire entirely anonymous. Absolutely no linkage between companies and questionnaires will be retained. The label from the completed questionnaire is designed to eliminate your company from those that we will have to recontact.

However, if this temporary identification makes you uncomfortable, then peel off the label before returning the questionnaire. We appreciate your help and we want you to feel comfortable in participating in the survey.

PEEL OFF LABEL WITH SAMPLE

IDENTIFICATION HERE

PLEASE RETURN THE QUESTIONNAIRE IN THE POSTAGE PAID RETURN ENVELOPE SENT WITH THE QUESTIONNAIRE. IF THE ENVELOPE HAS BEEN LOST, THE RETURN ADDRESS IS:

Margaret Anderson
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Office of Technology Assessment
U.S. Congress
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SECTION V: DEMOGRAPHICS

17. What is your job title?

_____

18. Which of the following lines of insurance does your company underwrite?

Health	1
Disability	2
Life	3

19. What percent of persons under health insurance policies issued by your company are in policies classified as:

Self-insured Administration	_____%
Individual	_____%
Small Groups	_____%
Large Groups	_____%
TOTAL	100%

16. Please indicate whether you:

	Agree Strongly	Agree Somewhat	Disagree Somewhat	Disagree Strongly
a. It's fair for insurers to use genetic tests to identify individuals with increased risk of disease.	1	2	3	4
b. An insurer should have the option of determining how to use genetic information in determining risks.	1	2	3	4
c. Genetic conditions, such as cystic fibrosis or Huntington's disease, are pre-existing conditions.	1	2	3	4
d. Carrier status for genetic conditions, such as cystic fibrosis or Tay-Sachs, are pre-existing conditions.	1	2	3	4
e. Genetic information is no different than other types of medical information.	1	2	3	4
f. Prenatal diagnosis indicates the fetus is affected with cystic fibrosis; the couple decide to continue the pregnancy. The health insurance carrier, which paid for the tests, informs the couple they will have no financial responsibility for the cystic fibrosis-related costs for the child.	1	2	3	4
g. Through prior genetic testing, the husband is known to be a carrier for cystic fibrosis. Before having children, the wife seeks genetic testing for cystic fibrosis. The insurance company declines to pay for the testing, since there is no history of cystic fibrosis in her family.	1	2	3	4

15. How likely do you think it is that your company will:

	Very Likely	Somewhat Likely	Somewhat Unlikely	Very Unlikely
In the next 5 years:				
a. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
b. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
c. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
d. Offer optional genetic testing and carrier testing	1	2	3	4
e. Use information derived from genetic tests for underwriting	1	2	3	4
f. Alter claims payment practices as new genetic tests come on line	1	2	3	4
In the next 10 years:				
g. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
h. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
i. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
j. Offer optional genetic testing and carrier testing	1	2	3	4
k. Use information derived from genetic tests for underwriting	1	2	3	4
l. Alter claims payment practices as new genetic tests come on line	1	2	3	4

Chapter 1
Introduction

Health insurance in the United States is not monolithic. U.S. health care financing, which totaled more than $800 billion in 1991, is a mixture of public and private funds. For the majority of Americans, however, access to health care—and the health insurance that makes such access possible—is provided through the private sector. Privately financed health insurance for medical expenses covers more than 189 million persons through self-funded companies, commercial insurance companies, Blue Cross and Blue Shield (BC/BS) plans, and managed care programs (e.g., health maintenance organizations (HMOs) and preferred provider organizations) (1). Among these entities, business practices vary widely within and among the categories, and each is subject to different State or Federal regulations (2).

The majority of Americans obtain health insurance through employment—either directly as employees or as family members of the employed. Most people covered in this manner obtain health insurance as members of large groups, with no diagnostic tests or physical examinations required for entry (i.e., no medical underwriting). Some individuals, however, obtain health insurance through small groups, which require some diagnostic tests or physical examinations, on which the insurance contract's coverage and costs are based. Finally, persons without group coverage can seek individual health insurance from commercial insurers, BC/BS plans, or HMOs.

Organizations that medically underwrite individual or group policies classify risks on actuarial data. Currently, about 10 to 15 percent of individuals with health care coverage are medically underwritten. This selection process—i.e., differentiation based on medical characteristics—is an integral part of the insurance mechanism. Risk classification is the foundation, in fact, for the concept of private insurance.

In the coming years, an increasing number of underwriting decisions and reimbursement policies will revolve around the tests, information, and services arising from the Human Genome Project. The number of DNA-based tests for genetic disorders and predispositions will almost certainly expand by an order of magnitude in the next decade. How insurers view such tests will affect their utilization. This background paper describes results from a 1991 OTA survey of U.S. health insurers' attitudes toward genetic tests and genetic information—both how they currently view information from various sources (e.g., genetic tests, other medical tests, or family histories) in underwriting decisions and how they might reimburse consumers for genetic tests. It also reports data on the role health insurers expect genetic tests and genetic information will play in their business practices over the coming decade.

HEALTH INSURANCE AND GENETICS

Perhaps the most widely raised social question stemming from the Human Genome Project is what effect genetic tests have (and will have) on health care access in the United States. Consumers fear exclusion from health care coverage due to genetic, or other, factors. Because health care access involves private health insurance for most citizens, concern focuses on this market.

Some commentators speculate that, overall, genetic analyses will mean fewer people will have access to private health insurance because such tests identify or refine risks. They argue genetic tests, in precluding more and more people from health insurance, will provide the best reason yet for a nationalized health care system. Others contend, however, that genetic assays could rule out an individual's risk for a disorder and hence increase access to health care coverage. That is, making use of genetic information would allow insurers to better assess risks, with the result that individuals at elevated risk will pay more (or be denied access), but people with low risk will pay less. Still others point out that as the number of identified genes increases, so will the number of people who will be identified as at risk, which could spread risk. The ultimate impact of genetic tests, then, will depend, in part, on the practices and attitudes of insurers toward tests for genetic disorders, as well as the morbidity and mortality associated with particular conditions (2).

SCOPE AND ORGANIZATION OF THIS BACKGROUND PAPER

For its assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (2), OTA found a paucity of information about health insurers' current attitudes and policies toward genetic tests or any future role such tests might play in their business practices. To gain some understanding about these issues, OTA surveyed commercial insurers, BC/BS plans, and selected HMOs that offered individual or medically underwritten group policies in June 1991. This survey did not extend to large group contracts or to the practices and attitudes of self-funded companies, which cover the largest percentage of individuals who have private health care benefits.

Results from OTA's survey of health insurers apply to a small slice of the insured population—the 12.7 million people who have individual or medically underwritten group coverage provided through survey respondents. Further, most of the information presented in the following chapters should not be construed to represent either the numbers or percentages of commercial entities, BC/BS plans, or HMOs that have dealt with the issues presented. Respondents were asked how they *would* treat certain conditions or scenarios presented (currently or in the future, depending on the questions), not whether they, in fact, *had* made such decisions.[1]

This background paper reports the complete results from OTA's survey of health insurers, but does not analyze them in a public policy context. That analysis is presented in the aforementioned report for which this survey was undertaken (2). Chapter 2 of the background paper describes general characteristics of the respondents and the populations they serve. Following this, data related to genetic tests, genetic information, and underwriting are discussed in chapter 3. Chapter 4 presents data about health insurers' policies toward reimbursing consumers for various genetic tests and services, and chapter 5 examines insurers' overall attitudes toward current and future use of genetic tests and information. Appendix A details the survey method, including population selection, and appendix B presents verbatim comments made by respondents in space provided for open ended statements. Survey instruments are reproduced in appendix C.

CHAPTER 1 REFERENCES

1. Health Insurance Association of America, *Source Book of Health Insurance Data 1991* (Washington, DC: Health Insurance Association of America, 1991).
2. U.S. Congress, Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA-BA-532 (Washington, DC: U.S. Government Printing Office, August 1992).

[1] In a few instances, as evident through question wording, OTA did ask about an actual practice—e.g., "To your knowledge, has your company ever reimbursed for carrier testing for cystic fibrosis?" As is clear from the survey questionnaires reproduced in appendix C, however, most questions inquired about how the respondent "would" treat a given situation.

11. For each category of coverage, how would these policies normally be affected by the following findings:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with waiting period at standard rates;
4 = Accepted with exclusion waiver at rated/risk-adjusted premium;
5 = Accepted without exclusion waiver or waiting period but at rated/risk-adjusted premium;
6 = Accepted with waiting period at rated/risk-adjusted premium; 7 = Declined

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
a. Presymptomatic testing reveals the likelihood of a serious, chronic future disease (e.g., for Huntington's disease)	_____	_____	_____
b. Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease (e.g., predisposition to heart disease)	_____	_____	_____
c. Carrier testing reveals the possibility that off-spring may have a serious, chronic condition or disease	_____	_____	_____
d. Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	_____	_____	_____

SECTION IV: GENERAL ATTITUDES

12. To your knowledge, has your company ever reimbursed for carrier testing for cystic fibrosis?
Yes _____(1)
No _____(2)

13. Has your company ever conducted an economic analysis of the costs and benefits of:

	Yes	No
a. Carrier testing as part of applicant screening	1	2
b. Genetic counseling of carriers who are covered	1	2
c. Carrier testing as part of prenatal coverage	1	2
d. Genetic testing as part of applicant screening	1	2

14. Under what conditions would a negative financial impact be likely to occur for your company: (CHECK ALL THAT APPLY)

a. Widespread availability of genetic tests to the medical/provider community _____(1)
b. Widespread availability of genetic tests with constraints on insurers' access to the results _____(2)
c. Adverse claims or underwriting results from antiselection _____(3)
d. Other (SPECIFY) _____ (4)

9. For individual policy applicants only, how would the coverage of a family member (e.g., spouse or adopted child) be affected if the policy applicant was negative, but the family member was asymptomatic but had a family history of:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates; 3 = Accepted with waiting period at standard rates; 4 = Accepted with exclusion waiver at rated/risk-adjusted premium; 5 = Accepted without exclusion waiver or waiting period but at rated/risk-adjusted premium; 6 = Accepted with waiting period at rated/risk-adjusted premium; 7 = Declined

	Individual/Non-group Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

10. For each category of coverage, do your standard policies provide coverage for:

1 = At patient request; 2 = Only if medically indicated; 3 = Not covered

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
Carrier tests for:			
a. Cystic fibrosis	_____	_____	_____
b. Tay-Sachs	_____	_____	_____
c. Sickle cell trait	_____	_____	_____
Prenatal tests for:			
d. Cystic fibrosis	_____	_____	_____
e. Tay-Sachs	_____	_____	_____
f. Sickle cell anemia	_____	_____	_____
g. Down Syndrome	_____	_____	_____
h. Other (SPECIFY)	_____	_____	_____
Genetic counseling	_____	_____	_____

Chapter 2
Profile of Respondents

In 1991, OTA conducted a survey of commercial health insurers, Blue Cross and Blue Shield (BC/BS) plans, and health maintenance organizations (HMOs) as part of its report, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (4). The survey collected information on insurers' underwriting practices and use of medical screening for individual and medically underwritten group policies. Additionally, it sought information about how insurers view and use genetic information and genetic tests, especially DNA-based tests for cystic fibrosis (CF) mutations. A 1986 OTA survey targeted a similar population, but the data collected for that survey focused on general medical testing (especially for the human immunodeficiency virus (HIV)), and did not examine genetic tests and genetic information (3).

RESPONDENT PROFILE

General industry profile questions asked by OTA included the number of people respondents insure in their plans, the number of applications received, and how those applications were rated. This chapter presents such data for each of the three populations OTA surveyed.[1] Appendix A describes how the population samples were derived.

Commercial Health Insurers

In the United States, approximately 1,250 for-profit companies are in the business of writing major medical expense policies (2), but increasingly few health insurers write policies for individuals or medically underwritten groups (4). Of 225 commercial health insurers initially mailed a survey, 81 insurance companies responded that they offered neither individual nor medically underwritten group policies. Of the 51 responding companies that did offer such policies, 29 companies offered individual coverage, 37 respondents offered medically underwritten group policies, and 15 companies offered both (table 2-1). Thirty-eight companies also wrote disability insurance, and 42 wrote life insurance. None of the companies included Medigap policies or statistics in their responses. (Medigap policies are designed to supplement Medicare coverage for the elderly.)

As an aggregate population, responding companies reported receiving a total of 940,745 applications for individual health insurance in 1990. The annual volume of applications ranged from 50 to 368,350 applications per company (table 2-2). Four companies alone accounted for 564,475 applications, or more than half the annual volume of the entire survey population. Responding companies reported receiving 625,134 applications for medically underwritten group coverage, with a range of 100 to 100,000 applications. Responding companies reported insuring a total of 2 million people under individual policies, and 2.3 million under medically underwritten group policies (table 2-3).

Companies also were asked to indicate the distribution of persons they covered under self-funded administrative policies, individual policies, medically underwritten groups, and large groups. All respondents had business encompassing these practices, but the proportions among companies varied widely.

The client mix within any single responding commercial insurer varied. People covered under self-funded administrative policies comprised between 1 and 70 percent of clients covered by commercial respondents, with an average of 25 percent. Two to 100 percent of persons were covered through individual policies, with an average of 50 percent. The percentage of persons who were covered under medically underwritten group policies of commercial insurers ranged from 1 to 100 percent and averaged 62 percent. Finally, commercial insurers responding to the OTA survey covered 6 to 96 percent of people under large group policies, with an average of 44 percent.

Blue Cross and Blue Shield Plans

Surveys were sent to both the medical director and the chief underwriter for 72 of the 73 BC/BS plans. (Puerto Rico's plan was excluded.) BC/BS plans often operate under considerably different condi-

[1] For chapters 2 through 5, the numbers in the text might not total 100 percent or sum to the actual number of responses for a particular survey population because "no response" is not included in the discussion, but is presented in the table.

Table 2-1—Respondent Profile: Companies That Offer Individual or Medically Underwritten Group Coverage

	Commercial insurers (n = 51)	BC/BS plans—underwriters/ medical directors (n = 29/18)	HMOs (n = 23)
Individual policies	29 companies	25/18 plans	11 HMOs
Medically underwritten group policies	37 companies	21/15 plans	20 HMOs
Nongroup/open enrollment	NA	8/7 plans	NA

NA = Not applicable.
SOURCE: Office of Technology Assessment, 1992.

Table 2-2—Number of Applications Received by OTA Survey Respondents

	Commercial insurers	BC/BS plans—underwriters/ medical directors	HMOs
Individual policies	940,745 (range: 50 to 368,350)	261,186/303,692 (range: 512 to 47,380)/ (range: 9 to 120,000)	69,554 (range: 24 to 43,000)
Medically underwritten group policies	625,134 (range: 100 to 100,000)	103,726/101,391 (range: 1,200 to 19,000)/ (range: 0 to 34,000)	414,977 (range: 150 to 350,000)
Nongroup/open enrollment	NA	29,360/13,768 (range: 60 to 25,000)/ (range: 0 to 6,168)	NA

NA = Not applicable.
SOURCE: Office of Technology Assessment, 1992.

tions from commercial carriers. Some plans hold open enrollment periods, all are regionally based, and many enjoy significant shares of their local health insurance market. These factors play a pivotal role in underwriting policies. Twenty-nine chief underwriters completed a survey and 18 medical directors returned surveys. Some overlap exists between the two populations, so the reported data are not additive, but are treated as two populations.[2] In addition to inquiring about medically underwritten groups and individuals, the BC/BS survey instrument asked how the questions applied to a third category: nongroup open enrollment policies.[3]

Of the 29 BC/BS plans represented by the underwriter survey, 25 of 29 write individual policies and 21 of 29 offer medically underwritten group policies. Eight of 29 BC/BS surveys returned by chief underwriters represented plans that offer open enrollment; each of these eight offers continuous, year-round open enrollment (table 2-1).

All 18 BC/BS plans represented by the medical director survey write individual policies, and 15 plans also offer medically underwritten group policies. Seven represented plans that offer continuous, year-round open enrollment. Twelve States require BC/BS plans to offer an open enrollment period—i.e., all applicants must be accepted for coverage regardless of their health status and with no medical underwriting. Three BC/BS plans represented by the underwriter survey also provide disability insurance and six wrote life insurance; 1 plan represented by the medical director survey also provides disability insurance and 1 wrote life insurance.

The responding BC/BS plans represented by the underwriter survey received 261,186 applications for individual health insurance in 1990, with a range of 512 to 47,380 applications. The medical director sample revealed that 303,692 individual insurance applications were received by these respondents, with a range of 9 to 120,000. BC/BS underwriters

[2] Because anonymity and confidentiality were guaranteed, OTA does not report the actual number of policies that overlapped, nor did OTA perform a comparative analysis between the underwriter and medical director responses from the same BC/BS plan.

[3] When BC/BS plans were first offered in the 1930s, all applicants were accepted for coverage regardless of their health status—i.e., open enrollment. Today, plans in 12 States have an open enrollment period, although most contracts have waiting periods for preexisting conditions.

SECTION III: GENETIC CONDITIONS

7. Does your company specifically inquire, for each category of coverage, about the following conditions in the application for health insurance in the personal history, family history, or neither:

1 = Personal history only; 2 = Family history; 3 = Neither

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
a. Hemophilia	_____	_____	_____
b. Tay-Sachs	_____	_____	_____
c. Huntington's disease	_____	_____	_____
d. Sickle cell anemia	_____	_____	_____
e. Cystic fibrosis	_____	_____	_____
f. Any other genetic disease (SPECIFY)	_____	_____	_____

8. For individual policy applicants only, how would the application normally be treated if a policy applicant was asymptomatic but had a family history of:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with waiting period at standard rates;
4 = Accepted with exclusion waiver at rated/risk-adjusted premium;
5 = Accepted without exclusion waiver or waiting period but at rated/risk-adjusted premium;
6 = Accepted with waiting period at rated/risk-adjusted premium; 7 = Declined

	Individual/Non-group Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

5. For each category of coverage, please indicate the importance of each of the following factors in determining insurability (not in rating):

1 = Very important; 2 = Important; 3 = Unimportant; 4 = Never used

	Individual/Non-group Policies	Medically Underwritten Groups
a. Age	_____	_____
b. Occupation	_____	_____
c. Smoking status	_____	_____
d. Lifestyle	_____	_____
e. Sex	_____	_____
f. Financial/credit status	_____	_____
g. Personal medical history of significant conditions	_____	_____
h. Family medical history of significant conditions	_____	_____
i. Genetic predisposition to significant conditions	_____	_____
j. Carrier risk for genetic diseases	_____	_____

6. For each category of coverage, how would you normally treat these policies if they disclosed the following conditions in an examination(s) or application:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with waiting period at standard rates;
4 = Accepted with exclusion waiver at rated/risk-adjusted premium;
5 = Accepted without exclusion waiver or waiting period but at rated/risk-adjusted premium;
6 = Accepted with waiting period at rated/risk-adjusted premium; 7 = Declined

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
a. Hypertension	_____	_____	_____
b. Diabetes mellitus	_____	_____	_____
c. Cerebrovascular disease	_____	_____	_____
d. Hemophilia	_____	_____	_____
e. Sickle cell anemia	_____	_____	_____

Table 2-3—Number of People Insured by OTA Survey Respondents

	Commercial Insurers	BC/BS plans—underwriters/ medical directors	HMOs
Individual policies	2.0 million (range: 171 to 240,000)	1.7 million/1.4 million (range: 1,500 to 690,559)/ (range: 0 to 324,800)	306,861 (range: 350 to 258,945)
Medically underwritten group policies	2.3 million (range: 1,000 to 382,000)	2.4 million/671,385 (range: 1,039 to 1,592,000)/ (range: 0 to 205,144)	4.2 million (range: 1,501 to 2 million)
Nongroup/open enrollment	NA	645,164/134,878 (range: 550 to 512,477)/ (range: 675 to 43,589)	NA

NA = Not applicable.
SOURCE: Office of Technology Assessment, 1992.

reported their plans received a total of 103,726 individual applications, with a range of 1,200 to 19,000 applications; medical directors reported receiving 101,391 medically underwritten group applications, with a range of 0 to 34,000. Finally, a total of 29,360 applications were received by underwriters during open enrollment, with a range of 60 to 25,000 applications received. Medical directors reported they received 13,768 applications during open enrollment, with a range of 0 to 6,168.

Underwriters for BC/BS plans responding to the OTA survey reported that their plans insure 1,736,270 people through individual policies, 2,394,703 in medically underwritten groups, and 645,164 under open enrollment contracts. Medical directors at BC/BS plans responding to the OTA survey said their plans insure 1,383,166 through individual policies, 671,385 in medically underwritten groups, and 134,878 under open enrollment contracts.

Based on the survey responses of chief underwriters, the fraction of persons covered through self-funded policies ranged from 1 to 62 percent, with an average of 23 percent. One to 49 percent of BC/BS clients were covered by individual policies, with an average of 14 percent. The percentage of persons covered under medically underwritten group policies ranged from 4 to 73 percent, and averaged 20 percent. Finally, underwriters from BC/BS plans responding to the OTA survey covered 19 to 82 percent of people under large group policies, with an average of 44 percent.

For BC/BS medical directors who responded to the OTA survey, a range of 0 to 66 percent of clients were covered under self-funded policies, with an average of 24 percent. One to 49 percent of persons were covered under individual policies, with an average of 15 percent. Coverage under medically underwritten group policies for this survey population ranged from 4 to 60 percent, with an average of 14 percent. Clients covered under large group policies also varied widely, ranging from 10 to 73 percent, with an average of 46 percent.

Health Maintenance Organizations

As of December 1990, there were 569 HMOs in the United States. OTA sent surveys to the 50 largest HMOs, as well as a sample of 28 plans that were the largest HMOs within a State or the largest by HMO model type. (Four HMO types exist: the staff plan, group plan, network plan, and the individual practice association plan.) Forty-three surveys were returned, of which 20 neither offered individual policies nor medically underwrite groups. Of the 23 HMOs responding that do offer such coverage, 11 HMOs accept individuals and 20 medically underwrite groups (table 2-1). Eighteen of the 23 HMOs responding are federally qualified plans. Of the 23 respondents, 1 wrote disability policies, and 4 wrote life insurance.

As a group, responding HMOs received 69,554 applications for individual coverage in 1990, with a range of 24 to 43,000; 414,977 applications were received for medically underwritten group coverage, with a range of 150 to 350,000. Survey respondents covered a total of 306,861 individual members, with membership ranging from 350 to 258,945. Those HMOs that offer medically underwritten group policies cover about 4.2 million people under such policies, with a range of 1,501 to 2 million people.

The percentage of persons within each HMO covered under self-funded policies ranged from 0 to 61 percent, with an average of about 4 percent (20 of the responding 43 HMOs had no self-funded policies). Zero to 34 percent of persons were covered through individual policies, with an average of 3 percent (11 HMOs had no individual policies). The percentage of persons covered under medically underwritten group policies ranged from 0 to 100 percent, and averaged 68 percent. Finally, HMOs responding to the OTA survey covered 0 to 99 percent of their clients under large group policies, with an average of 25 percent.

TREATMENT OF APPLICATIONS

The outcome of underwriting is risk classification, the final evaluation of whether the applicant for insurance will be covered on a standard or substandard basis, or not at all. Not all insurers view specific conditions the same. A medical condition or impairment that makes an applicant uninsurable to one insurer could be excluded from coverage by another, be included in a policy at a rated (higher-priced) premium, or be ignored altogether. This section describes data related to the treatment of applications for existing clientele. Chapter 3 describes data on how respondents *would* treat applications under specific scenarios.

Commercial Health Insurers

Most applicants for individual health insurance are classified as standard and can purchase coverage without additional premiums or limitations (i.e., exclusions). Over half (18 of 29) of commercial insurers responding to the OTA survey provided standard coverage to at least 60 percent of their individual applicants. Three-quarters of the respondents (30 of 38) underwriting small groups also cover 60 to 100 percent of group members on a standard basis.

Substandard policies can include an exclusion waiver, a rated premium, or both. Exclusion waivers temporarily or permanently exclude a medical condition from coverage. The exclusion may be for a specific condition, such as gallstones, or for an entire organ system, such as reproductive disorders. More than half (18 of 29) of responding commercial insurers reported that 0 to 19 percent of their individual policies carried an exclusion waiver. (Information on the duration of the waiver was not gathered in this survey.) Four companies imposed exclusions for 20 to 34 percent of their individual coverage applicants. Thirty-three of 38 commercial respondents that offer medically underwritten group coverage required exclusion waivers for 0 to 20 percent of applicants.

Sixteen of 29 commercial insurers that offer individual coverage reported that the increased risk associated with 1 to 20 percent of their applicants required a rated premium. The cost of additional premiums usually ranges from 25 to 100 percent of the standard premium, although some insurers use higher ratings (1). In this survey, OTA found that 18 commercial companies that offer medically underwritten group coverage never charge applicants a rated (higher priced) premium.

All 39 companies that offer individual policies declined some portion of applicants; responses ranged from 2 to 22 percent of applicants. Similarly, all 27 companies offering medically underwritten group coverage declined between 1 and 30 percent of applicants for these policies.

Blue Cross and Blue Shield Plans

Although BC/BS plans generally do not screen for high-risk applicants as exhaustively as do commercial carriers, the risk classification that is used once a high-risk applicant is identified varies little from the approach used by commercial carriers (3). A majority of BC/BS plans represented by the underwriter survey (17 of 25) do not offer standard coverage for their individual applicants; 7 BC/BS plans reported offering standard rates for 25 to 85 percent of individual applicants. About half (11 of 21) of BC/BS plans offering medically underwritten group coverage do not offer standard rates to any applicants. Seven respondents offer standard rates to 10 to 25 percent of applicants for medically underwritten group coverage.

For BC/BS plans represented by a medical director survey, 10 of 18 plans that offer individual coverage do not offer standard coverage to any applicants. Five of the 18 plans that offer individual coverage did so at standard rates to 60 percent or more of all applicants. For medically underwritten groups, one-third (5 of 15) of plans do not offer standard coverage to any applicants. Four of 15 BC/BS plans represented by a medical director survey that offer medically underwritten group coverage offered standard rates to less than 30 percent of applicants. Another four BC/BS plans

SECTION II: UNDERWRITING PRACTICES

4. For each category of coverage, please estimate the proportion of all health insurance applicants from whom you require:

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
a. A personal health history	_____%	_____%	_____%
b. A family health history	_____%	_____%	_____%

IF A FAMILY HISTORY IS REQUIRED, ON WHOM WOULD INFORMATION BE REQUESTED. CHECK ALL THAT APPLY.

[ ] Spouse (1)
[ ] Parents (2)
[ ] Grandparents (3)
[ ] Siblings (4)
[ ] Children (5)
[ ] Other (SPECIFY) _____ (6)

c. An attending physician statement (APS)	_____%	_____%	_____%

IF AN APS IS REQUIRED FOR ANY INDIVIDUALS, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)

d. Physical exam:	_____%	_____%	_____%

IF AN EXAM IS EVER REQUIRED, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)
[ ] Any significant diagnosis or symptoms identified in APS (6)

e. Blood or urine screens:	_____%	_____%	_____%

PLEASE ANSWER THE FOLLOWING QUESTIONS (#5-11) AS THEY APPLY TO YOUR MOST COMMONLY PURCHASED PRODUCT. IS THIS PRODUCT (CHECK ONE):

Traditional _____ (1)
PPO _____ (2)
HMO _____ (3)

SECTION I: INDIVIDUAL AND GROUP STATISTICS

	Individual/Non-group Policies	Medically Underwritten Groups	Nongroup Open Enrollment
1. What is the approximate number of persons that you currently insure through:	_____	_____	_____
2. What is the approximate number of applications received by your company per year for coverage under:	_____	_____	_____
3. What portion of those applications are:			
a. Accepted at standard rates without exclusion waiver or waiting period	_____%	_____%	_____%
b. Covered with an exclusion waiver, but standard premium	_____%	_____%	_____%
c. Covered with a waiting period, but standard premium	_____%	_____%	_____%
d. Covered with a rated/risk-adjusted premium, but not exclusion waiver or waiting period	_____%	_____%	_____%
e. Covered with an exclusion waiver and a rated/risk-adjusted premium	_____%	_____%	_____%
f. Covered with a waiting period and a rated/risk-adjusted premium	_____%	_____%	_____%
g. Declined by your company	_____%	_____%	_____%
h. Other (SPECIFY)	_____%	_____%	_____%
_____	_____%	_____%	_____%
_____	_____%	_____%	_____%
TOTAL	100%	100%	100%

offered standard rates to more than 75 percent of applicants.

BC/BS plans generally do not offer coverage at standard rates to open enrollment applicants; seven of eight BC/BS underwriters that work for plans with open enrollment reported that applicants for this type of coverage are not offered standard rates. Three of seven BC/BS medical directors that work for plans with open enrollment said they do not offer individual coverage to any applicants at standard rates. Most plans attempt to hold down premium rates for open enrollment subscribers by providing less comprehensive benefits relative to medically underwritten applicants. Others require open enrollment subscribers to pay higher premiums than underwritten applicants for identical coverage. Open enrollment coverage of high-risk applicants usually entails waiting periods before initial benefits may be paid and may impose limitations on coverage of preexisting conditions (3).

The majority of BC/BS plans represented by underwriter surveys (23 of 25) offering individual coverage do so with standard rates, but with exclusion waivers for 0 to 50 percent of applicants. However, of the 21 plans offering medically underwritten group coverage, over half (14 plans) do not offer coverage at standard rates with an exclusion waiver to any applicants. The remaining five responding plans offered this coverage to less than 10 percent of applicants. None of the eight BC/BS underwriters' plans offered open enrollment coverage at standard rates with an exclusion waiver.

Eight of 18 BC/BS plan medical directors said their plans do not offer standard coverage with an exclusion waiver to anyone applying for individual coverage; the remaining eight BC/BS plans offer standard coverage with an exclusion waiver to less than 27 percent of applicants for individual coverage. Eight of 15 medical directors of BC/BS plans that offer medically underwritten group policies said they do not offer standard coverage with an exclusion waiver to any applicants; the remaining seven BC/BS plans offer this type of coverage to less than 11 percent of all medically underwritten group applicants. For open enrollment, a majority (5 of 7) of medical directors from BC/BS plans that offer such coverage said they offer standard rates with an exclusion waiver to any open enrollment applicant.

Underwriters from 15 of the 25 BC/BS plans offering individual policies responded that more than 50 percent of their applicants are offered coverage at a standard premium but with a waiting period, as do 13 of 21 BC/BS plans offering medically underwritten group coverage. Underwriters at four of eight BC/BS plans offering open enrollment said their plans offer applicants standard rates, but require waiting periods.

Medical directors from 11 of the 18 BC/BS plans that write individual coverage said more than 58 percent of their plans' applicants are offered policies at a standard premium but with a waiting period. Six of 18 BC/BS plans do not offer standard rates with a waiting period to any medically underwritten group applicants, but medical directors from six other BC/BS plans reported their plans offer such coverage to more than 65 percent of their applicants. Three of 7 BC/BS plans offering open enrollment do not give standard rates with a waiting period to any applicants, while two of seven give this coverage to all applicants.

Requiring a rated premium with no waiting period or exclusion waiver was uncommon for plans offering individual coverage—only one plan covered applicants this way among surveys returned by chief underwriters. Although a majority of chief underwriters at BC/BS plans that medically underwrite groups (12 of 21) reported they never offered applicants a rated premium with no waiting period or exclusion waiver, a few plans did: 6 did less than 50 percent of the time and 2 did for more than 80 percent of their applicants. However, no plans offering open enrollment covered applicants this way.

No medical directors from the 18 BC/BS plans that write individual policies offered such coverage at a rated premium without a waiting period or exclusion waiver. Similarly, medical directors from 11 of 15 BC/BS plans said they never offered medically underwritten group coverage with a rated premium and no waiting period or exclusion waiver. A majority (5 of 7) of medical directors from BC/BS plans offering open enrollment said they did not offer this type of coverage to any applicant.

Only 1 of the 25 underwriters from BC/BS plans offering individual coverage responded he or she did so with a rated premium and an exclusion waiver—to 1 percent of applicants. Underwriters from 22 of 25 BC/BS plans offering individual coverage said their plans did not cover any applicants with a waiting period and a rated premium. Six BC/BS

plans offering medically underwritten group policies covered less than 25 percent of applicants with a waiting period and a rated premium, but 13 plans represented by underwriters never offered this coverage. No open enrollment plans offered coverage with a waiting period or an exclusion waiver and a rated premium.

None of the medical directors from BC/BS plans that offer individual policies said their plan covered any applicants with a rated premium and an exclusion waiver. Medical directors from 12 of 15 BC/BS plans that offer medically underwritten group policies said their plans do not cover any applicants with a rated premium and an exclusion waiver. Fifteen of 18 medical directors from BC/BS plans that offer individual coverage said their plans do not cover any applicants with a waiting period and a rated premium. Medical directors from 10 of the 15 BC/BS plans that offer medically underwritten group coverage said their plans do not cover any applicants with a waiting period and a rated premium.

For BC/BS plans represented by the underwriter population, 19 of 21 plans that offer individual coverage declined applicants between 0 and 25 percent of the time. Nearly all responding underwriters from BC/BS plans (20 of 21) said they declined applicants less than 35 percent of the time. Medical directors from 15 of the 18 BC/BS plans that offer individual coverage reported their plans declined applicants between 0 and 25 percent of the time. Thirteen of the 15 BC/BS plans returned by a medical director declined applicants for medically underwritten group coverage less than 3 percent of the time.

Health Maintenance Organizations

All 11 HMOs offering individual coverage accept more than 50 percent of their applicants at standard rates. Three-quarters (16 of 20 respondents) of those HMOs offering medically underwritten group coverage offer standard rates to more than 50 percent of their applicants. The majority of HMOs offering individual coverage (9 of 11) do not use exclusion waivers, and a similar proportion of HMOs offering medically underwritten group coverage (15 of 20) also do not use exclusion waivers. Similar proportions were found for HMOs covering applicants with rated premiums: 10 of the 11 HMOs offering individual coverage and 13 of the 20 offering medically underwritten coverage never provide coverage with a rated premium.

Clearly, HMO practices are either to accept applicants or to decline them. Rarely did HMO survey respondents report accepting an applicant with a restriction on the policy. More than half of responding HMOs that offer individual coverage (6 of 11) declined applicants less than 25 percent of the time. The remaining 5 respondents declined applicants for coverage less than 45 percent of the time. For HMOs offering medically underwritten group coverage, the proportion of declined applicants was similar: 15 of the 20 offering medically underwritten group coverage declined coverage less than 25 percent of the time.

CHAPTER 2 REFERENCES

1. Health Insurance Association of America, *A Course in Individual Health Insurance: Parts A and B* (Chicago, IL: Health Insurance Association of America, 1983).
2. Iglehart, J.K., "The American Health Care System—Private Insurance," *New England Journal of Medicine* 326:1715-1720, 1992.
3. U.S. Congress, Office of Technology Assessment, *Medical Testing and Health Insurance*, OTA-H-384 (Washington, DC: U.S. Government Printing Office, August 1988).
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CONGRESSIONAL OFFICE OF TECHNOLOGY ASSESSMENT

SURVEY OF HEALTH INSURERS' ATTITUDES AND PRACTICES REGARDING GENETIC TESTING FOR CYSTIC FIBROSIS

ATTN: CHIEF UNDERWRITER

Please Respond by July 19, 1991

The Congressional Office of Technology Assessment (OTA) is contacting health insurers who offer individual coverage in a national survey of attitudes and practices regarding cystic fibrosis screening. This questionnaire has been directed to you as the person in your organization whose responsibilities include underwriting. We request your assistance in answering some questions about genetic testing and underwriting in your company. **If you are not the Chief Underwriter, we would appreciate it if you would please forward the questionnaire to the appropriate person.**

For the purposes of this survey, OTA has adopted the following definitions:

> By *carrier testing*, we mean testing an unaffected individual to reveal the possibility that off-spring may have a serious chronic condition or disease (e.g., cystic fibrosis or sickle cell disease).
>
> By *genetic testing*, we mean testing applicants or policyholders for certain inherited characteristics either presymptomatically to reveal future serious chronic disease (e.g., for Huntington's disease) or for risk oriented purposes (e.g., predisposition to heart disease).

This is an important study that has been requested by the U.S. Congress, and is designed to represent the attitudes and practices of health insurers. We need to know how insurers view the technologies of genetic testing in terms of their current and future applications in health insurance.

Please read each question and mark the space that most nearly corresponds to your answer. Please feel free to qualify your answers. Space has been provided at the end for comments and opinions that you feel are not adequately represented by the survey questions. The survey responses will be kept strictly anonymous as well as confidential.

PLEASE NOTE: This survey focuses on three health insurance populations---(1) *Medically underwritten Individuals/nongroup* who seek insurance independently and without any association with an employer or membership group of any kind; (2) *Medically underwritten groups*, i.e., those groups whose members must be medically underwritten; and (3) *Nongroup open enrollment*, individuals/nongroup who seek open enrollment coverage, i.e., without medical underwriting.

****

Conversions should be excluded from your responses. In addition, we prefer that you exclude Medigap insurance from your responses. If because of reporting or other reasons, you must include Medigap policies, please check the box below:

[ ] YES, Medigap policies and statistics are included in our responses to this survey.

****

Does your plan have an open enrollment period? [ ] YES (1) [ ] NO (2)
If yes, is it continuous? [ ] YES (1) [ ] NO (2)

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us as any other opinions, concerns, or suggestions related to genetic testing and insurance that you feel our questions did not address. These comments will be strictly anonymous but may be incorporated in our report to Congress. Please write these comments below.

_____

_____

_____

_____

_____

_____

We have attached a peel-off identification number on the questionnaire. This is the only link between the companies who were sampled and the questionnaires returned. We would prefer that you leave the identification number on the questionnaire when you return it. Our staff will remove the label upon receipt, making the questionnaire entirely anonymous. Absolutely no linkage between companies and questionnaires will be retained. The label from the completed questionnaire is designed to eliminate your company from those that we will have to recontact.

However, if this temporary identification makes you uncomfortable, then peel off the label before returning the questionnaire. We appreciate your help and we want you to feel comfortable in participating in the survey.

_____

PEEL OFF LABEL WITH SAMPLE

IDENTIFICATION HERE

_____

PLEASE RETURN THE QUESTIONNAIRE IN THE POSTAGE PAID RETURN ENVELOPE SENT WITH THE QUESTIONNAIRE. IF THE ENVELOPE HAS BEEN LOST, THE RETURN ADDRESS IS:

Margaret Anderson
Biological Applications Program
Office of Technology Assessment
U.S. Congress
Washington, DC 20510-8025

Chapter 3
Underwriting Practices

An underwriter's objective is to know as much about the applicant's health status as the applicant. Any health insurance policy based on medical underwriting requires the applicant (and each family member for family policies) to complete a health history questionnaire and to release medical records. In some cases, insurers might also require physical examinations or laboratory tests.

UNDERWRITING PRACTICES

For commercial health insurers offering individual coverage, the majority (23 of 29) surveyed by OTA required a personal health history of all applicants. The same is true for commercial companies offering medically underwritten coverage: 29 of 37 required one of all applicants.

For Blue Cross and Blue Shield (BC/BS) plans represented by the underwriter survey, 22 of 25 plans offering individual coverage required a personal health history of all applicants; 17 of 21 plans offering medically underwritten group coverage required one of all applicants. Underwriters at six of the eight BC/BS plans with open enrollment coverage said their plans did not require a personal history from any applicants. Sixteen of 18 BC/BS plans represented by a medical director survey required a personal health history of all applicants. Thirteen of 15 BC/BS plans represented by a medical director survey required one of all applicants as well. Of those BC/BS plans from medical directors that had open enrollment, 4 of 6 did not require a personal health history from any applicants. For health maintenance organizations (HMOs), 7 of 11 plans offering individual coverage required a personal health history of all applicants. Nine of 20 HMOs required one of all medically underwritten group applicants; all of the remaining plans required a personal health history for less than 40 percent of their applicants.

Family health histories were required of all individual applicants for 14 of 29 commercial insurers; 12 individual insurers did not require one of any applicants. For commercial insurers offering medically underwritten group coverage, nearly half (16 of 37) did not require a family history from any applicants, while 12 required one from all applicants. A majority of BC/BS plans (20 of 25) represented by an underwriter survey never required a family history of individual applicants or medically underwritten group applicants (19 of 21), or open enrollment applicants (7 of 8). Sixteen of 18 BC/BS plans represented by medical directors did not require a family history of any individual applicants. Fourteen of 15 BC/BS plans represented by the underwriter population did not require one from any medically underwritten group applicants. The same holds true for HMOs, with 9 of 11 that offer individual coverage not requiring a family history of any applicants and 14 of 20 never requiring one of medically underwritten group applicants.

Of those commercial insurers requiring a family health history, six routinely request information about the applicant's parents, and five respondents request information about an applicant's spouse and children. Of the few BC/BS plans represented by an underwriter survey that required a family history, information on an applicant's spouse and children is most often requested. Four required information about a spouse and five seek information about children. Health histories on spouse (2 plans) and children (2 plans) are the only ones used by BC/BS plans represented by medical directors. Finally, for HMOs using a family history, information is obtained most often on an applicant's spouse (6 plans) and children (6 plans).

Varying widely are company procedures pertaining to the proportion of applicants required to provide further evidence of their health status through an attending physician statement (APS), physical examination, or blood/urine test. The standard APS form calls for a complete description of a patient's complaints, any abnormal findings (including laboratory and other test results), treatment or operations, present condition, if known, and other medical information with a bearing on an applicant's health, such as smoking or alcohol use. For children under 6 months of age, additional information might be sought regarding birth weight and the presence of any disease or abnormality (2).

For both medically underwritten groups and individual policies, the APS is the most common

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supplemental source of information for underwriting beyond the health data provided directly through the insurance application (2). For individual applicants, a quarter of commercial insurers (10 of 39) required an APS for less than 25 percent of applicants, 12 required one for between 25 and 50 percent of applicants, and 9 for over 50 percent of applicants. Twenty-four commercial plans required an APS for less than 25 percent of medically underwritten group applicants.

Overall, close to half (12 of 25) of underwriters from BC/BS plans offering individual coverage required an APS for less than 25 percent of applicants; 13 of 21 offering medically underwritten coverage required an APS for less than 25 percent of applicants. Underwriters from seven of the eight BC/BS open enrollment plans said they never required an APS of applicants. Eight of 18 BC/BS plans for the medical director population required an APS for 25 to 50 percent of individual applicants, seven required one from less than 25 percent of applicants. Medical directors from all 15 BC/BS plans that offer medically underwritten group coverage said they required an APS for less than 50 percent of applicants. Over half the HMOs (6 of 11) that offer individual coverage required an APS for 50 to 75 percent of applicants, while four required one for less than 20 percent of applicants. Fifty percent (10 of 20) of HMOs did not require an APS for any medically underwritten group applicants, 8 required them for less than 10 percent of applicants.

For commercial companies, an APS was triggered most often by reports of any significant (39 companies) or selected (31 companies) diagnosis or symptoms on the application, or because of a Medical Information Bureau, Inc. (MIB) report (26 companies). Applications for individual insurance—health, life, or disability—carry an explanation about MIB. MIB's reports alert a potential insurer to omissions or misrepresentation of facts by an applicant (3). In the BC/BS underwriter/medical director surveys, any significant (19 plans/11 plans) or selected (16 plans/10 plans) diagnosis or symptoms reported on the application triggered an APS. Twelve HMOs required an APS because of any significant diagnosis or symptoms in the application, and 11 HMOs required one because of selected diagnoses or symptoms.

Physical examinations of individual health insurance applicants are much less common than other underwriting practices. Five of 29 commercial insurers did not require physical exams of any individual applicants, 22 required a physical exam of less than 40 percent of applicants. Thirty-four of 37 companies required a physical exam from less than 25 percent of medically underwritten group applicants.

Seventeen of 25 BC/BS plans represented by the medical director population did not require a physical exam of any individual applicants. Physical exams are not required of any medically underwritten group applicants in 16 of 21 BC/BS plans. Medical directors at 10 of 18 BC/BS plans that offer individual coverage said their plans did not require a physical exam of any applicants. The remaining plans required them of less than 20 percent of applicants. Of the 15 BC/BS plans represented by the medical director population, 12 do not require a physical exam of any medically underwritten group applicants. For the 11 HMOs that write individual policies, physical exams are required for less than 30 percent of applicants. Only one of 20 HMOs requires a physical exam for medically underwritten group coverage.

If commercial insurers require a physical exam, it is usually triggered because of selected diagnoses or symptoms reported on an application (21 plans), or an MIB report (22 plans). Underwriters at six BC/BS plans reported that selected diagnoses or symptoms in the application, and any significant diagnosis or symptoms in the APS, can trigger a physical exam. Four BC/BS plans represented by the medical director population said that any significant diagnosis or symptoms in the APS prompts a physical exam, as they can for four HMOs.

Insurers generally use the standard blood tests and urinalysis that are commonly ordered by physicians as part of a general physical evaluation. Such panels can detect indicators of use of illicit drugs, as well as nicotine and prescription medications for diabetes, heart disease, and hypertension. The insurer's interest in prescription medicine is twofold; first, to identify applicants who are not forthcoming in their health history questionnaire and, second, to determine whether known hypertensive applicants, for example, are conscientiously following prescribed treatment (2).

Twenty of 29 commercial companies required blood or urine screens of less than 30 percent of individual applicants; 33 of 37 commercial compa-

SECTION VI: DEMOGRAPHICS

21. What is your job title?

    _____

22. Which of the following lines of insurance does your company underwrite?

    Health 1

    Disability 2

    Life 3

23. What percent of persons under HMO policies issued by your company are in policies classified as:

    Self-insured Administration _____%

    Individual _____%

    Community-rated Groups _____%

    Experience-rated Groups _____%

    TOTAL 100%

20. Please indicate whether you:

	Agree Strongly	Agree Somewhat	Disagree Somewhat	Disagree Strongly
a. It's fair for HMOs to use genetic tests to identify individuals with increased risk of disease.	1	2	3	4
b. An HMO should have the option of determining how to use genetic information in determining risks.	1	2	3	4
c. Genetic conditions, such as cystic fibrosis or Huntington's disease, are pre-existing conditions.	1	2	3	4
d. Carrier status for genetic conditions, such as cystic fibrosis or Tay-Sachs, are pre-existing conditions.	1	2	3	4
e. Genetic information is no different than other types of medical information.	1	2	3	4
f. Prenatal diagnosis indicates the fetus is affected with cystic fibrosis; the couple decide to continue the pregnancy. The HMO, which paid for the tests, informs the couple they will have no financial responsibility for the cystic fibrosis-related costs for the child.	1	2	3	4
g. Through prior genetic testing, the husband is known to be a carrier for cystic fibrosis. Before having children, the wife seeks genetic testing for cystic fibrosis. The HMO declines to pay for the testing, since there is no history of cystic fibrosis in her family.	1	2	3	4

nies required blood or urine screens of less than 30 percent of medically underwritten group applicants. Eleven commercial companies did not require them of any medically underwritten group applicants. Blood or urine screens are not required of individual applicants by underwriters at 20 of 25 BC/BS plans. Nineteen of 21 BC/BS plans represented by an underwriter survey did not require blood or urine screens of any medically underwritten group applicants. Medical directors from 15 of 18 BC/BS plans said they did not require blood or urine screens from any individual applicants; all 15 plans that offer medically underwritten group coverage never required a blood or urine screen. Nine of the 11 HMOs that offer individual coverage said blood or urine screens are required of less than 20 percent of applicants. Nineteen of 20 HMOs never required them of any medically underwritten group applicants.

FACTORS IN INSURABILITY

Insurability is not just a matter of health status; several factors are involved in an underwriter's decision to accept or deny an application, to exclude coverage for a condition, or to charge a higher premium. When asked to indicate which nonmedical underwriting factors could affect acceptance of an individual application, commercial insurers most commonly cited smoking habits, age, and occupation. For medically underwritten group applicants, insurers cited age, occupation, and sex (table 3-1).

An individual applicant's smoking status is considered "important" or "very important" by 24 of 29 commercial insurers. Twenty-three of 29 commercial insurers offering individual insurance said age was important or very important. An applicant's occupation is important or very important to 21 (41 percent) insurers of individuals. Eighteen (35 percent) commercial insurers of group applicants consider age, occupation, and gender to be important factors in determining insurability.

Personal and family medial histories were the most important factors in determining insurability for respondents regardless of whether they were from a commercial insurer, HMO, or BC/BS plan. For commercial insurers, for example, all individual and group insurers thought a personal history of significant conditions was very important. However, only 16 of 29 individual insurers and 17 of 37 commercial group insurers thought a family medical history was important. Insurers of both individuals and groups found genetic predispositions as well as carrier risk for genetic diseases to be relatively unimportant. Genetic predisposition was a very important criterion to 4 of 29 commercial insurers that offer individual policies, important to 6, unimportant to 3, and never used by 16. Eighteen of 37 group insurers found genetic predispositions to be important, with an equal number never using it in determining insurability. Carrier risk for genetic disease was considered important in determining insurability by 7 of 29 companies that insured individuals and by 10 of 37 group insurers. Similar results were obtained for BC/BS plans and HMOs (table 3-1).

Information on Specific Conditions

When certain conditions are detected either in an examination or an application, how do they affect the rating of applicants by insurers? The majority of commercial insurers would not accept individual applicants with standard rates for any of the conditions listed in the OTA survey (table 3-2). A large proportion would decline the applicant. Fewer applicants with hypertension were declined than those who had cerebrovascular disease, diabetes, or cystic fibrosis (CF). HMOs generally accepted individual applicants with the listed conditions, but often with an exclusion waiver and a rated premium. Eight of 11 HMOs that offer individual coverage declined individual applicants with hemophilia and CF (table 3-2). Individual applicants with the listed conditions were most often declined coverage from BC/BS plans (table 3-3). Those applicants with hypertension were declined least often, while applicants with hemophilia and sickle cell anemia were declined most often.

Commercial insurers declined to cover the majority of medically underwritten groups with members who had one of the conditions in table 3-2, except for groups with applicants who had hypertension. In fact, medically underwritten groups with appliants who had hypertension were frequently accepted with standard rates by commercial insurers, BC/BS plans, and HMOs (tables 3-2 and 3-3). When medically underwritten group policies were accepted with applicants having one of the other conditions listed in the OTA survey, most BC/BS plans required either a rated premium or a waiting period (table 3-3), and again, applicants were most often declined

Table 3-1—Factors in Determining Insurability

Question: For each category of coverage, please indicate the importance of each of the following factors in determining insurability (not in rating):

	Respondent	Very important	Important	Unimportant	Never used	No response[a]
Individual policies						
Age	*Commercials*	11 (38%)	12 (41%)	5 (17%)	1 (3%)	0 (0%)
	HMOs	0 (0%)	3 (27%)	7 (64%)	1 (9%)	1 (9%)
	BC/BS plans-U[b]	0 (0%)	9 (36%)	7 (28%)	8 (32%)	1 (4%)
	BC/BS plans-M	3 (17%)	6 (33%)	4 (22%)	5 (28%)	0 (0%)
Occupation	*Commercials*	3 (10%)	18 (62%)	7 (24%)	1 (3%)	0 (0%)
	HMOs	0 (0%)	2 (18%)	3 (27%)	5 (45%)	1 (9%)
	BC/BS plans-U	0 (0%)	3 (12%)	10 (40%)	11 (44%)	1 (4%)
	BC/BS plans-M	0 (0%)	6 (33%)	3 (17%)	9 (50%)	0 (0%)
Smoking status	*Commercials*	9 (31%)	15 (52%)	2 (71%)	3 (10%)	0 (0%)
	HMOs	1 (9%)	5 (45%)	1 (9%)	3 (27%)	1 (9%)
	BC/BS plans-U	3 (12%)	9 (36%)	4 (16%)	8 (32%)	1 (4%)
	BC/BS plans-M	3 (17%)	5 (28%)	1 (6%)	9 (50%)	0 (0%)
Lifestyle	*Commercials*	1 (3%)	10 (34%)	3 (10%)	14 (48%)	1 (3%)
	HMOs	0 (0%)	3 (27%)	2 (18%)	5 (45%)	1 (9%)
	BC/BS plans-U	1 (4%)	5 (20%)	6 (24%)	12 (48%)	1 (4%)
	BC/BS plans-M	1 (6%)	5 (28%)	1 (6%)	11 (61%)	0 (0%)
Sex	*Commercials*	5 (17%)	4 (14%)	7 (24%)	13 (45%)	0 (0%)
	HMOs	0 (0%)	0 (0%)	2 (18%)	8 (73%)	1 (9%)
	BC/BS plans-U	0 (0%)	3 (12%)	7 (28%)	14 (56%)	1 (4%)
	BC/BS plans-M	1 (6%)	5 (28%)	3 (17%)	9 (50%)	0 (0%)
Financial/credit status	*Commercials*	2 (7%)	11 (38%)	9 (31%)	7 (24%)	0 (0%)
	HMOs	0 (0%)	0 (0%)	3 (27%)	7 (64%)	1 (9%)
	BC/BS plans-U	0 (0%)	0 (0%)	0 (0%)	24 (96%)	1 (4%)
	BC/BS plans-M	0 (0%)	0 (0%)	0 (0%)	18 (100%)	0 (0%)
Personal medical history of significant conditions	*Commercials*	29(100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	HMOs	9 (82%)	0 (0%)	0 (0%)	1 (9%)	1 (9%)
	BC/BS plans-U	22 (88%)	1 (4%)	0 (0%)	1 (4%)	1 (4%)
	BC/BS plans-M	16 (89%)	0 (0%)	0 (0%)	2 (11%)	0 (0%)
Family medical history of significant conditions	*Commercials*	5 (17%)	11 (38%)	9 (31%)	4 (14%)	0 (0%)
	HMOs	1 (9%)	0 (0%)	2 (18%)	7 (64%)	1 (9%)
	BC/BS plans-U	0 (0%)	6 (24%)	4 (16%)	14 (56%)	1 (4%)
	BC/BS plans-M	0 (0%)	4 (22%)	4 (22%)	10 (56%)	0 (0%)
Genetic predisposition to significant conditions	*Commercials*	4 (14%)	6 (21%)	3 (10%)	16 (55%)	0 (0%)
	HMOs	0 (0%)	3 (27%)	1 (18%)	6 (55%)	1 (9%)
	BC/BS plans-U	1 (4%)	2 (8%)	5 (20%)	16 (64%)	1 (4%)
	BC/BS plans-M	0 (0%)	3 (17%)	1 (6%)	14 (78%)	0 (0%)
Carrier risk for genetic disease	*Commercials*	2 (7%)	5 (17%)	6 (21%)	16 (55%)	0 (0%)
	HMOs	0 (0%)	2 (18%)	1 (18%)	7 (64%)	1 (9%)
	BC/BS plans-U	0 (0%)	2 (8%)	5 (20%)	17 (68%)	1 (4%)
	BC/BS plans-M	0 (0%)	3 (17%)	1 (6%)	14 (78%)	0 (0%)

for coverage by BC/BS plans when they had cerebrovascular disease, hemophilia, or sickle cell anemia.

Inquiries About Genetic Conditions

Do applications for either individual or medically underwritten group insurance coverage contain questions about genetic conditions? OTA asked insurers whether questions on genetic conditions were included in either a personal history, a family history, or neither. For individual policies, the majority of commercial insurers did not inquire about any of the listed genetic conditions in either the personal or family history (table 3-4). Five of 29 commercial

19. How likely do you think it is that your HMO will:

	Very Likely	Somewhat Likely	Somewhat Unlikely	Very Unlikely
In the next 5 years:				
a. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
b. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
c. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
d. Offer optional genetic testing and carrier testing	1	2	3	4
e. Use information derived from genetic tests for underwriting	1	2	3	4
f. Alter claims payment practices as new genetic tests come on line	1	2	3	4
In the next 10 years:				
g. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
h. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
i. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
j. Offer optional genetic testing and carrier testing	1	2	3	4
k. Use information derived from genetic tests for underwriting	1	2	3	4
l. Alter claims payment practices as new genetic tests come on line	1	2	3	4

15. How would individual policies and medically underwritten policies normally be affected by the following findings:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates; 3 = Accepted with exclusion waiver at rated premium; 4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies	Medically Underwritten Groups
a. Presymptomatic testing reveals the likelihood of a serious, chronic future disease (e.g., for Huntington's disease)	_____	_____
b. Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease (e.g., predisposition to heart disease)	_____	_____
c. Carrier testing reveals the possibility that off-spring may have a serious, chronic condition or disease	_____	_____
d. Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	_____	_____

SECTION V: GENERAL ATTITUDES

16. To your knowledge, has your company ever reimbursed for carrier testing for cystic fibrosis?
Yes _____(1)
No _____(2)

17. Has your company ever conducted an economic analysis of the costs and benefits of:

	Yes	No
a. Carrier testing as part of applicant screening	1	2
b. Genetic counseling of carriers who are covered	1	2
c. Carrier testing as part of prenatal coverage	1	2
d. Genetic testing as part of applicant screening	1	2

18. Under what conditions would a negative financial impact be likely to occur for your company: (CHECK ALL THAT APPLY)

a. Widespread availability of genetic tests to the medical/provider community _____(1)
b. Widespread availability of genetic tests with constraints on HMOs' access to the results ____(2)
c. Adverse claims or underwriting results from antiselection _____(3)
d. Other (SPECIFY) _____ (4)

Table 3-1—Factors in Determining Insurability—Continued

Question: For each category of coverage, please indicate the importance of each of the following factors in determining insurability (not in rating):

	Respondent	Very important	Important	Unimportant	Never used	No response[a]
Medically underwritten group policies						
Age	*Commercials*	4 (11%)	14 (38%)	11 (30%)	8 (22%)	0 (0%)
	HMOs	3 (15%)	6 (30%)	0 (0%)	10 (50%)	1 (5%)
	BC/BS plans-U[b]	1 (5%)	9 (43%)	4 (19%)	7 (33%)	0 (0%)
	BC/BS plans-M	3 (20%)	5 (33%)	4 (27%)	3 (20%)	0 (0%)
Occupation	*Commercials*	4 (11%)	14 (38%)	12 (32%)	7 (19%)	0 (0%)
	HMOs	4 (20%)	6 (30%)	4 (20%)	5 (25%)	1 (5%)
	BC/BS plans-U	1 (5%)	7 (33%)	5 (24%)	8 (38%)	0 (0%)
	BC/BS plans-M	1 (6%)	9 (60%)	1 (6%)	4 (28%)	0 (0%)
Smoking status	*Commercials*	2 (5%)	14 (38%)	10 (27%)	11 (30%)	0 (0%)
	HMOs	2 (10%)	4 (20%)	2 (10%)	11 (55%)	1 (5%)
	BC/BS plans-U	1 (5%)	7 (33%)	5 (24%)	8 (38%)	0 (0%)
	BC/BS plans-M	0 (0%)	4 (27%)	2 (13%)	9 (60%)	0 (0%)
Lifestyle	*Commercials*	1 (3%)	7 (19%)	7 (19%)	20 (54%)	2 (5%)
	HMOs	1 (5%)	6 (30%)	2 (10%)	10 (50%)	1 (5%)
	BC/BS plans-U	1 (5%)	6 (29%)	3 (14%)	12 (57%)	0 (0%)
	BC/BS plans-M	1 (6%)	4 (27%)	3 (20%)	7 (47%)	0 (0%)
Sex	*Commercials*	0 (0%)	6 (16%)	12 (32%)	19 (51%)	0 (0%)
	HMOs	0 (0%)	5 (25%)	1 (5%)	13 (65%)	1 (5%)
	BC/BS plans-U	1 (5%)	4 (19%)	5 (24%)	11 (52%)	0 (0%)
	BC/BS plans-M	1 (6%)	6 (40%)	3 (20%)	5 (33%)	0 (0%)
Financial/credit status	*Commercials*	1 (3%)	4 (11%)	11 (30%)	20 (54%)	1 (3%)
	HMOs	3 (15%)	3 (15%)	1 (5%)	12 (65%)	1 (5%)
	BC/BS plans-U	1 (5%)	3 (14%)	1 (5%)	16 (76%)	0 (0%)
	BC/BS plans-M	0 (0%)	1 (6%)	1 (6%)	13 (87%)	0 (0%)
Personal medical history of significant conditions	*Commercials*	36 (95%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)
	HMOs	15 (75%)	1 (5%)	0 (0%)	3 (15%)	1 (5%)
	BC/BS plans-U	18 (86%)	1 (5%)	0 (0%)	2 (10%)	0 (0%)
	BC/BS plans-M	15 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Family medical history of significant conditions	*Commercials*	3 (8%)	14 (37%)	10 (27%)	9 (24%)	1 (3%)
	HMOs	4 (20%)	3 (15%)	2 (10%)	10 (50%)	1 (5%)
	BC/BS plans-U	1 (5%)	3 (14%)	4 (19%)	13 (62%)	0 (0%)
	BC/BS plans-M	0 (0%)	4 (27%)	3 (20%)	8 (53%)	0 (0%)
Genetic predisposition to significant conditions	*Commercials*	0 (0%)	12 (32%)	6 (16%)	18 (49%)	1 (3%)
	HMOs	0 (0%)	3 (15%)	2 (10%)	13 (65%)	2 (10%)
	BC/BS plans-U	1 (5%)	1 (5%)	4 (19%)	15 (71%)	0 (0%)
	BC/BS plans-M	0 (0%)	3 (20%)	1 (7%)	11 (63%)	0 (0%)
Carrier risk for genetic disease	*Commercials*	1 (3%)	9 (24%)	9 (24%)	17 (46%)	1 (3%)
	HMOs	0 (0%)	3 (15%)	2 (10%)	13 (65%)	2 (10%)
	BC/BS plans-U	1 (5%)	0 (0%)	5 (24%)	15 (71%)	0 (0%)
	BC/BS plans-M	0 (0%)	3 (20%)	2 (13%)	10 (67%)	0 (0%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

insurers that offer individual coverage inquired about Tay-Sachs, Huntington disease, sickle cell anemia, and CF in the personal history; 7 insurers inquired about hemophilia in the personal history. However, genetic conditions were of greater interest to HMOs and BC/BS plans. Inquiries in the personal history about hemophilia were the most common.

More than half of commercial insurers (26 of 37) that offer medically underwritten group coverage never inquired about the listed genetic conditions in either the personal or family history. Eight commercial insurers responded that they inquired about all of the genetic conditions in OTA's survey in the personal history. Fewer HMOs and BC/BS plans

Table 3-2—Treatment of Applicants with Specific Conditions: Commercials and HMOs

How would you normally treat either an individual policy applicant or medically underwritten groups that disclosed the following conditions in an examination(s) or application:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver at rated premium	Declined	No response[a]
Individual policies							
Hypertension	*Commercials*	5 (17%)	2 (7%)	2 (7%)	13 (45%)	0 (0%)	7 (24%)
	HMOs	2 (18%)	0 (0%)	2 (18%)	0 (0%)	1 (9%)	6 (55%)
Diabetes mellitus	*Commercials*	1 (3%)	0 (0%)	2 (7%)	7 (24%)	15 (52%)	4 (14%)
	HMOs	2 (18%)	0 (0%)	1 (9%)	0 (0%)	2 (18%)	6 (55%)
Cerebrovascular disease	*Commercials*	0 (0%)	1 (3%)	0 (0%)	5 (17%)	16 (56%)	7 (24%)
	HMOs	1 (9%)	0 (0%)	0 (0%)	0 (0%)	6 (55%)	4 (36%)
Hemophilia	*Commercials*	1 (3%)	0 (0%)	0 (0%)	0 (0%)	26 (90%)	2 (7%)
	HMOs	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (73%)	3 (27%)
Cystic fibrosis	*Commercials*	1 (3%)	0 (0%)	0 (0%)	0 (0%)	26 (90%)	2 (7%)
	HMOs	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (73%)	3 (27%)
Sickle cell anemia	*Commercials*	1 (3%)	0 (0%)	0 (0%)	0 (0%)	25 (86%)	3 (10%)
	HMOs	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (64%)	4 (36%)
Medically underwritten group policies							
Hypertension	*Commercials*	14 (38%)	0 (0%)	3 (8%)	7 (19%)	0 (0%)	13 (35%)
	HMOs	11 (55%)	0 (0%)	1 (5%)	1 (5%)	2 (10%)	5 (25%)
Diabetes mellitus	*Commercials*	1 (3%)	2 (5%)	1 (3%)	6 (16%)	13 (35%)	14 (38%)
	HMOs	6 (30%)	0 (0%)	1 (5%)	2 (10%)	4 (20%)	7 (35%)
Cerebrovascular disease	*Commercials*	1 (3%)	0 (0%)	0 (0%)	4 (11%)	21 (57%)	11 (30%)
	HMOs	4 (20%)	0 (0%)	1 (5%)	1 (5%)	7 (35%)	7 (35%)
Hemophilia	*Commercials*	0 (0%)	1 (3%)	0 (0%)	2 (5%)	30 (81%)	4 (11%)
	HMOs	3 (15%)	0 (0%)	2 (10%)	0 (0%)	10 (50%)	5 (25%)
Cystic fibrosis	*Commercials*	0 (0%)	1 (3%)	1 (3%)	1 (3%)	31 (84%)	3 (8%)
	HMOs	2 (10%)	0 (0%)	1 (5%)	2 (10%)	10 (50%)	5 (25%)
Sickle cell anemia	*Commercials*	0 (0%)	0 (0%)	1 (3%)	2 (5%)	31 (84%)	3 (8%)
	HMOs	4 (20%)	0 (0%)	1 (5%)	2 (10%)	9 (45%)	4 (20%)

[a]Percentages may not add to 100 due to rounding.

SOURCE: Office of Technology Assessment, 1992.

that offered medically underwritten group coverage were interested in the genetic conditions than the HMOs and BC/BS plans that offered individual coverage. More than half of all HMOs did not inquire about the listed conditions in either the personal or family history. Similar numbers were found from responding underwriter and medical directors of BC/BS plans (table 3-4).

Effect of Genetic Test Results on Insurability

Do genetic test results have an effect on insurability? When presymptomatic testing reveals the likelihood of a serious, chronic future disease (e.g., Huntington disease) 17 of 29 commercial insurers would decline an individual applicant, while 8 would accept the applicant at standard rates (table 3-5). Fifteen of 37 commercial insurers that cover medically underwritten groups would decline the applicant, however, 10 insurers would accept the group at standard rates (table 3-5).

Underwriters at 11 of 25 BC/BS plans that provide individual coverage said they would decline an applicant if presymptomatic testing revealed a likelihood of disease (e.g., Huntington disease); 6 would accept the applicant at standard rates. The

13. For individual policy applicants only, how would the coverage of a family member (e.g., spouse or adopted child) be affected if the policy applicant was negative, but the family member was asymptomatic but had a family history of:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with exclusion waiver at rated premium;
4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

14. Do your standard individual policies and medically underwritten policies provide coverage for:

1= At patient request; 2 = Only if medically indicated; 3 = Not covered

	Individual Policies	Medically Underwritten Groups
Carrier tests for:		
a. Cystic fibrosis	_____	_____
b. Tay-Sachs	_____	_____
c. Sickle cell trait	_____	_____
Prenatal tests for:		
d. Cystic fibrosis	_____	_____
e. Tay-Sachs	_____	_____
f. Sickle cell anemia	_____	_____
g. Down Syndrome	_____	_____
h. Other (SPECIFY)	_____	_____
Genetic counseling	_____	_____

SECTION IV: GENETIC CONDITIONS

11. Does your company specifically inquire, for each category of coverage, about the following conditions in the HMO application in the personal history, family history, or neither:

1 = Personal history only; 2 = Family history; 3 = Neither

	Individual Policies	Medically Underwritten Groups
a. Hemophilia	_____	_____
b. Tay-Sachs	_____	_____
c. Huntington's disease	_____	_____
d. Sickle cell anemia	_____	_____
e. Cystic fibrosis	_____	_____
f. Any other genetic disease (SPECIFY)	_____	_____

12. For individual policy applicants <u>only</u>, how would the application normally be treated if a policy applicant was asymptomatic but had a family history of:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with exclusion waiver at rated premium;
4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

Table 3-3—Treatment of Applicants with Specific Conditions: BC/BS plans

How would you normally treat either an individual policy applicant or medically underwritten groups that disclosed the following conditions in an examination(s) or application:

Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with waiting period at standard rates	Accepted with exclusion waiver or waiting period/ rated premium	Accepted without exclusion waiver or waiting period/ rated premium	Accepted with waiting period at rated premium	Declined	No response[a]
Individual policies								
Hypertension	*BC/BS plans-U*[b]	4 (16%)	6 (24%)	8 (32%)	0 (0%)	0 (0%)	2 (8%)	5 (20%)
	BC/BS plans-M	3 (17%)	4 (22%)	5 (28%)	0 (0%)	1 (6%)	2 (11%)	3 (17%)
Diabetes mellitus	*BC/BS plans-U*	0 (0%)	4 (16%)	4 (16%)	0 (0%)	0 (0%)	14 (56%)	3 (12%)
	BC/BS plans-M	0 (0%)	2 (11%)	2 (11%)	0 (0%)	2 (11%)	9 (50%)	3 (17%)
Cerebrovascular disease	*BC/BS plans-U*	0 (0%)	5 (20%)	4 (16%)	0 (0%)	0 (0%)	16 (64%)	0 (0%)
	BC/BS plans-M	0 (0%)	0 (0%)	3 (17%)	0 (0%)	1 (6%)	14 (78%)	0 (0%)
Hemophilia	*BC/BS plans-U*	0 (0%)	2 (8%)	2 (8%)	0 (0%)	0 (0%)	21 (84%)	0 (0%)
	BC/BS plans-M	0 (0%)	0 (0%)	3 (17%)	0 (0%)	1 (6%)	13 (72%)	1 (6%)
Sickle cell anemia	*BC/BS plans-U*[c]	1 (4%)	4 (16%)	2 (8%)	0 (0%)	0 (0%)	18 (72%)	0 (0%)
	BC/BS plans-M	0 (0%)	0 (0%)	3 (17%)	0 (0%)	1 (6%)	13 (72%)	1 (6%)
Medically underwritten group policies								
Hypertension	*BC/BS plans-U*	5 (24%)	1 (5%)	5 (24%)	0 (0%)	1 (5%)	1 (5%)	6 (29%)
	BC/BS plans-M	2 (13%)	0 (0%)	4 (27%)	0 (0%)	0 (0%)	2 (13%)	4 (27%)
Diabetes mellitus	*BC/BS plans-U*	1 (5%)	0 (0%)	3 (14%)	0 (0%)	4 (19%)	8 (38%)	4 (19%)
	BC/BS plans-M	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	6 (40%)	4 (27%)
Cerebrovascular disease	*BC/BS plans-U*	1 (5%)	1 (5%)	2 (10%)	0 (0%)	2 (10%)	13 (62%)	2 (5%)
	BC/BS plans-M	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	12 (80%)	0 (0%)
Hemophilia	*BC/BS plans-U*	1 (5%)	0 (0%)	1 (5%)	0 (0%)	2 (10%)	17 (80%)	0 (0%)
	BC/BS plans-M	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	12 (88%)	1 (7%)
Sickle cell anemia	*BC/BS plans-U*	1 (5%)	0 (0%)	1 (5%)	0 (0%)	2 (10%)	15 (70%)	0 (0%)
	BC/BS plans-M	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	12 (80%)	1 (7%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
[c]Due to an editing error, "cystic fibrosis" was inadvertently dropped from the survey instrument that was mailed to the BC/BS populations.

SOURCE: Office of Technology Assessment, 1992.

Table 3-4—Inquiries About Genetic Conditions

Question	Respondent	Personal history	Family history	Neither	No response[a]
Does your company specifically inquire, for each category of coverage, about the following conditions in the application for health insurance in the personal history, family history, or neither:					
Individual policies					
Hemophilia	*Commercials*	7 (24%)	0 (0%)	21 (73%)	1 (3%)
	HMOs	6 (55%)	0 (0%)	4 (36%)	1 (9%)
	BC/BS plans-U[b]	14 (56%)	0 (0%)	9 (36%)	2 (8%)
	BC/BS plans-M	7 (39%)	0 (0%)	11 (61%)	0 (0%)
Tay-Sachs	*Commercials*	5 (17%)	0 (0%)	23 (79%)	1 (3%)
	HMOs	4 (36%)	2 (9%)	5 (46%)	1 (9%)
	BC/BS plans-U	10 (40%)	0 (0%)	13 (52%)	2 (8%)
	BC/BS plans-M	8 (44%)	0 (0%)	10 (56%)	0 (0%)
Huntington disease	*Commercials*	5 (17%)	0 (0%)	23 (79%)	1 (3%)
	HMOs	4 (36%)	1 (9%)	5 (46%)	1 (9%)
	BC/BS plans-U	10 (40%)	0 (0%)	13 (52%)	2 (8%)
	BC/BS plans-M	7 (39%)	0 (0%)	11 (61%)	0 (0%)
Sickle cell anemia	*Commercials*	5 (17%)	0 (0%)	23 (79%)	1 (3%)
	HMOs	5 (46%)	1 (9%)	4 (36%)	1 (9%)
	BC/BS plans-U	12 (48%)	0 (0%)	12 (48%)	1 (4%)
	BC/BS plans-M	8 (44%)	0 (0%)	10 (56%)	0 (0%)
Cystic fibrosis	*Commercials*	5 (17%)	0 (0%)	23 (79%)	1 (3%)
	HMOs	5 (46%)	1 (9%)	4 (36%)	1 (9%)
	BC/BS plans-U	13 (52%)	0 (0%)	11 (44%)	1 (4%)
	BC/BS plans-M	8 (44%)	0 (0%)	10 (56%)	0 (0%)
Medically underwritten group policies					
Hemophilia	*Commercials*	8 (22%)	2 (5%)	26 (70%)	1 (3%)
	HMOs	6 (30%)	1 (5%)	12 (60%)	1 (5%)
	BC/BS plans-U	11 (52%)	0 (0%)	9 (43%)	1 (5%)
	BC/BS plans-M	7 (47%)	0 (0%)	8 (53%)	0 (0%)
Tay-Sachs	*Commercials*	8 (22%)	2 (5%)	26 (70%)	1 (3%)
	HMOs	5 (25%)	1 (5%)	13 (65%)	1 (5%)
	BC/BS plans-U	9 (43%)	0 (0%)	11 (52%)	1 (5%)
	BC/BS plans-M	7 (47%)	0 (0%)	8 (53%)	0 (0%)
Huntington disease	*Commercials*	8 (22%)	2 (5%)	26 (70%)	1 (3%)
	HMOs	5 (25%)	1 (5%)	13 (65%)	1 (5%)
	BC/BS plans-U	9 (43%)	0 (0%)	11 (52%)	1 (5%)
	BC/BS plans-M	7 (47%)	0 (0%)	8 (53%)	0 (0%)
Sickle cell anemia	*Commercials*	8 (22%)	2 (5%)	26 (70%)	1 (3%)
	HMOs	7 (35%)	1 (5%)	11 (55%)	1 (5%)
	BC/BS plans-U	11 (52%)	0 (0%)	10 (48%)	0 (0%)
	BC/BS plans-M	7 (47%)	0 (0%)	8 (53%)	0 (0%)
Cystic fibrosis	*Commercials*	8 (22%)	2 (5%)	26 (70%)	1 (3%)
	HMOs	6 (30%)	1 (5%)	12 (60%)	1 (5%)
	BC/BS plans-U	11 (52%)	0 (0%)	10 (48%)	0 (0%)
	BC/BS plans-M	7 (47%)	0 (0%)	8 (53%)	0 (0%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

9. For each category of coverage, please indicate the importance of each of the following factors in determining insurability (not in rating):

1 = Very important; 2 = Important; 3 = Unimportant; 4 = Never used

	Individual Policies	Medically Underwritten Groups
a. Age	_____	_____
b. Occupation	_____	_____
c. Smoking status	_____	_____
d. Lifestyle	_____	_____
e. Sex	_____	_____
f. Financial/credit status	_____	_____
g. Personal medical history of significant conditions	_____	_____
h. Family medical history of significant conditions	_____	_____
i. Genetic predisposition to significant conditions	_____	_____
j. Carrier risk for genetic diseases	_____	_____

10. How would you normally treat either an individual policy applicant or medically underwritten groups that disclosed the following conditions in an examination(s) or application:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with exclusion waiver at rated premium;
4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies	Medically Underwritten Groups
a. Hypertension	_____	_____
b. Diabetes mellitus	_____	_____
c. Cerebrovascular disease	_____	_____
d. Hemophilia	_____	_____
e. Cystic fibrosis	_____	_____
f. Sickle cell anemia	_____	_____

SECTION III: UNDERWRITING PRACTICES

8. For each category of coverage, please estimate the proportion of all HMO applicants from whom you require:

	Individual Policies	Medically Underwritten Groups
a. A personal health history	_____%	_____%
b. A family health history	_____%	_____%

IF A FAMILY HISTORY IS REQUIRED, ON WHOM WOULD INFORMATION BE REQUESTED. CHECK ALL THAT APPLY.

[ ] Spouse (1)
[ ] Parents (2)
[ ] Grandparents (3)
[ ] Siblings (4)
[ ] Children (5)
[ ] Other (SPECIFY) _____ (6)

c. An attending physician statement (APS)	_____%	_____%

IF AN APS IS REQUIRED FOR ANY INDIVIDUALS, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)

d. Physical exam:	_____%	_____%

IF AN EXAM IS EVER REQUIRED, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)
[ ] Any significant diagnosis or symptoms identified in APS (6)

e. Blood or urine screens:	_____%	_____%

Table 3-5—Effect of Genetic Test Results on Insurability: Commercials and HMOs

How would individual policies and medically underwritten policies normally be affected by the following findings:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver at rated premium	Declined	No response[a]
Individual policies							
Presymptomatic testing reveals the likelihood of a serious chronic future disease	*Commercials*	8 (28%)	1 (4%)	0 (0%)	0 (0%)	17 (59%)	2 (8%)
	HMOs	2 (18%)	0 (0%)	0 (0%)	0 (0%)	4 (36%)	5 (46%)
Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease	*Commercials*	12 (41%)	2 (7%)	2 (7%)	5 (17%)	5 (17%)	3 (10%)
	HMOs	4 (36%)	0 (0%)	1 (9%)	0 (0%)	1 (9%)	5 (46%)
Carrier testing reveals the possibility that offspring may have a serious, chronic condition or disease	*Commercials*	16 (55%)	3 (10%)	1 (4%)	0 (0%)	6 (21%)	3 (10%)
	HMOs	6 (55%)	0 (0%)	1 (9%)	0 (0%)	0 (0%)	4 (36%)
Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	*Commercials*	6 (21%)	2 (7%)	0 (0%)	0 (0%)	19 (65%)	2 (7%)
	HMOs	1 (9%)	0 (0%)	0 (0%)	0 (0%)	4 (36%)	6 (55%)
Medically underwritten group policies							
Presymptomatic testing reveals the likelihood of a serious chronic future disease	*Commercials*	10 (27%)	3 (8%)	0 (0%)	1 (3%)	15 (40%)	8 (22%)
	HMOs	6 (30%)	0 (0%)	1 (5%)	1 (5%)	5 (25%)	7 (35%)
Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease	*Commercials*	21 (57%)	3 (8%)	0 (0%)	2 (5%)	4 (11%)	7 (19%)
	HMOs	10 (50%)	0 (0%)	1 (5%)	0 (0%)	3 (15%)	6 (30%)
Carrier testing reveals the possibility that offspring may have a serious, chronic condition or disease	*Commercials*	22 (59%)	3 (8%)	0 (0%)	0 (0%)	4 (11%)	8 (22%)
	HMOs	9 (45%)	0 (0%)	2 (10%)	1 (5%)	3 (15%)	5 (25%)
Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	*Commercials*	6 (16%)	1 (3%)	0 (0%)	1 (3%)	24 (65%)	5 (13%)
	HMOs	4 (20%)	0 (0%)	0 (0%)	0 (0%)	8 (40%)	8 (40%)

[a]Percentages may not add to 100 due to rounding.

SOURCE: Office of Technology Assessment, 1992.

effect of such a test result would cause a medically underwritten group application to be declined by 9 of 21 underwriters at BC/BS plans (table 3-6).

Medical directors at 8 of 18 BC/BS plans said they would decline individual coverage if presymptomatic testing revealed predispostion for future, chronic disease predisposition, while 5 would accept the applicant at standard rates. Six of 15 BC/BS plans would decline medically underwritten group coverage because of presymptomatic test results, and 3 would accept the applicant at standard rates.

Table 3-6—Effect of Genetic Test Results on Insurability: BC/BS plans

How would individual policies and medically underwritten policies normally be affected by the following findings:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with waiting period at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver or waiting period/ rated premium	Accepted with waiting period at rated premium	Declined	No response[a]
Individual policies									
Presymptomatic testing reveals the likelihood of a serious chronic future disease	*BC/BS plans-U*[b]	6 (24%)	2 (8%)	3 (12%)	0 (0%)	0 (0%)	0 (0%)	11 (44%)	3 (12%)
	BC/BS plans-M	6 (33%)	2 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (44%)	2 (11%)
Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease	*BC/BS plans-U*	10 (40%)	2 (8%)	5 (20%)	0 (0%)	0 (0%)	0 (0%)	5 (20%)	3 (12%)
	BC/BS plans-M	8 (44%)	1 (6%)	2 (11%)	0 (0%)	0 (0%)	0 (0%)	5 (28%)	2 (11%)
Carrier testing reveals the possibility that offspring may have a serious, chronic condition or disease	*BC/BS plans-U*	10 (40%)	2 (8%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	3 (12%)	4 (16%)
	BC/BS plans-M	7 (39%)	2 (11%)	2 (11%)	0 (0%)	1 (6%)	0 (0%)	3 (17%)	3 (17%)
Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	*BC/BS plans-U*	5 (20%)	1 (4%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	14 (56%)	4 (16%)
	BC/BS plans-M	3 (17%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	1 (6%)	10 (56%)	3 (17%)
Medically underwritten group policies									
Presymptomatic testing reveals the likelihood of a serious chronic future disease	*BC/BS plans-U*	6 (29%)	0 (0%)	3 (14%)	0 (0%)	0 (0%)	0 (0%)	9 (43%)	3 (14%)
	BC/BS plans-M	4 (27%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	6 (40%)	3 (20%)
Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease	*BC/BS plans-U*	9 (43%)	1 (5%)	5 (24%)	0 (0%)	0 (0%)	0 (0%)	4 (19%)	2 (9%)
	BC/BS plans-M	5 (33%)	1 (7%)	0 (0%)	0 (0%)	3 (20%)	0 (0%)	3 (20%)	3 (20%)
Carrier testing reveals the possibility that offspring may have a serious, chronic condition or disease	*BC/BS plans-U*	9 (43%)	2 (10%)	4 (19%)	0 (0%)	0 (0%)	0 (0%)	3 (14%)	3 (14%)
	BC/BS plans-M	4 (27%)	1 (7%)	1 (7%)	0 (0%)	2 (13%)	0 (0%)	2 (13%)	5 (33%)
Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	*BC/BS plans-U*	3 (14%)	0 (0%)	1 (5%)	0 (0%)	1 (5%)	1 (5%)	13 (62%)	2 (9%)
	BC/BS plans-M	1 (7%)	0 (0%)	1 (7%)	0 (0%)	0 (0%)	1 (7%)	9 (60%)	3 (20%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.

SOURCE: Office of Technology Assessment, 1992.

SECTION II: INDIVIDUAL AND GROUP STATISTICS

	Individual Policies	Medically Underwritten Groups
5. What is the approximate number of persons that you currently insure through:	_____	_____
6. What is the approximate number of applications received by your company per year for coverage under:	_____	_____
7. What portion of those applications are:		
a. Accepted at standard rates	____%	____%
b. Covered with an exclusion waiver, but standard premium	____%	____%
c. Covered with a rated premium, but not exclusion waiver	____%	____%
d. Covered with an exclusion waiver and a rated premium	____%	____%
e. Declined by your company	____%	____%
f. Other (SPECIFY)		
_____	____%	____%
_____	____%	____%
_____	____%	____%
TOTAL	100%	100%

SECTION I: BACKGROUND

1. Do you offer coverage for either self-paying individuals (other than on a conversion basis) or medically underwritten groups?

   Yes _____(1)
   No _____(2)

IF YOU ARE NOT OFFERING EITHER OF THESE TYPES OF COVERAGE, THIS COMPLETES YOUR SURVEY. THANK YOU VERY MUCH. PLEASE RETURN IT IN THE PRE-ADDRESSED POSTAGE-PAID ENVELOPE.

2. Is your plan federally qualified? [ ] Yes (1) [ ] No (2)

   If no, is Federal qualification pending? [ ] Yes (1) [ ] No (2)

   If yes, do you have a non-federally qualified subsidiary? [ ] Yes (1) [ ] No (2)

3. Does your plan have an open enrollment period (i.e., no medical screening) for self-payers?

   [ ] Yes (1) [ ] No (2)

   If yes, is it continuous? [ ] Yes (1) [ ] No (2)

4. Which model type is your plan? Check all that apply, but if more than one type is offered, indicate which is primary, secondary, etc. by the number of patients covered.

   Staff Model Plan _____

   Group Model Plan _____

   Network Model Plan _____

   IPA Model Plan _____

Of the 11 HMOs that cover individuals, 4 would decline an applicant if presymptomatic testing revealed the likelihood of a chronic, future disease and 2 would accept the applicant at standard rates. Six of 20 HMOs that cover medically underwritten groups would do so at standard rates, while 5 HMOs would decline the application.

When risk-oriented testing reveals that an individual carries markers associated with a serious, chronic future disease (e.g., predisposition to heart disease) 12 of 29 commercial insurers would accept individual applicants at standard rates; 5 would decline coverage. The use of an exclusion waiver to exclude the condition would be used by four plans, while five plans would use a rated premium rather than an exclusion waiver. More than half of commercial insurers (21 of 37) that cover medically underwritten groups would accept the applicant at standard rates, 8 would offer standard rates but would have an exclusion waiver for the specific condition.

If an individual applicant is found to carry markers for a chronic, future disease, 10 of 25 BC/BS plans represented by an underwriter survey would accept the application at standard rates, while 5 would decline coverage. Similar proportions were found for medically underwritten group coverage, with underwriters at 9 of 21 BC/BS plans responding that an application would be accepted at standard rates, and 4 responding that coverage would be declined.

The results of risk-oriented testing did not affect individual insurability at 8 of 18 BC/BS plans represented by the medical director population, as they would be accepted with standard rates. However, medical directors at 5 of 18 plas said they would decline coverage because of evidence of disease markers. One-third of underwriters at BC/BS plans (5 of 15) that cover medically underwritten groups said they would accept such groups at standard rates even if disease markers were detected within the group; 3 would decline such applications.

Four of 11 HMOs that accept individuals for coverage would still do so at standard rates even if risk-oriented testing revealed the possibility of a serious, chronic future disease. Half of the HMOs (10 of 20) that cover medically underwritten groups would do so at standard rates in light of such risk-oriented testing results; 3 would deny the application.

When carrier tests reveal the possibility that children may have a serious, chronic condition or disease, 16 of 29 commercial insurers would accept the applicant with standard rates, but 6 would decline the applicant. Three commercial insurers would accept the individual applicant with an exclusion waiver (presumably for the specific condition revealed by carrier testing). Over half of commercial insurers that provide coverage to medically underwritten groups (22 of 37) would accept the applicant with standard rates, while 8 would decline coverage.

Ten of 25 BC/BS plans represented by the underwriter population would accept an individual applicant at standard rates even if carrier tests revealed that children might have a serious condition or disease; 3 would decline coverage. A waiting period would be used by six BC/BS plans for individual applicants. Nine of 21 BC/BS plans represented by a medical director survey would provide coverage at standard rates to medically underwritten groups with members who had carrier test results; 4 would require a waiting period.

Results of carrier testing would not affect insurability or rating for individual applicants at 7 of 18 BC/BS plans represented by a medical director survey, while 2 plans would require an exclusion waiver and 2 would require a waiting period. Similar proportions were found for medical directors at BC/BS plans (table 3-6).

Carrier test results would not cause any of the 11 HMOs that accept individual applicants to decline coverage; 6 would accept at standard rates and one HMO would accept the applicant with an exclusion waiver and charge a rated premium. Nine of the 20 HMOs that provide medically underwritten group coverage would do so at standard rates in light of carrier test results, and three would decline coverage.

If prenatal diagnosis reveals a fetus is affected with a serious, chronic condition or disease, 19 of 29 commercial insurers would decline an applicant. Six commercial insurers would accept the individual applicant at standard rates. It should be noted however, that if a pregnant woman is already covered, her baby is covered at birth (1), so the prenatal diagnosis would affect coverage only for pregnant women who are not currently covered. Twenty-four of 37 commercial insurers that cover

Table 3-7—Effect of Genetic Test Information on Insurability: Commercials and HMOs

For *individual policy applicants only*, how would the application normally be treated if a policy applicant was asymptomatic but had a family history of:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver but at rated premium	Declined	No response[a]
Hemophilia	*Commercials*	26 (90%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)
Tay-Sachs	*Commercials*	25 (86%)	1 (3%)	0 (0%)	0 (0%)	1 (3%)	2 (7%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)
Huntington disease	*Commercials*	17 (59%)	3 (10%)	0 (0%)	0 (0%)	6 (21%)	3 (10%)
	HMOs	9 (82%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	1 (9%)
Sickle cell anemia	*Commercials*	23 (79%)	1 (3%)	0 (0%)	1 (3%)	2 (7%)	2 (7%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)
Cystic fibrosis	*Commercials*	26 (90%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (91%)
Duchenne muscular dystrophy	*Commercials*	23 (79%)	2 (7%)	0 (0%)	0 (0%)	1 (3%)	3 (10%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)
ADA deficiency	*Commercials*	25 (86%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	3 (10%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)
Down syndrome	*Commercials*	27 (93%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	10 (91%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)

[a]Percentages may not add to 100 due to rounding.
SOURCE: Office of Technology Assessment, 1992.

medically underwritten groups would decline coverage, while 6 would accept at standard rates.

Underwriters at 14 of 25 BC/BS plans would decline coverage to individual applicants if prenatal diagnosis revealed the fetus had a serious condition or disease, 5 would accept the applicant at standard rates. Thirteen of 21 BC/BS plans represented by the underwriter population would decline a medically underwritten group application as a result of such a prenatal diagnosis. A similar distribution of medical directors would decline coverage due to prenatal test results (table 3-6).

Four of 11 HMOs that offer individual coverage would decline an applicant if prenatal test results revealed a fetus had a serious condition, and only 1 would accept the applicant at standard rates. Eight of 20 HMOs that cover medically underwritten groups would decline the application, while 4 HMOs would accept the application with standard rates.

Effect of Genetic Information on Insurability

How do health insurers treat applicants that are asymptomatic but have family histories of genetic conditions? OTA found that a family history of a genetic condition did not always mean the applicant would be declined. In fact, the majority of such applicants would be accepted at standard rates. The majority of commercial insurers accepted individual applicants at standard rates when a family history of a genetic condition was revealed (table 3-7). Applicants for commercial health insurance who had a family history of hemophilia, Tay-Sachs, sickle cell anemia, CF, ADA deficiency ("Bubble Boy disease"), and Down syndrome all would be accepted at standard rates more than 80 percent of the time. Fifty-nine percent of individual applicants for commercial insurance with a family history of Huntington disease and 79 percent with a history of Duchenne muscular dystrophy would be accepted at standard rates. The majority of HMOs accepted individual applicants at standard rates when they were asymptomatic, but had a family history of a genetic condition (table 3-7). The majority of underwriters and medical directors from BC/BS plans responding to the OTA survey accepted individual applicants at standard rates regardless of family history for genetic conditions (table 3-8).

CONGRESSIONAL OFFICE OF TECHNOLOGY ASSESSMENT

SURVEY OF HMOs' ATTITUDES AND PRACTICES REGARDING GENETIC TESTING FOR CYSTIC FIBROSIS

ATTN: MEDICAL DIRECTOR

Please Respond by July 19, 1991

The Congressional Office of Technology Assessment (OTA) is contacting health insurers and HMOs who offer individual coverage in a national survey of attitudes and practices regarding cystic fibrosis screening. This questionnaire has been directed to you as the person in your organization whose responsibilities include medical decisionmaking. We request your assistance in answering some questions about genetic testing and medical decisionmaking in your company. **If you are not the Medical Director, we would appreciate it if you would please forward the questionnaire to the appropriate person.**

For the purposes of this survey, OTA has adopted the following definitions:

> By *carrier testing*, we mean testing an unaffected individual to reveal the possibility that off-spring may have a serious chronic condition or disease (e.g., cystic fibrosis or sickle cell disease).
>
> By *genetic testing*, we mean testing applicants or policyholders for certain inherited characteristics either presymptomatically to reveal future serious chronic disease (e.g., for Huntington's disease) or for risk oriented purposes (e.g., predisposition to heart disease).

This is an important study that has been requested by the U.S. Congress, and is designed to represent the attitudes and practices of health insurers and HMOs. We need to know how insurers view the technologies of genetic testing in terms of their current and future applications in health insurance.

Please read each question and mark the space that most nearly corresponds to your answer. Please feel free to qualify your answers. Space has been provided at the end for comments and opinions that you feel are not adequately represented by the survey questions. The survey responses will be kept strictly anonymous as well as confidential.

PLEASE NOTE: This survey focuses on two HMO populations–(1) *Individuals*, non-conversion self-payers who seek HMO membership independently and without any association with an employer or membership group of any kind; and (2) *Medically underwritten groups*, i.e., those groups whose members must be medically underwritten.

****

Conversions should be excluded from your responses. In addition, we prefer that you exclude applicants for supplemental Medicare coverage from your responses. If because of reporting or other reasons, you must include Medicare policies, please check the box below:

[ ] YES, Medicare policies and statistics are included in our responses to this survey.

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us as any other opinions, concerns, or suggestions related to genetic testing and insurance that you feel our questions did not address. These comments will be strictly anonymous but may be incorporated in our report to Congress. Please write these comments below.

_____

_____

_____

_____

_____

_____

We have attached a peel-off identification number on the questionnaire. This is the only link between the companies who were sampled and the questionnaires returned. We would prefer that you leave the identification number on the questionnaire when you return it. Our staff will remove the label upon receipt, making the questionnaire entirely anonymous. Absolutely no linkage between companies and questionnaires will be retained. The label from the completed questionnaire is designed to eliminate your company from those that we will have to recontact.

However, if this temporary identification makes you uncomfortable, then peel off the label before returning the questionnaire. We appreciate your help and we want you to feel comfortable in participating in the survey.

_____

PEEL OFF LABEL WITH SAMPLE

IDENTIFICATION HERE

_____

PLEASE RETURN THE QUESTIONNAIRE IN THE POSTAGE PAID RETURN ENVELOPE SENT WITH THE QUESTIONNAIRE. IF THE ENVELOPE HAS BEEN LOST, THE RETURN ADDRESS IS:

Margaret Anderson
Biological Applications Program
Office of Technology Assessment
U.S. Congress
Washington, DC 20510-8025

Table 3-8—Effect of Genetic Information on Insurability: BC/BS plans

For *individual policy applicants only*, how would the application normally be treated if a policy applicant was asymptomatic but had a family history of:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with waiting period at standard rates	Accepted without exclusion waiver or waiting period/ rated premium	Accepted with exclusion waiver at rated premium	Accepted with waiting period at rated premium	Declined	No response[a]
Hemophilia	*BC/BS plans-U*[b]	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Tay-Sachs	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Huntington disease	*BC/BS plans-U*	15 (60%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	3 (12%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Sickle cell anemia	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Cystic fibrosis	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Duchenne muscular dystrophy	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
ADA deficiency	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Down syndrome	*BC/BS plans-U*	17 (68%)	1 (4%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (30%)	0 (0%)	0 (0%)	1 (7%)	1 (7%)	1 (7%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

Table 3-9—Coverage of a Family Member with Family History of Disease: Commercials and HMOs

For *individual policy applicants only*, how would the coverage of a family member (e.g., spouse or adopted child) be affected if the policy applicant was negative, but the family member was asymptomatic but had a family history of:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver but at rated premium	Declined	No response[a]
Hemophilia	*Commercials*	26 (90%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
Tay-Sachs	*Commercials*	25 (86%)	2 (7%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
Huntington disease	*Commercials*	18 (62%)	3 (10%)	0 (0%)	0 (0%)	5 (17%)	3 (10%)
	HMOs	7 (64%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	3 (27%)
Sickle cell anemia	*Commercials*	25 (86%)	1 (3%)	0 (0%)	1 (3%)	0 (0%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
Cystic fibrosis	*Commercials*	26 (90%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
Duchenne muscular dystrophy	*Commercials*	25 (86%)	1 (3%)	0 (0%)	0 (0%)	1 (3%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
ADA deficiency	*Commercials*	26 (90%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)
Down syndrome	*Commercials*	26 (90%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)	2 (7%)
	HMOs	8 (73%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (27%)

[a]Percentages may not add to 100 due to rounding.
SOURCE: Office of Technology Assessment, 1992.

How would coverage decisions be handled for a family member on an individual insurance policy when the applicant had a family member who was asymptomatic but had a family history of genetic conditions? Commercial insurers appear to handle applications the same whether it is a family member or the individual applying for the policy who has the family history of genetic disease (table 3-9): The majority of applications would be accepted at standard rates regardless of the specific genetic condition. Similar results were found for responding HMOs, as well as underwriters and medical directors from BC/BS plans (table 3-10).

CHAPTER 3 REFERENCES

1. Payne, J., Health Insurance Association of America, Inc., Washington, DC, personal communication, January 1992.
2. U.S. Congress, Office of Technology Assessment, *Medical Testing and Health Insurance*, OTA-H-384 (Washington, DC: U.S. Government Printing Office, August 1988).
3. U.S. Congress, Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA-BA-532 (Washington, DC: U.S. Government Printing Office, August 1992).

SECTION V: DEMOGRAPHICS

17. What is your job title?

    _____

18. Which of the following lines of insurance does your company underwrite?

    Health 1

    Disability 2

    Life 3

19. What percent of persons under health insurance policies issued by your company are in policies classified as:

    Self-insured Administration _____%

    Individual _____%

    Medically Underwritten Groups _____%

    Large Groups _____%

    TOTAL 100%

16. Please indicate whether you:

	Agree Strongly	Agree Somewhat	Disagree Somewhat	Disagree Strongly
a. It's fair for insurers to use genetic tests to identify individuals with increased risk of disease.	1	2	3	4
b. An insurer should have the option of determining how to use genetic information in determining risks.	1	2	3	4
c. Genetic conditions, such as cystic fibrosis or Huntington's disease, are pre-existing conditions.	1	2	3	4
d. Carrier status for genetic conditions, such as cystic fibrosis or Tay-Sachs, are pre-existing conditions.	1	2	3	4
e. Genetic information is no different than other types of medical information.	1	2	3	4
f. Prenatal diagnosis indicates the fetus is affected with cystic fibrosis; the couple decide to continue the pregnancy. The health insurance carrier, which paid for the tests, informs the couple they will have no financial responsibility for the cystic fibrosis-related costs for the child.	1	2	3	4
g. Through prior genetic testing, the husband is known to be a carrier for cystic fibrosis. Before having children, the wife seeks genetic testing for cystic fibrosis. The insurance company declines to pay for the testing, since there is no history of cystic fibrosis in her family.	1	2	3	4

Table 3-10—Coverage of a Family Member with a Family History of Disease: BC/BS plans

For *individual policy applicants only*, how would the coverage of a family member (e.g., spouse or adopted child) be affected if the policy applicant was negative, but the family member was asymptomatic but had a family history of:

	Respondent	Accepted with standard rates	Accepted with exclusion waiver at standard rates	Accepted with waiting period at standard rates	Accepted with exclusion waiver at rated premium	Accepted without exclusion waiver or waiting period/ rated premium	Accepted with waiting period at rated premium	Declined	No response[a]
Hemophilia	*BC/BS plans-U*[b]	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Tay-Sachs	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Huntington disease	*BC/BS plans-U*	15 (60%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	3 (12%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Sickle cell anemia	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Cystic fibrosis	*BS/BC plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Duchenne muscular dystrophy	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
ADA deficiency	*BC/BS plans-U*	16 (64%)	0 (0%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (13%)	1 (7%)
Down syndrome	*BC/BS plans-U*	17 (68%)	1 (4%)	6 (24%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
	BC/BS plans-M	9 (60%)	0 (0%)	3 (30%)	0 (0%)	0 (0%)	1 (7%)	1 (7%)	1 (7%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.

SOURCE: Office of Technology Assessment, 1992.

15. How likely do you think it is that your company will:

	Very Likely	Somewhat Likely	Somewhat Unlikely	Very Unlikely
In the next 5 years:				
a. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
b. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
c. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
d. Offer optional genetic testing and carrier testing	1	2	3	4
e. Use information derived from genetic tests for underwriting	1	2	3	4
f. Alter claims payment practices as new genetic tests come on line	1	2	3	4
In the next 10 years:				
g. Require genetic testing for applicants with family histories of serious conditions	1	2	3	4
h. Require carrier tests for applicants at risk of transmitting serious genetic diseases to offspring	1	2	3	4
i. Require genetic testing for applicants with no known risk to genetic disease	1	2	3	4
j. Offer optional genetic testing and carrier testing	1	2	3	4
k. Use information derived from genetic tests for underwriting	1	2	3	4
l. Alter claims payment practices as new genetic tests come on line	1	2	3	4

11. How would individual policies and medically underwritten policies normally be affected by the following findings:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with exclusion waiver at rated premium;
4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies	Medically Underwritten Groups
a. Presymptomatic testing reveals the likelihood of a serious, chronic future disease (e.g., for Huntington's disease)	_____	_____
b. Risk oriented testing reveals that an individual carries markers associated with a serious, chronic future disease (e.g., predisposition to heart disease)	_____	_____
c. Carrier testing reveals the possibility that off-spring may have a serious, chronic condition or disease	_____	_____
d. Prenatal diagnosis reveals fetus affected with a serious, chronic condition or disease	_____	_____

SECTION IV: GENERAL ATTITUDES

12. To your knowledge, has your company ever reimbursed for carrier testing for cystic fibrosis?
Yes _____(1)
No _____(2)

13. Has your company ever conducted an economic analysis of the costs and benefits of:

	Yes	No
a. Carrier testing as part of applicant screening	1	2
b. Genetic counseling of carriers who are covered	1	2
c. Carrier testing as part of prenatal coverage	1	2
d. Genetic testing as part of applicant screening	1	2

14. Under what conditions would a negative financial impact be likely to occur for your company: (CHECK ALL THAT APPLY)

a. Widespread availability of genetic tests to the medical/provider community _____(1)
b. Widespread availability of genetic tests with constraints on insurers' access to the results _____(2)
c. Adverse claims or underwriting results from antiselection _____(3)
d. Other (SPECIFY) _____ (4)

Chapter 4
Coverage and Reimbursement

Will health insurers pay for voluntary screening and followup counseling? And will health insurance companies authorize payment for prenatal screening or testing of newborn children? Answers to these questions carry significant cost implications. They also will likely affect the degree to which carrier screening for cystic fibrosis (CF) becomes commonplace, since many people will be unwilling to pay out-of-pocket the costs of the assays (1). From the perspective of the commercial laboratory that provides genetic tests to medical providers and patients, the issue of reimbursement is crucial to business—current and future.

OTA asked health insurers covering individuals and medically underwritten groups about their coverage of certain genetic tests and services. Are they covered "at patient request," where there is no family history (i.e., screening)? Are they covered "only if medically indicated," where a family history exists? Or, are they "not covered"?

REIMBURSEMENT FOR GENETIC TESTS AND SERVICES

No commercial company reimburses for CF carrier tests for screening purposes. The survey also found that carrier tests for CF—as well as for Tay-Sachs and sickle cell—are not covered for any reason by 12 of 29 commercial insurers that offer individual coverage. Twelve respondents (41 percent) cover CF carrier assays if medically indicated. With respect to prenatal tests for CF, about 41 percent (12 respondents) that write individual policies reimburse for such tests when medically indicated.

For the 37 commercial companies offering medically underwritten group policies, carrier tests for CF (and, again, for sickle cell or Tay-Sachs) are not covered by any company when done solely at patient request. CF mutation analysis is covered by 24 of 37 companies if medically indicated. Ten companies offering medically underwritten group coverage do not cover any of the carrier or prenatal tests asked about in OTA's survey. Sixty-two percent of companies (23 respondents) that offer medically underwritten group policies cover prenatal tests for CF when medically indicated (table 4-1).

Two of 25 Blue Cross and Blue Shield (BC/BS) plans offering individual coverage would reimburse CF carrier screening at patient request. Sixteen of these BC/BS plans (64 percent) cover them if they are medically indicated and seven do not cover them. Three of 25 BC/BS plans cover prenatal testing for CF at a patient's request, seven if medically indicated, and three not at all. Of 21 BC/BS plans offering coverage to medically underwritten groups, CF carrier screening is covered at patient request by only 2 companies (10 percent), if medically indicated by 11 companies (52 percent), and not at all by 8 companies (38 percent) (table 4-1). Data on coverage for CF prenatal tests by BC/BS plans that cover medically underwritten groups are also presented in table 4-1.

For the 11 health maintenance organizations (HMOs) that offer health insurance to individuals, 1 HMO (9 percent) covers CF carrier tests at patient request and 7 HMOs (64 percent) reimburse for them if medically indicated. For the 20 HMOs that offer medically underwritten group contracts, 1 HMO (5 percent) covers CF carrier tests at patient request, 13 respondents (45 percent) reimburse for them if medically indicated, and 2 (10 percent) do not cover them at all. Table 4-1 presents these results as well as how HMOs cover prenatal tests for CF.

From OTA's survey results, it is evident that carrier and prenatal tests often are not covered under individual and medically underwritten group policies unless they are medically necessary—i.e., unless a family history exists. Such policies can have a significant impact on both the rate at which CF carrier screening becomes routine and the ultimate utilization of CF mutation analysis.

OTA found that genetic counseling was not covered by 18 commercial companies offering individual coverage and 17 offering medically underwritten group coverage. Six commercial insurance companies offering individual policies and 16 that medically underwrite groups cover genetic counseling only if it is medically indicated. Two commercial companies offering each type of cover-

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Table 4-1—Reimbursement for Genetic Tests and Genetic Counseling

Question	Respondent	At patient request	Medically indicated only	Not covered	No response[a]
Do your standard individual policies and medically underwritten policies provide coverage for:					
Individual policies					
Carrier tests for CF?	*Commercials*	0 (0%)	12 (41%)	12 (41%)	5 (18%)
	HMOs	2 (18%)	7 (64%)	0 (0%)	2 (18%)
	BC/BS plans-U[b]	2 (8%)	16 (64%)	7 (28%)	0 (0%)
	BC/BS plans-M	0 (0%)	11 (61%)	5 (28%)	2 (11%)
Carrier tests for Tay-Sachs?	*Commercials*	0 (0%)	12 (41%)	12 (41%)	5 (18%)
	HMOs	2 (18%)	7 (64%)	0 (0%)	2 (18%)
	BC/BS plans-U	2 (8%)	16 (64%)	7 (28%)	0 (0%)
	BC/BS plans-M	0 (0%)	11 (61%)	5 (28%)	2 (11%)
Carrier tests for sickle cell trait?	*Commercials*	0 (0%)	12 (41%)	12 (41%)	5 (18%)
	HMOs	3 (27%)	6 (55%)	0 (0%)	2 (18%)
	BC/BS plans-U	2 (8%)	16 (64%)	7 (28%)	0 (0%)
	BC/BS plans-M	0 (0%)	11 (61%)	5 (28%)	2 (11%)
Prenatal tests for CF?	*Commercials*	0 (0%)	12 (41%)	14 (48%)	3 (10%)
	HMOs	1 (9%)	7 (64%)	1 (9%)	2 (18%)
	BC/BS plans-U	3 (12%)	19 (76%)	3 (12%)	0 (0%)
	BC/BS plans-M	1 (5%)	13 (73%)	2 (11%)	2 (11%)
Prenatal tests for Tay-Sachs?	*Commercials*	0 (0%)	11 (38%)	15 (52%)	3 (10%)
	HMOs	2 (18%)	8 (73%)	0 (0%)	1 (9%)
	BC/BS plans-U	3 (12%)	19 (76%)	3 (12%)	0 (0%)
	BC/BS plans-M	1 (5%)	13 (73%)	2 (11%)	2 (11%)
Prenatal tests for sickle cell anemia?	*Commercials*	0 (0%)	11 (38%)	15 (52%)	3 (10%)
	HMOs	1 (9%)	8 (73%)	0 (0%)	2 (18%)
	BC/BS plans-U	3 (12%)	19 (76%)	3 (12%)	0 (0%)
	BC/BS plans-M	1 (5%)	13 (73%)	2 (11%)	2 (11%)
Prenatal tests for Down syndrome?	*Commercials*	1 (4%)	10 (34%)	15 (52%)	3 (10%)
	HMOs	1 (9%)	9 (82%)	0 (0%)	1 (9%)
	BC/BS plans-U	3 (12%)	19 (76%)	3 (12%)	0 (0%)
	BC/BS plans-M	1 (5%)	13 (73%)	2 (11%)	2 (11%)
Genetic counseling?	*Commercials*	2 (7%)	6 (21%)	18 (62%)	3 (10%)
	HMOs	1 (9%)	6 (56%)	1 (9%)	3 (9%)
	BC/BS plans-U	1 (4%)	9 (36%)	13 (52%)	2 (8%)
	BC/BS plans-M	0 (0%)	8 (44%)	8 (44%)	2 (12%)

age (individual and medically underwritten) reimburse for genetic counseling performed at patient request (table 4-1). Similar results for BC/BS plans and HMOs are also presented in table 4-1.

COVERAGE FOR CYSTIC FIBROSIS CARRIER TESTS

In contrast to questions that inquire about what the respondent's company policy would be, respondents were also asked whether they were aware if their organization had ever actually reimbursed for CF carrier tests. Regardless of the type of respondent, CF carrier testing has been reimbursed at roughly the same frequency for all (table 4-2). For commercial insurers, 11 of the 51 respondents (22 percent) said their companies had reimbursed for such tests, and 35 respondents (69 percent) indicated their companies had not. Of the 23 HMOs that responded to the OTA survey, 7 (30 percent) had reimbursed for CF carrier testing, and 14 (61 percent) had not. Of the 29 BC/BS plans represented by the underwriter survey, 7 (24 percent) had reimbursed for CF carrier testing, and 18 (62 percent) had not. Five of the 18 (28 percent) BC/BS plans represented by a medical director survey had reimbursed for CF carrier testing, and 12 (67 percent) had not.

9. For individual policy applicants only, how would the coverage of a family member (e.g., spouse or adopted child) be affected if the policy applicant was negative, but the family member was asymptomatic but had a family history of:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates; 3 = Accepted with exclusion waiver at rated premium; 4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

10. Do your standard individual policies and medically underwritten policies provide coverage for:

1 = At patient request; 2 = Only if medically indicated; 3 = Not covered

	Individual Policies	Medically Underwritten Groups
Carrier tests for:		
a. Cystic fibrosis	_____	_____
b. Tay-Sachs	_____	_____
c. Sickle cell trait	_____	_____
Prenatal tests for:		
d. Cystic fibrosis	_____	_____
e. Tay-Sachs	_____	_____
f. Sickle cell anemia	_____	_____
g. Down Syndrome	_____	_____
h. Other (SPECIFY)	_____	_____
Genetic counseling	_____	_____

SECTION III: GENETIC CONDITIONS

7. Does your company specifically inquire, for each category of coverage, about the following conditions in the application for health insurance in the personal history, family history, or neither:

1= Personal history only; 2 = Family history; 3 = Neither

	Individual Policies	Medically Underwritten Groups
a. Hemophilia	_____	_____
b. Tay-Sachs	_____	_____
c. Huntington's disease	_____	_____
d. Sickle cell anemia	_____	_____
e. Cystic fibrosis	_____	_____
f. Any other genetic disease (SPECIFY)	_____	_____

8. For individual policy applicants only, how would the application normally be treated if a policy applicant was asymptomatic but had a family history of:

1= Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates;
3 = Accepted with exclusion waiver at rated premium;
4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies
a. Hemophilia	_____
b. Tay-Sachs	_____
c. Huntington's disease	_____
d. Sickle cell anemia	_____
e. Cystic fibrosis	_____
f. Duchenne muscular dystrophy	_____
g. ADA deficiency ("Bubble Boy disease")	_____
h. Down Syndrome	_____

Table 4-1—Reimbursement for Genetic Tests and Genetic Counseling—Continued

Question	Respondent	At patient request	Medically indicated only	Not covered	No response[a]
Medically underwritten groups					
Carrier tests for CF?	*Commercials*	0 (0%)	24 (65%)	10 (27%)	3 (8%)
	HMOs	1 (5%)	13 (65%)	2 (10%)	4 (20%)
	BC/BS plans-U	2 (10%)	11 (52%)	8 (38%)	0 (0%)
	BC/BS plans-M	0 (0%)	9 (60%)	4 (27%)	2 (13%)
Carrier tests for Tay-Sachs?	*Commercials*	0 (0%)	22 (59%)	11 (30%)	4 (11%)
	HMOs	1 (10%)	13 (60%)	2 (10%)	7 (20%)
	BC/BS plans-U	2 (10%)	11 (52%)	8 (38%)	0 (0%)
	BC/BS plans-M	0 (0%)	9 (60%)	4 (27%)	2 (13%)
Carrier tests for sickle cell trait?	*Commercials*	0 (0%)	23 (62%)	10 (27%)	4 (11%)
	HMOs	2 (10%)	12 (60%)	2 (10%)	4 (20%)
	BC/BS plans-U	2 (10%)	11 (52%)	8 (38%)	0 (0%)
	BC/BS plans-M	0 (0%)	9 (60%)	4 (27%)	2 (13%)
Prenatal tests for CF?	*Commercials*	1 (3%)	23 (62%)	10 (27%)	3 (8%)
	HMOs	2 (10%)	14 (70%)	0 (0%)	4 (20%)
	BC/BS plans-U	3 (14%)	14 (67%)	4 (19%)	0 (0%)
	BC/BS plans-M	1 (7%)	11 (73%)	1 (7%)	2 (13%)
Prenatal tests for Tay-Sachs?	*Commercials*	1 (3%)	24 (65%)	10 (27%)	2 (5%)
	HMOs	3 (15%)	14 (70%)	0 (0%)	3 (15%)
	BC/BS plans-U	3 (14%)	14 (67%)	4 (19%)	0 (0%)
	BC/BS plans-M	1 (7%)	11 (73%)	1 (7%)	2 (13%)
Prenatal tests for sickle cell anemia?	*Commercials*	1 (3%)	24 (65%)	10 (27%)	2 (5%)
	HMOs	2 (10%)	14 (70%)	0 (0%)	4 (20%)
	BC/BS plans-U	3 (14%)	14 (67%)	4 (19%)	0 (0%)
	BC/BS plans-M	1 (7%)	11 (73%)	1 (7%)	2 (13%)
Prenatal tests for Down syndrome?	*Commercials*	2 (5%)	23 (62%)	10 (27%)	2 (5%)
	HMOs	2 (10%)	15 (75%)	0 (0%)	3 (15%)
	BC/BS plans-U	3 (14%)	14 (67%)	4 (19%)	0 (0%)
	BC/BS plans-M	1 (7%)	11 (73%)	1 (7%)	2 (13%)
Genetic counseling	*Commercials*	2 (5%)	16 (43%)	17 (46%)	2 (5%)
	HMOs	2 (10%)	12 (60%)	1 (5%)	5 (25%)
	BC/BS plans-U	1 (5%)	7 (33%)	12 (57%)	1 (5%)
	BC/BS plans-M	0 (0%)	6 (40%)	7 (47%)	2 (13%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

ECONOMIC ANALYSIS OF GENETIC TESTS

To determine whether insurance companies have looked into the economic implications of various genetic tests, OTA asked if companies had ever conducted an economic analysis of the costs and benefits of various testing schemes. OTA found that no commercial insurer had conducted an economic analysis of the costs and benefits of carrier or other genetic tests as part of applicant screening. In addition, no commercial company had conducted an economic analysis of the costs and benefits of genetic counseling of carriers who are covered. One commercial company reported it had done an analysis of the costs and benefits of carrier tests as part of prenatal coverage, but 48 of 51 companies had not (table 4-3).

Survey respondents from HMOs had not conducted an economic analysis of the costs and benefits of carrier testing for either applicant screening or prenatal coverage. No economic analysis had been conducted by HMOs on genetic testing for applicant screening. One company conducted an economic analysis of the costs and benefits of genetic counseling of carriers who are covered.

Similar results were found for BC/BS plans. One of the 29 BC/BS plans represented by an underwriter

Table 4-2—Coverage for Cystic Fibrosis Carrier Tests

Respondent	Yes	No	No response[a]
Commercials	11 (22%)	35 (69%)	5 (9%)
HMOs	7 (30%)	14 (61%)	2 (9%)
BC/BS plans-U[b]	7 (24%)	18 (62%)	4 (14%)
BC/BS plans-M	5 (28%)	12 (67%)	1 (5%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

survey had conducted an economic analysis of the costs and benefits of genetic counseling of carriers who are covered, and 1 had conducted an economic analysis of carrier testing as part of prenatal coverage. None of the BC/BS plans represented by the underwriter survey had conducted an economic analysis of carrier or genetic testing as a part of applicant screening.

One of the 18 BC/BS plans represented by the medical director survey had conducted an economic analysis of carrier testing as part of prenatal coverage. Otherwise, none of the medical directors at the responding BC/BS plans had conducted an economic analysis of carrier or genetic testing as part of applicant screening, or of genetic counseling of carriers who are covered.

PERSPECTIVES ON FUTURE REIMBURSEMENT FOR GENETIC TESTS

As new genetic tests come on line, will insurers alter their claims payment practices? When asked if they would alter claims payment practices in the next 5 years, nearly half of commercial insurers (23 of 51; 45 percent) considered it "very unlikely," while one quarter (12; 24 percent) found it "somewhat likely"; only two companies thought it was likely (table 4-4). When commercial insurers were asked to project ahead a decade, 23 of 51 companies responded that it would be very or somewhat likely that their company would alter claims payment practices as new genetic tests came on line; 28 companies thought it would be somewhat or very unlikely.

Underwriters from 10 BC/BS plans responded it was "somewhat likely" that claims payment practices would be altered as new genetic tests came on line, 9 thought it "somewhat unlikely" and 7 thought it was "very unlikely." More BC/BS underwriters thought it was "somewhat likely" (11 of 29) in 10 years. Six BC/BS plans represented by an underwriter survey thought it was "very likely" and seven thought it "very unlikely."

Table 4-3—Economic Analyses of Genetic Tests and Genetic Counseling by Insurers

Question	Respondent	Yes	No	No response[a]
Has your company ever conducted an economic analysis of:				
Carrier testing as part of applicant screening?	*Commercials*	0 (0%)	50 (98%)	1 (2%)
	HMOs	0 (0%)	20 (87%)	3 (13%)
	BC/BS plans-U[b]	0 (0%)	28 (94%)	1 (3%)
	BC/BS plans-M	0 (0%)	16 (89%)	2 (11%)
Carrier testing as part of prenatal coverage?	*Commercials*	1 (2%)	48 (94%)	2 (4%)
	HMOs	0 (10%)	20 (87%)	3 (13%)
	BC/BS plans-U	1 (13%)	27 (94%)	1 (13%)
	BC/BS plans-M	1 (6%)	15 (83%)	2 (11%)
Genetic testing as part of applicant screening?	*Commercials*	0 (0%)	49 (96%)	2 (4%)
	HMOs	0 (0%)	20 (87%)	3 (13%)
	BC/BS plans-U	0 (0%)	28 (97%)	1 (3%)
	BC/BS plans-M	0 (0%)	16 (89%)	2 (11%)
Genetic counseling of carriers who are covered?	*Commercials*	0 (0%)	49 (96%)	2 (4%)
	HMOs	1 (4%)	19 (83%)	3 (13%)
	BC/BS plans-U	1 (3%)	27 (94%)	1 (3%)
	BC/BS plans-M	0 (0%)	16 (89%)	2 (11%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

5. For each category of coverage, please indicate the importance of each of the following factors in determining insurability (not in rating):

1 = Very important; 2 = Important; 3 = Unimportant; 4 = Never used

	Individual Policies	Medically Underwritten Groups
a. Age	_____	_____
b. Occupation	_____	_____
c. Smoking status	_____	_____
d. Lifestyle	_____	_____
e. Sex	_____	_____
f. Financial/credit status	_____	_____
g. Personal medical history of significant conditions	_____	_____
h. Family medical history of significant conditions	_____	_____
i. Genetic predisposition to significant conditions	_____	_____
j. Carrier risk for genetic diseases	_____	_____

6. How would you normally treat either an individual policy applicant or medically underwritten groups that disclosed the following conditions in an examination(s) or application:

1 = Accepted with standard rates; 2 = Accepted with exclusion waiver at standard rates; 3 = Accepted with exclusion waiver at rated premium; 4 = Accepted without exclusion waiver but at rated premium; 5 = Declined

	Individual Policies	Medically Underwritten Groups
a. Hypertension	_____	_____
b. Diabetes mellitus	_____	_____
c. Cerebrovascular disease	_____	_____
d. Hemophilia	_____	_____
e. Cystic fibrosis	_____	_____
f. Sickle cell anemia	_____	_____

SECTION II: UNDERWRITING PRACTICES

4. For each category of coverage, please estimate the proportion of all health insurance applicants from whom you require:

	Individual Policies	Medically Underwritten Groups
a. A personal health history	_____%	_____%
b. A family health history	_____%	_____%

IF A FAMILY HISTORY IS REQUIRED, ON WHOM WOULD INFORMATION BE REQUESTED. CHECK ALL THAT APPLY.

[ ] Spouse (1)
[ ] Parents (2)
[ ] Grandparents (3)
[ ] Siblings (4)
[ ] Children (5)
[ ] Other (SPECIFY) _____ (6)

c. An attending physician statement (APS)	_____%	_____%

IF AN APS IS REQUIRED FOR ANY INDIVIDUALS, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)

d. Physical exam:	_____%	_____%

IF AN EXAM IS EVER REQUIRED, WHICH OF THE FOLLOWING WOULD TRIGGER THE REQUIREMENT. CHECK ALL THAT APPLY.

[ ] Any significant diagnosis or symptoms reported on application (1)
[ ] Selected diagnoses or symptoms reported on application (2)
[ ] Any significant conditions reported in family history (3)
[ ] Selected conditions reported in family history (4)
[ ] M.I.B. report (5)
[ ] Any significant diagnosis or symptoms identified in APS (6)

e. Blood or urine screens:	_____%	_____%

Medical directors from 4 of 18 BC/BS plans responded that it was "somewhat likely" that claims payment practices would be altered as new genetic tests came on line. However, nine medical directors from BC/BS plans thought it was "somewhat unlikely" that payment practices would be altered. In 10 years, seven underwriters from BC/BS plans thought it was "somewhat likely" and six thought it was "somewhat unlikely" (table 4-4).

Seven of 23 HMOs thought it was "very likely" or "somewhat likely" that they would alter their claims payment practices as new genetic tests came on line, nine HMOs thought it would be "very unlikely" and five responded it would be "somewhat unlikely." In 10 years, only two HMOs thought it would be "very likely" they would alter claims payment practices, five HMOs responded it would be "somewhat likely," eight thought it would be "somewhat unlikely" and five thought it would be "very unlikely."

CHAPTER 4 REFERENCES

1. U.S. Congress, Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA-BA-532 (Washington, DC: U.S. Government Printing Office, August 1992).
2. U.S. Congress, Office of Technology Assessment, *Genetic Counseling and Cystic Fibrosis Carrier Screening—Results of a Survey*, OTA-BP-BA-97 (Washington, DC: U.S. Government Printing Office, September 1992).

Table 4-4—Projected Reimbursement Practices by Insurers in 5 and 10 Years

Question	Respondent	Very likely	Somewhat likely	Somewhat unlikely	Very unlikely	No response[a]
How likely do you think it is that your company/HMO will in the next 5 years:						
Alter claims payment practices as new genetic tests come on line	*Commercials*	7 (14%)	12 (24%)	16 (31%)	16 (31%)	0 (0%)
	HMOs	1 (4%)	5 (22%)	9 (39%)	6 (26%)	2 (9%)
	BC/BS plans-U[b]	1 (5%)	10 (34%)	9 (31%)	7 (24%)	2 (6%)
	BC/BS plans-M	1 (6%)	4 (22%)	9 (50%)	2 (11%)	2 (11%)
In the next 10 years:						
Alter claims payment practices as new genetic tests come on line	*Commercials*	7 (14%)	12 (24%)	16 (31%)	16 (31%)	0 (0%)
	HMOs	1 (4%)	5 (22%)	9 (26%)	6 (26%)	2 (9%)
	BC/BS plans-U	6 (22%)	11 (38%)	3 (10%)	7 (24%)	2 (6%)
	BC/BS plans-M	1 (6%)	7 (39%)	6 (33%)	2 (11%)	2 (11%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

Do you offer coverage for either individuals or medically underwritten groups?

Yes _____ (1)
No _____ (2)

IF YOU ARE NOT OFFERING EITHER OF THESE TYPES OF COVERAGE, THIS COMPLETES YOUR SURVEY. THANK YOU VERY MUCH. PLEASE RETURN IT IN THE PRE-ADDRESSED POST-PAID ENVELOPE.

SECTION I: INDIVIDUAL AND GROUP STATISTICS

	Individual Policies	Medically Underwritten Groups
1. What is the approximate number of persons that you currently insure through:	_____	_____
2. What is the approximate number of applications received by your company per year for coverage under:	_____	_____
3. What portion of those applications are:		
a. Accepted at standard rates	_____%	_____%
b. Covered with an exclusion waiver, but standard premium	_____%	_____%
c. Covered with a rated premium, but not exclusion waiver	_____%	_____%
d. Covered with an exclusion waiver and a rated premium	_____%	_____%
e. Declined by your company	_____%	_____%
f. Other (SPECIFY)	_____%	_____%
_____	_____%	_____%
_____	_____%	_____%
TOTAL	100%	100%

CONGRESSIONAL OFFICE OF TECHNOLOGY ASSESSMENT

SURVEY OF HEALTH INSURERS' ATTITUDES AND PRACTICES REGARDING GENETIC TESTING FOR CYSTIC FIBROSIS

ATTN: MEDICAL DIRECTOR

Please Respond by July 15, 1991

The Congressional Office of Technology Assessment (OTA) is contacting health insurers who offer individual coverage in a national survey of attitudes and practices regarding cystic fibrosis screening. This questionnaire has been directed to you as the person in your organization whose responsibilities include medical decisionmaking. We request your assistance in answering some questions about genetic testing and medical decisionmaking in your company. **If you are not the Medical Director, we would appreciate it if you would please forward the questionnaire to the appropriate person.**

For the purposes of this survey, OTA has adopted the following definitions:

> By *carrier testing*, we mean testing an unaffected individual to reveal the possibility that off-spring may have a serious chronic condition or disease (e.g., cystic fibrosis or sickle cell disease).
>
> By *genetic testing*, we mean testing applicants or policyholders for certain inherited characteristics either presymptomatically to reveal future serious chronic disease (e.g., for Huntington's disease) or for risk oriented purposes (e.g., predisposition to heart disease).

This is an important study that has been requested by the U.S. Congress, and is designed to represent the attitudes and practices of health insurers. We need to know how insurers view the technologies of genetic testing in terms of their current and future applications in health insurance.

Please read each question and mark the space that most nearly corresponds to your answer. Please feel free to qualify your answers. Space has been provided at the end for comments and opinions that you feel are not adequately represented by the survey questions. The survey responses will be kept strictly anonymous as well as confidential.

PLEASE NOTE: This survey focuses on two health insurance populations—(1) *Individuals* who seek insurance independently and without any association with an employer or membership group of any kind; and (2) *Medically underwritten groups*, i.e., those groups whose members must be medically underwritten.

****

Conversions should be excluded from your responses. In addition, we prefer that you exclude Medigap insurance from your responses. If because of reporting or other reasons, you must include Medigap policies, please check the box below:

[ ] YES, Medigap policies and statistics are included in our responses to this survey.

Chapter 5
General Attitudes Toward Genetic Tests and Information

Besides current or anticipated reimbursement practices for genetic tests, OTA also asked several questions to gauge health insurers' general attitudes toward genetic tests and genetic information. This chapter reports results from these questions. Additionally, general attitudes of respondents can be gleaned from the verbatim comments offered by some respondents, presented in appendix B.

IMPACT OF GENETIC TESTS ON BUSINESS PRACTICES

As genetic tests become widely available, one important consideration for insurers will be the financial impact such tests might have on their business. OTA asked survey participants about whether they believed certain scenarios involving the availability of genetic tests would lead to a negative financial impact for their company.

The majority of commercial insurers (30 of 51; 59 percent) said a negative financial impact would not occur if genetic tests were widely available to the medical community. A majority of chief underwriters at Blue Cross and Blue Shield (BC/BS) plans (20 of 29; 69 percent) responded similarly, as did 6 of 18 medical directors at BC/BS plans (33 percent). Respondents from health maintenance organizations (HMOs), however, were equally divided in their opinions of whether widespread availability of genetic tests to the medical provider community would result in a negative financial impact for their HMOs (table 5-1).

In contrast, table 5-1 shows that a clear majority of respondents from commercial insurers, BC/BS plans, and HMOs thought a negative financial impact would likely occur if genetic tests were widely available, but had constraints on insurers' access to the results. Similarly, a majority of survey respondents from all populations clearly thought a negative financial impact would result for their companies if the availability of genetic tests resulted in adverse claims or underwriting results due to adverse selection (table 5-1). A handful of respondents among the total survey population also wrote in that a negative financial impact also would be likely if genetic tests became mandated benefits for which they would not ordinarily have reimbursed.

ATTITUDES TOWARD GENETIC INFORMATION

As discussed in chapter 3, health insurers that offer individual or medically underwritten group policies clearly weigh several factors in determining both insurability and rating. Included among the factors that respondents considered "very impor-

Table 5-1—Impact of Genetic Tests on Insurers

Question	Respondent	Yes	No	No response[a]
Under what conditions would a negative financial impact be likely to occur for your company (check all that apply):				
Widespread availability of genetic tests to the medical provider community.	*Commercials*	19 (37%)	30 (59%)	2 (4%)
	HMOs	10 (44%)	10 (44%)	3 (13%)
	BC/BS plans-U[b]	7 (24%)	20 (69%)	2 (7%)
	BC/BS plans-M	6 (33%)	11 (61%)	1 (6%)
Widespread availability of genetic tests with constraints on insurers' access to results.	*Commercials*	34 (67%)	15 (29%)	2 (4%)
	HMOs	16 (70%)	4 (17%)	3 (13%)
	BC/BS plans-U	17 (59%)	10 (35%)	2 (7%)
	BC/BS plans-M	11 (61%)	6 (33%)	1 (6%)
Adverse claims or underwriting results from antiselection.	*Commercials*	47 (92%)	2 (4%)	2 (4%)
	HMOs	18 (78%)	2 (9%)	3 (13%)
	BC/BS plans-U	27 (93%)	0 (0%)	2 (7%)
	BC/BS plans-M	16 (89%)	1 (6%)	1 (6%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.

SOURCE: Office of Technology Assessment, 1992.

Table 5-2—Genetic Information as Medical Information or Preexisting Conditions

Question	Respondent	Agree strongly	Agree somewhat	Disagree somewhat	Disagree strongly	No response[a]
Genetic information is no different than other types of medical information	*Commercials*	17 (33%)	10 (20%)	12 (23%)	10 (20%)	2 (4%)
	HMOs	7 (30%)	6 (26%)	5 (22%)	3 (13%)	2 (9%)
	BC/BS plans-U[b]	6 (21%)	14 (48%)	6 (21%)	1 (3%)	2 (7%)
	BC/BS plans-M	5 (28%)	5 (28%)	4 (22%)	2 (11%)	2 (11%)
Genetic conditions such as cystic fibrosis or Huntington disease are preexisting conditions	*Commercials*	14 (28%)	9 (18%)	17 (33%)	8 (16%)	3 (6%)
	HMOs	12 (52%)	8 (35%)	1 (4%)	0 (0%)	2 (9%)
	BC/BS plans-U	8 (28%)	7 (24%)	8 (28%)	5 (17%)	1 (3%)
	BC/BS plans-M	10 (56%)	2 (11%)	3 (17%)	1 (6%)	2 (11%)
Carrier status for genetic conditions such as cystic fibrosis or Tay-Sachs are preexisting conditions	*Commercials*	8 (16%)	12 (24%)	16 (31%)	13 (25%)	2 (4%)
	HMOs	5 (22%)	12 (52%)	0 (0%)	4 (17%)	2 (9%)
	BC/BS plans-M	4 (14%)	6 (21%)	7 (24%)	9 (31%)	3 (10%)
	BC/BS plans-U	7 (39%)	3 (17%)	2 (11%)	4 (22%)	2 (11%)

[a] Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the chief underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

Table 5-3—General Attitudes of Insurers Toward Genetic Information and Genetic Tests

Statement	Respondent	Agree strongly	Agree somewhat	Disagree somewhat	Disagree strongly	No response[a]
An insurer should have the option of determining how to use genetic information in determining risks.	*Commercials*	19 (37%)	19 (37%)	9 (22%)	3 (6%)	1 (2%)
	HMOs	2 (9%)	15 (65%)	4 (17%)	0 (0%)	2 (9%)
	BC/BS plans-U[b]	9 (31%)	15 (52%)	4 (14%)	0 (0%)	1 (3%)
	BC/BS plans-M	8 (44%)	6 (33%)	0 (0%)	3 (17%)	1 (6%)
It's fair for insurers to use genetic tests to identify individuals with increased risk of genetic disease.	*Commercials*	11 (22%)	23 (45%)	11 (22%)	4 (8%)	2 (4%)
	HMOs	3 (13%)	14 (61%)	2 (9%)	2 (9%)	2 (9%)
	BC/BS plans-U	4 (14%)	17 (59%)	4 (14%)	2 (7%)	2 (7%)
	BC/BS plans-M	0 (0%)	11 (61%)	2 (11%)	4 (22%)	1 (6%)

[a]Percentages may not add to 100 due to rounding.
[b]BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

tant" or "important," were personal medical history of significant conditions, family medical history of significant conditions, and carrier risk for genetic disease—although the importance respondents placed on any single factor varied. Many, in fact, considered certain factors unimportant or never used them in decisionmaking.

Overall, how do health insurers view genetic information, regardless of the source (i.e., a positive test or elevated risk for carrier status or disease because of a known family history)? Results from OTA's survey found a majority of respondents, both as an aggregate population and as individual subsets, agreed with the statement, "Genetic information is no different than other types of medical information" (table 5-2). Underscoring this finding are results that the majority of health insurers, collectively, agree "strongly" or "somewhat" that genetic conditions such as cystic fibrosis (CF) or Huntington disease are preexisting conditions, but that carrier status for diseases such as Tay-Sachs or CF is not a preexisting condition (table 5-2).

Third-party payors already use genetic information in making decisions about individual policies or medically underwritten groups, and health insurers clearly believe it is fair for them to have access to information known to the applicant. Survey respondents were asked whether "an insurer should have the option of determining how to use genetic information in determining risks." A majority of all respondents agreed strongly or somewhat with this statement (table 5-3).

OTA also sought the reactions of commercial insurers, HMOs, and BC/BS plans to a hypothetical situation based on a real life case. Respondents were asked to indicate whether they "agree" strongly,"

Appendix C
Survey Instruments

As part of the 1992 assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA surveyed commercial health insurers that offer policies to individuals or medically underwritten groups, Blue Cross and Blue Shield plans, and selected health maintenance organizations. The instruments were tailored slightly for each population, but the substance for all three questionnaires was unchanged. The following are reproductions of the survey questionnaires. For Blue Cross and Blue Shield plans, identical surveys were sent separately to chief underwriters and medical directors, but only the former is reproduced.

our State-mandated requirement to offer some type of coverage to all applicants.

2. Not all questions were completed since we currently do not require testing of any kind or family history information in our medical underwriting process. We do not specifically inquire on the application for coverage about genetic conditions listed in the survey. However, applicants with these known conditions are not considered standard risks and would be declined coverage with our company. Payment for some genetic testing is covered under some of our health insurance policies depending on the diagnosis and if the services are determined to be medically necessary.
3. The responses are a result of our "Corporate Medical Policy Committees" input. Our corporation is nonprofit and is founded on a social/community mission and responsibility. Therefore, we accept all applicants. Due to fiscal difficulties, we are *considering implementing* a waiting period of one year even in our group business. We will still accept all but apply the waiting period.
4. Our position on treatment of genetic testing and applying such information in our underwriting practices will be directly affected by the position of the other insurers. This is necessary to assure that adverse selection is avoided.
5. While I do not support insurer-required genetic testing, I feel insurers must be permitted to use applicant-initiated testing results on the same basis as other medical information.
6. Currently we rider individuals with certain conditions. In 1992, we plan to stop "ridering" and begin "risk adjusting premiums." At that time, we will become much more concerned about genetic disorders. However, we do not anticipate requiring genetic testing.
7. This survey was answered with 1990 statistics; it excludes LTC [long-term care] as a line of business. The only "open enrollment" for individual plan members is limited to noneligible group members; Hawaii does not medically underwrite groups.
8. The questions asked do not take a number of factors into account (i.e., it is not stated if currently covered, requesting coverage, are symptoms and treatment currently being rendered, etc.)
9. Our underwriting practices and decisions are highly regulated by the State Department of Insurance, which severely limits our ability to consistently apply sound and equitable risk evaluation techniques.
10. The public should demand that health insurers and employers follow their earlier mission of spreading risk, rather than avoiding risk. Additionally, coverage for genetic testing should be provided if medically necessary; criteria which probably need to be refined. If my responses seem confusing, be aware that we ask for medical histories from nongroup applicants [as a method of collecting data], but we are resolute in neither denying coverage nor rating surcharges for high risk individuals. Of course, we don't make a lot of profit with these practices.

Health Maintenance Organizations

1. As an IPA-fee-for-service [independent practice association] HMO in our State, we can not exclude preexisting conditions. Therefore, we are at a distinct disadvantage with other competitors in the field who are permitted such an approach. We therefore are always experiencing adverse selection and show hemophiliacs, AIDS patients, etc.—far in excess of random population statistics.

"agree somewhat," "disagree somewhat," or "disagree strongly," with:

> Prenatal diagnosis indicates the fetus is affected with cystic fibrosis; the couple decides to continue the pregnancy. The health insurance carrier, which paid for the tests, informs the couple they will have no financial responsibility for the CF-related costs for the child.

For commercial vendors, three medical directors (6 percent) agreed strongly or somewhat. Thirteen individuals (25 percent) in this population disagreed somewhat and 34 (67 percent) disagreed strongly. Among medical directors at HMOs, 3 respondents (13 percent) agree to some extent, but 18 respondents (78 percent) disagreed, 15 (65 percent) of them strongly. For chief underwriters of BC/BS plans, six respondents agreed (21 percent), either strongly or somewhat. Eight BC/BS chief underwriters (28 percent) indicated they disagreed somewhat, and 14 (48 percent) disagreed strongly. Among medical directors of BC/BS plans, 1 (6 percent) agreed strongly, 1 (6 percent) agreed somewhat, and 15 (84 percent) disagreed strongly or somewhat.

USE OF GENETIC TESTS

Health insurers do not *need* genetic tests to find out genetic information. Currently, it is less expensive to ask a question or request medical records, and applicants disclose genetic information as part of the battery of questions they respond to in personal and family history inquiries. OTA is unaware of any insurer who currently underwrites individual or medically underwritten groups and requires carrier or presymptomatic tests (e.g., for Huntington or adult polycystic kidney diseases) (1,2), although OTA's survey findings indicate that insurers generally believe that it is fair for them to use genetic tests to identify those at increased risk of disease, and that they should decide how to use that information in risk classification (table 5-3). Thus, what about the possibility of requiring genetic tests as a condition of coverage in the future?

Even a decade from now, OTA's survey found that the majority of respondents do not expect to require genetic tests of applicants—whether or not they have a family history of serious genetic conditions—nor do they anticipate requiring carrier assays. Requiring carrier screening as a condition of consideration for insurance is viewed as even more remote than mandating genetic assays for those who have family histories of serious disorders (table 5-4).

For example, OTA found that a minority of commercial insurers who responded believe it will be "very likely" (2 respondents; 4 percent) or "somewhat likely" (17 respondents; 33 percent) that in 10 years they will require genetic testing for applicants who have a family history of serious conditions. No BC/BS chief underwriter considered it "very likely" that its plan would require genetic testing in the next decade for applicants who had family histories of serious disorders. Medical directors at BC/BS plans were of a similar opinion: No medical director viewed mandatory genetic testing of applicants with family histories as very likely before the turn of the century (table 5-4).

Of medical directors at HMOs, 3 of 23 (13 percent) thought their HMO would require applicants to have a genetic test if a family history of a serious disorder existed, and 5 others (22 percent) said they considered it "somewhat likely" tests would be required in this manner—again, in the next 10 years. A similar distribution of responses was revealed when respondents were queried about requiring carrier tests for applicants at risk of passing on serious genetic conditions to their offspring (table 5-4).

Few respondents believe their company will require genetic tests in either 5 or 10 years, but what about optional testing? Commercial health insurers and BC/BS plans do not anticipate that optional testing or screening will be part of their company's policy in 5 or 10 years. It is interesting to note that a majority of HMO-based medical directors who responded to OTA's survey said they considered it "very likely" or "somewhat" likely that their HMO would offer optional genetic testing and carrier testing in 10 years (12 respondents; 52 percent) (table 5-4). The difference in response between the HMO population versus the commercial insurers and BC/BS plans could reflect HMOs' longer standing history with and emphasis on managed and preventive care.

Thus, over the next decade, OTA's survey indicates the vast majority of health insurers that offer individual coverage or medically underwrite groups do not anticipate requiring applicants to undergo genetic screening for disease, predisposition, or carrier status. Thus, whether or not genetic information is available to health insurers hinges on whether

Table 5-4—Projected Use of Genetic Tests by Insurers in 5 and 10 Years

Question	Respondent	Very likely	Somewhat likely	Somewhat unlikely	Very unlikely	No response[a]
How likely do you think it is that your company/HMO will in the next 5 years:						
Require genetic testing for applicants with family histories of serious conditions?	*Commercials*	1 (2%)	3 (6%)	16 (31%)	31 (61%)	0 (0%)
	HMOs	1 (4%)	4 (17%)	7 (39%)	9 (39%)	2 (9%)
	BC/BS plans-U[b]	0 (0%)	1 (3%)	11 (38%)	15 (52%)	2 (7%)
	BC/BS plans-M	0 (0%)	2 (11%)	5 (28%)	10 (56%)	1 (6%)
Require carrier tests for applicants at risk of transmitting serious genetic disease to offspring?	*Commercials*	2 (4%)	13 (25%)	35 (69%)	1 (2%)	0 (0%)
	HMOs	2 (9%)	3 (13%)	5 (22%)	11 (48%)	2 (9%)
	BC/BS plans-U	0 (0%)	1 (3%)	12 (41%)	14 (48%)	2 (7%)
	BC/BS plans-M	0 (0%)	1 (6%)	6 (33%)	10 (56%)	1 (6%)
Require genetic testing for applicants with no known risk of genetic disease?	*Commercials*	0 (0%)	0 (0%)	4 (8%)	47 (92%)	0 (0%)
	HMOs	1 (4%)	0 (0%)	2 (9%)	18 (78%)	2 (9%)
	BC/BS plans-U	0 (0%)	1 (3%)	6 (21%)	20 (69%)	2 (7%)
	BC/BS plans-M	0 (0%)	0 (0%)	3 (17%)	14 (78%)	1 (6%)
Offer optional genetic testing and carrier testing?	*Commercials*	0 (0%)	3 (6%)	18 (35%)	30 (59%)	0 (0%)
	HMOs	4 (17%)	6 (26%)	6 (26%)	5 (22%)	2 (9%)
	BC/BS plans-U	1 (3%)	5 (17%)	9 (31%)	12 (41%)	2 (9%)
	BC/BS plans-M	1 (6%)	1 (6%)	7 (39%)	7 (39%)	2 (11%)
How likely do you think it is that your company/HMO will in the next 10 years:						
Require genetic testing for applicants with family histories of serious conditions?	*Commercials*	2 (4%)	17 (33%)	14 (28%)	18 (35%)	0 (0%)
	HMOs	3 (13%)	5 (22%)	9 (39%)	3 (13%)	3 (13%)
	BC/BS plans-U	0 (0%)	10 (34%)	8 (28%)	9 (31%)	2 (7%)
	BC/BS plans-M	0 (0%)	3 (17%)	6 (33%)	8 (44%)	1 (6%)
Require carrier tests for applicants at risk of transmitting serious genetic disease to offspring?	*Commercials*	1 (2%)	13 (25%)	16 (31%)	21 (41%)	0 (0%)
	HMOs	3 (13%)	4 (17%)	9 (39%)	4 (17%)	3 (13%)
	BC/BS plans-U	0 (0%)	9 (31%)	9 (31%)	9 (31%)	2 (7%)
	BC/BS plans-M	0 (0%)	3 (17%)	6 (33%)	8 (44%)	1 (6%)
Require genetic testing for applicants with no known risk of genetic disease?	*Commercials*	0 (0%)	4 (8%)	8 (16%)	39 (76%)	0 (0%)
	HMOs	1 (4%)	0 (0%)	6 (26%)	13 (57%)	3 (13%)
	BC/BS plans-U	0 (0%)	3 (10%)	9 (31%)	15 (52%)	2 (7%)
	BC/BS plans-M	0 (0%)	1 (6%)	3 (17%)	13 (72%)	1 (6%)
Offer optional genetic testing and carrier testing?	*Commercials*	0 (0%)	12 (24%)	17 (33%)	22 (43%)	0 (0%)
	HMOs	5 (22%)	7 (30%)	6 (26%)	2 (9%)	3 (13%)
	BC/BS plans-U	3 (10%)	10 (34%)	5 (17%)	9 (31%)	2 (7%)
	BC/BS plans-M	2 (11%)	3 (16%)	4 (22%)	7 (39%)	2 (11%)

[a] Percentages may not add to 100 due to rounding.
[b] BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.
SOURCE: Office of Technology Assessment, 1992.

individuals who seek personal policies, or are part of medically underwritten groups, become aware of their genetic status because of general family history, because they have sought a genetic test because of family history, or because they have been screened in some other context (2). Even then, a majority of respondents to OTA's survey reported they thought it "somewhat unlikely" or "very unlikely" that they would be using genetic *information* for underwriting (table 5-5).

CHAPTER 5 REFERENCES

1. Raymond, H.E., Health Insurance Association of America, Washington, DC, personal communication, December 1991.
2. U.S. Congress, Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, OTA-BA-532 (Washington, DC: U.S. Government Printing Office, August 1992).

Appendix B
Qualitative Comments From the Survey

Space was provided at the end of the questionnaire for any general comments a respondent wished to make. Additionally, several respondents wrote opinions, concerns, and suggestions related to an item in the margin. These open-ended comments of the survey participants provide additional detail and context on current attitudes and concerns among health insurers about genetic tests and genetic information. Where necessary for clarification, bracketed text has been added by OTA.

Commercial Health Insurers

1. So far so good. As long as no one [i.e., other insurance companies] is testing we are not at risk beyond that contemplated by our rate structure. As soon as genetic predisposition is employed on a widespread basis we will be forced to follow suit.
2. We currently do not employ genetic testing for underwriting. However, if it ever becomes a nationally accepted policy, we would utilize it judiciously in order to remain competitive.
3. Genetic testing should be on a level playing field (i.e., applicants and insurers should have equal access to the same information to prevent antiselection).
4. Considering the thousands of other significant medical impairments insurance companies must contend with, the incidence of genetically transmitted disease is a relatively insignificant matter!
5. Individuals with genetic impairments should not be excluded from health coverage. Federally subsidized plans may be needed to supplement what is available from commercial carriers.
6. Required genetic testing to obtain health insurance in general will not be beneficial to applicants for health insurance or to insurance companies. Rated group premiums should be adequate in most cases to compensate for extra risk. If an applicant at high risk to serious genetic disease submits genetic test results on his own which are favorable, then group premium can be adjusted appropriately downward.
7. Our company has more than 1 million health insurance policies in force for individuals and families. The great majority of these are guarantee-issue hospital indemnity policies with waiting periods (ordinarily 1 year) for preexisting conditions. For this part of our business, every applicant is eligible at standard rates. I completed the questionnaire as it pertained to a much smaller segment of our business. This is a medically underwritten, hospital-medical-surgical policy with a lifetime aggregate benefit, in most instances, of 1 million dollars. We will receive about 36,000 applications for this kind of policy in '91. Underwriting is performed from the application and APS [attending physician statement] information. We do not use paramedical exams or tests, and have no plans for genetic testing. We are not an MIB member [Medical Information Bureau, Inc.].
8. If possibility of future disease is 100 percent from testing we might consider using info for underwriting. If it is only a lesser probability, then I doubt if we could use that info.
9. Although incremental in its effect on indemnity industry, the genetic testing referenced will ultimately expand to numerous additional conditions. A broad view of insurance industry cost/risk should be taken from the inception to provide satisfactory protection from additional burden to the premium paying public.
10. This questionnaire appears to me to be poorly conceived and executed; many of the questions appear to be unfairly loaded or betray an ignorance of customary health insurance underwriting practices. Genetic testing is an important societal issue, and intellectually flawed and/or politically motivated exercises seem unlikely to advance the public good in this, or any other, area.
11. This survey appears entirely premature. The insurance industry is not considering screening for genetic diseases. No testing is available yet that is practical. We just want to underwrite symptomatic genetic conditions just like everything else.
12. As an insurer, we are not anxious to begin testing for underwriting purposes; however, if an applicant has already taken the test, it is *critically important* that we have the opportunity to access the test results.
13. We have no plans to perform genetic tests on our applicants. If, however, a genetic test has been done it is extremely important that we know what the applicant knows about his or her own condition. Adverse selection against any one company could jeopardize its financial status and ability to pay future claims.
14. This was a lot of information you requested to be answered in a relatively short period of time!

Blue Cross and Blue Shield Plans

1. Our answer regarding coverage of persons or families at risk for serious genetic disorders is predicated on

4. U.S. Congress, Office of Technology Assessment, *AIDS and Health Insurance—An OTA Survey*, NTIS PB88-170204 (Springfield, VA: National Technical Information Service, February 1988).

5. U.S. Congress, Office of Technology Assessment, *Medical Testing and Health Insurance*, OTA-H-384 (Washington, DC: U.S. Government Printing Office, August 1988).

Table 5-5—Projected Use of Genetic Information by Insurers in 5 and 10 Years

Question	Respondent	Very likely	Somewhat likely	Somewhat unlikely	Very unlikely	No response[a]
How likely do you think it is that your company/HMO will in the next 5 years:						
Use information derived from genetic tests for underwriting?	*Commercials*	7 (14%)	12 (24%)	16 (31%)	16 (31%)	0 (0%)
	HMOs	1 (4%)	5 (22%)	9 (26%)	6 (26%)	2 (9%)
	BC/BS plans-U[b]	3 (10%)	8 (28%)	10 (34%)	6 (21%)	2 (7%)
	BC/BS plans-M	1 (6%)	2 (11%)	7 (39%)	7 (39%)	1 (6%)
In the next 10 years:						
Use information derived from genetic tests for underwriting?	*Commercials*	12 (24%)	20 (39%)	11 (22%)	7 (14%)	1 (2%)
	HMOs	3 (13%)	6 (26%)	8 (35%)	3 (13%)	3 (13%)
	BC/BS plans-U	5 (17%)	13 (45%)	3 (10%)	6 (21%)	2 (7%)
	BC/BS plans-M	1 (6%)	5 (28%)	6 (33%)	5 (28%)	1 (6%)

[a] Percentages may not add to 100 due to rounding.
[b] BC/BS plans-U represents the underwriter population and BC/BS plans-M, the medical director population.

SOURCE: Office of Technology Assessment, 1992.

Appendix A
Survey Method

OTA conducted and managed all aspects of the survey, with input and advice on the survey instrument and study design from a contractor, industry officials, the Advisory Panel, and workshop participants.

Study Design

The OTA survey of health insurers was conducted by mail from June 21 to September 29, 1991. The general approach was similar to a 1987 survey OTA conducted for the report *Medical Testing and Health Insurance* (4,5), although the target population differed slightly, as did the method of ensuring anonymity and confidentiality.

Survey Populations

The overall survey population derived from three sources. The commercial health insurer population was obtained from a Health Insurance Association of America (HIAA) list of member companies that offer policies to either individuals or medically underwritten groups. The Blue Cross and Blue Shield (BC/BS) survey population was derived from the BC/BS Association's directory (1), and the health maintenance organization (HMO) population was derived from the Group Health Association of America (GHAA) 1991 National Directory of HMOs (2).

For the commercial insurers, OTA sent a copy of the survey and an HIAA letter of endorsement to medical directors of the 225 commercial health insurers identified by HIAA as those that offered either individual or medically underwritten group coverage. The list OTA obtained was 4 years old and in that time well over half of those companies had stopped offering individual coverage (3). The reported response rate for commercial insurers reflects those repondents who returned surveys stating they did not offer either type of coverage, but makes no adjustment for nonrespondents who might also not offer such coverage.

Both the chief underwriter and the chief medical director at 72 of 73 BC/BS plans (Puerto Rico was excluded) were sent surveys; a letter of endorsement from the national BC/BS Association also accompanied this survey. Finally, OTA sent surveys to medical directors at the 50 largest HMOs, as well as to an additional 28 plans that were not among the 50 largest U.S. plans, but were the largest HMO within a State or the largest by HMO model type. (Four HMO model types exist: the staff, group, network, and independent practice association model plans.)

A followup letter was mailed to those whose replies were not received within 3 weeks of the first mailing.

Questionnaire Development

Three separate survey questionnaires were developed to account for slight variations in the types of products each population offers, but the substance of the questions was the same (app. C). The instruments contained some items comparable to the 1987 OTA survey performed for *Medical Testing and Health Insurance* (4). Representatives of HIAA, BC/BS Association, and GHAA reviewed multiple drafts of the questionnaires and provided input on industry practices.

Confidentiality

A respondent identification number was placed on the last page of each questionnaire. This permitted improved sample tracking and allowed identification of duplicate returns. The numbered sticker was affixed using a peel-off label that could be removed by respondents who wished to remain anonymous. Respondents were encouraged to leave the peel-off label on the survey and informed that it would be removed after receipt. After OTA received the questionnaires, the peel-off labels were removed, making the data both anonymous and confidential.

Sample Disposition

Fifty-one commercial insurers that underwrite individual or medically underwritten groups responded. An additional 81 commercial insurance companies responded that they no longer wrote either type of policy. The overall response rate among the 225 organizations was 59 percent. Of the 72 BC/BS surveys sent out, 29 chief underwriters completed a survey (40 percent response rate), as did 18 chief medical directors (25 percent response rate). Of the 78 surveys sent to HMOs, 43 surveys were returned (55 percent response rate); 20 of these respondents offered neither individual nor medically underwritten groups.

Appendix A References

1. Blue Cross and Blue Shield Association Directory (Chicago, IL: Blue Cross and Blue Shield Association, 1990).
2. Group Health Association of America, *1991 National Directory* (Washington, DC: GHAA, 1991).
3. Raymond, H., Health Insurance Association of America, Washington DC, personal communication, December 1991.

JOHN H. GIBBONS
DIRECTOR

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

October 14, 1992

The Honorable Louis W. Sullivan, M.D.
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Mr. Secretary:

I am pleased to enclose OTA's Background Paper, *Genetic Testing, and Health Insurers: Results of a Survey*. This study was prepared in response to a request from the House Committee on Energy and Commerce; and the House Committee on Science, Space, and Technology. It was endorsed by Congressman David R. Obey.

As our knowledge of human genetic diseases improves and our ability to diagnose and predict them increases, concern is often raised about denial or restriction of health care insurance. To assess health insurers' views and practices towards genetic tests and information, OTA surveyed commercial insurers, Blue Cross and Blue Shield plans, and health maintenance organizations that offer individual or medically underwritten group policies. OTA undertook the survey in support of its assessment *Cystic Fibrosis and DNA Test: Implications of Carrier Screening*, which was published in August 1992.

This Background Paper presents results from the 1991 OTA survey that pertain to the broader topic of health insurers' practices and attitudes toward genetic information and genetic tests for diseases other than cystic fibrosis. Survey findings are presented that relate to: how health insurers currently view information from various sources (e.g., genetic tests, other medical tests) in underwriting decisions, reimbursement policies for certain genetic tests, and expectations about the impact and use of genetic tests and information on health insurance.

We will be happy to answer any questions you may have about this Background Paper, and I invite you to call me or Robyn Nishimi, Project Director, at 8-6690.

Sincerely,

John H. Gibbons

Enclosure:
Press Release
Background Paper

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JOHN H. GIBBONS
DIRECTOR

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

PRESS ADVISORY
October 14, 1992

Contact: Jean McDonald
(202) 228-6204

OTA RELEASES SURVEY RESULTS ON GENETIC TESTS AND HEALTH INSURANCE

The ongoing project to map human genes will almost certainly expand the number of DNA-based tests for genetic disorders by an order of magnitude over the next decade. How health insurers view such tests will affect their use, says the congressional Office of Technology Assessment (OTA).

An OTA background paper issued today describes the results from a 1991 OTA survey of U.S. health insurers' attitudes toward genetic tests and genetic information -- both their attitudes toward genetic information in making determinations of insurability and how they might reimburse consumers for genetic tests. The survey supports OTA's August 1992 assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening*, requested by the House Committees on Science, Space, and Technology, and on Energy and Commerce, and Rep. David R. Obey.

Results from OTA's survey of health insurers apply to a small slice of the insured population -- the 12.7 million people who have individual or medically underwritten group coverage through survey respondents. Respondents were asked how they would treat certain conditions or scenarios, not whether they had already encountered them. OTA surveyed commercial health insurers, Blue Cross and Blue Shield plans (BC/BS), and health maintenance organizations (HMOs).

All respondents -- commercial insurers, HMOs, and BC/BS plans -- reported that personal and family medical histories were the most important factors in determining insurability. The most important determinants in deciding about insurability and rates are smoking habits, age, occupation, and sex.

For individual policies, the majority of commercial insurers did not ask applicants about any of several genetic conditions listed by OTA (including cystic fibrosis and hemophilia) in either the personal or family history. More than half the HMOs and BC/BS underwriters also did not inquire about the listed conditions. OTA found that a family history of a genetic condition did not always mean the applicant would be declined; in fact, a majority would be accepted at standard rates.

(more)

When presymptomatic testing reveals the likelihood of a serious, chronic future disease (i.e. Huntington disease), more than half the commercial insurers would decline an individual applicant, while about a quarter would accept the applicant at standard rates. Slightly less than half of BC/BS plans that provide individual coverage said they would decline such an applicant, and about a quarter would accept the applicant at standard rates.

When tests show that an applicant is a carrier of a serious genetic condition that could be passed on to his or her children, slightly more than half of commercial insurers and slightly less than half of BC/BS plans that write individual policies would accept the applicant. Carrier test results would not cause any of the HMOs to decline coverage.

From OTA's survey results, it is evident that carrier and prenatal tests often are not reimbursed under individual and medically underwritten group policies unless a family history exists.

OTA found that none of the insurers responding had conducted an economic analysis of the costs and benefits of carrier or other genetic tests as part of applicant screening. In addition, none had conducted an economic analysis of the costs and benefits of genetic counseling of carriers who are covered. Almost none had conducted an economic analysis of carrier testing as part of prenatal coverage.

The majority of commercial insurers and chief underwriters at BC/BS said a negative financial impact for their companies would not occur if genetic tests were widely available to the medical community. HMO respondents, however, were equally divided. But all insurers agreed that a negative financial impact for their companies would likely occur if genetic tests were widely available, but with constraints on insurers' access to the results. Similarly a majority of respondents thought a negative financial impact would result if the availability of genetic tests resulted in adverse claims or underwriting results due to adverse selection.

Copies of the 75-page background paper *Genetic Tests and Health Insurance: Results of a Survey* for congressional use may be obtained by calling 4-9241. Copies for noncongressional use are available at the Superintendent of Documents, Government Printing Office (GPO), Washington, D. C. 20402-9325; phone (202) 783-3238. The stock number is 052-003-01310-0; the price is $5.00.

OTA is a nonpartisan analytical agency that serves the U.S. Congress. Its purpose is to aid Congress in the complex and often highly technical issues that increasingly affect our society.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

July 23, 1991

To: Felix De La Cruz, NICHD
Judith Fradkin, NIDDK
Patricia Moritz, NCNR

From: Director, Ethical, Legal and Social Implications Program, NCHGR

Re: CF RFA Policy Development

I am writing to bring you up to date on the outcome of our meeting on July 12.

I have enclosed a copy of a memo which we have sent to Dr. Raub, alerting him to problems with the policy regarding clinical costs of carrier testing performed as a part of research studies supported by our RFA.

As you can see, this preliminary memo anticipates a formal request from all of us to Dr. Healy to reconsider the NIH's interpretation of PHS policy in this case. The feeling within NCHGR, after further discussion, is that our official request for a policy change would be most persuasively made after the initial review of the applications, when we have concrete cases of meritorious research to discuss and the views of the reviewers as well as the applicants to consider.

After further discussion, we have also decided not to invite applicants to suggest amendments to their proposals at this stage in the process. The NCHGR Office of Scientific Review feels that, because many applicants would be unable to respond in time, or would misinterpret the action to their detriment, such an invitation would not ultimately serve to improve the competition. Instead, the reviewers will be instructed to take the restrictions of the RFA into account in evaluating the merits of proposed study designs, and to indicate when otherwise meritorious projects could be improved scientifically if the restrictions were eased. If the policy changes, these applicants could then be invited to supplement their current proposals.

I know that this plan diverges from the course we identified on July 12, and I do wish to preserve the collaborative spirit in which we set that course. However, it is the Review Office's

responsibility to manage the process at this point, and I have become convinced that the current plan provides a more orderly approach to our common goal.

Please call me with any questions you may have. Otherwise, I look forward to seeing you at the review meeting on August 1 and 2.

Eric T. Juengst, Ph.D.

attachment

cc: Dr. Elke Jordan
Dr. Mark Guyer
Dr. Bettie Graham
Dr. Nancy Pearson
Ms. Linda Engel
Dr. Elizabeth Thompson

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 605
(301) 496-0844

July 23, 1991

TO: Deputy Director, NIH

FROM: Deputy Director, NCHGR

SUBJECT: Grant support for CF carrier testing performed as part of clinical research studies.

I am writing to bring you up to date on our request for applications for "Studies of Testing and Counseling for Cystic Fibrosis Mutations," (RFA HG-91-01), and to alert you to the possible need to determine the limits of PHS policy governing clinical laboratory costs for this RFA. As you know, the RFA currently states that:

> The laboratory costs of testing are ineligible for NIH research grant support since they are considered part of the clinical care of the individuals involved in the studies.

The response to this RFA has been excellent (32 applications despite a short lead time). A number of applicants questioned the extension of our laboratory costs policy to costs involved in performing tests for CF mutations in subjects without known family histories of the disease, and were invited to develop their arguments in writing. As a result, ten of the applications request some support for laboratory costs involved in performing such tests.

While it is true that CF carrier screening is recommended as a standard part of clinical care for individuals who have a family history of cystic fibrosis, it has not yet become the standard of care for such testing to be offered to the general population. Clinical screening for individuals without known family histories of CF would be contrary to the recommendations of the NIH Workshop (March 1990) and the American Society of Human Genetics (1990), pending the outcome of the clinical research our RFA seeks to support. In short, one of the primary scientific goals of this RFA to clarify whether such testing should be considered part of the clinical care of these individuals or not. Our survey of other ICD's indicates that NIH-supported pilot studies of other genetic diagnostic tests have included the laboratory costs of such "experimental" testing.

Advances in testing technology have brought the cost of testing for multiple (4-6) CF mutations down substantially in the last year: applicants are requesting support in the range of $45 to $75 per test instead of the $300/test cited in the early literature. As a result, support for these costs can be accommodated within the financial limits of the current RFA.

The initial review group will meet on August 1 and 2 to discuss the applications submitted against this RFA, and we will seek their advice on the scientific dimensions of this policy question. We will let you know after the review whether further consideration of this issue seems necessary. Meanwhile, thank you for your preliminary consideration, and please feel free to call me with any question you may have.

Elke Jordan

Elke Jordan, Ph.D.
Deputy Director

cc: Eric Juengst, NCHGR
Felix De La Cruz, NICHHD
Patricia Moritz, NCNR
Judith Fradkin, NIDDK

FY1 Para

Dave

Which do you wish to display?
  1: Only the paragraphs found
  2: Only the 1st paragraph in each item found
  3: Complete statement by the member
  4: Full text of each item found

    Choose ONE number.....4

LEGI-SLATE Report for the 102nd Congress Thu, April 25, 1991 3:18pm (EDT)

Text of the Congressional Record
    Showing the Full Text of Each Item

    On 04/22/91
AND Contained in the Extensions of Remarks Section
AND Attributed to Rep. George W. Gekas (R-PA)
AND With Reference to 'CYSTIC FIBROSIS'

==========

Congressional Record dated Monday, April 22, 1991
Extensions of Remarks Section

Remarks by GEKAS (R-PA)
        THE CLONING OF THE CYSTIC FIBROSIS GENE: AN AMERICAN BIOMEDICAL RESEARCH SUCCESS STORY [CR page E-1354, 18 lines]

Attributed to GEKAS (R-PA)

THE CLONING OF THE CYSTIC FIBROSIS GENE: AN AMERICAN BIOMEDICAL RESEARCH SUCCESS STORY

HON. GEORGE W. GEKAS

OF PENNSYLVANIA

IN THE HOUSE OF REPRESENTATIVES

Monday, April 22, 1991

Mr. GEKAS. Mr. Speaker, this is a continuation from the text of remarks I submitted for printing on April 17, 1991. The remarks that appear in today's Record were made by Dr. Francis S. Collins at the March 13, 1991, Congressional Biomedical Research Caucus briefing on cystic fibrosis. I will conclude this extension tomorrow with remarks from Dr. Richard Boucher.

Text Inserted by GEKAS (R-PA)
        Finding the Burned Out Lightbulb: The Identification of the Cystic

Finding the Burned Out Lightbulb: The Identification of the Cystic Fibrosis Gene

(Remarks by Francis S. Collins, M.D., Ph.D.

I would like to thank the Congressional Biomedical Research Caucus for the opportunity to speak. I applaud the efforts by this group to increase understanding and dialogue between the scientific and political communities. I would also like to take this opportunity to thank the members of the Congress for their consistent and enthusiastic support of biomedical research in this country, especially at times of budget constraint. I am quite confident that we would not be here today discussing the cloning of the cystic fibrosis gene were it not for that substantial investment at a great many levels.

I am a physician and a scientist at the University of Michigan. I spend about two-thirds of my time running a research laboratory which is studying human genetic disease, especially cystic fibrosis, neurofibromatosis, and Huntington disease. With the other third of my time I see patients with a wide variety of genetic conditions who come to my clinic. I am constantly challenged and frequently frustrated, by the ravages of genetic disease and the suffering it induces, not only for those who are affected but for their families. So often, as with cystic fibrosis, genetic disease is particularly cruel because it strikes children and young adults. It is also fair to say that none of us can be very confident of escaping this particular burden; it is estimated that we all carry 4 to 5 severe recessive genes but we are unaware of their presence. As we have gained an increased understanding of the genetic basis of common diseases, such as coronary artery disease, hypertension, diabetes, cancer, and even alcoholism, it is clear that genetic influences play a major role in the health of all of us. A major challenge of the coming decades is to unravel these complex genetic influences and to use this information to develop a more effective medical approach.

I was first introduced to cystic fibrosis as a clinical problem during my internship in Internal Medicine. At that time, in the middle 1970's, there was very little known about the basic defect, and survival was not as good as it is today, when the average person with CF survives into their late twenties. Knowing that I was headed for a career in genetics, I read as much as I could about the disorder, but concluded that at that time there were few options for gaining an increased understanding of the disease. I never realized that ten years later this would become a major research activity of my own.

In fact, my research training was somewhat unorthodox. I had obtained a Ph.D. in physical chemistry prior to going to medical school, and made that non-traditional shift because of the sense that I wanted to be involved in something with more direct human applications. After finishing my medicine residency I entered a fellowship in human genetics at Yale where I learned the basics of molecular biology, in a program ably directed by Leon Rosenberg who spoke to you so eloquently at your first meeting. Along the way I was supported at various intervals by training grant support funded by taxpayer dollars. As a graduate student I was funded by an NSF graduate fellowship, and as a post-doctoral fellow at Yale I received support from an NIH training grant. I could not have obtained scientific training without these programs, and these grants continue to be absolutely crucial for the support of a wide range of budding biomedical scientists.

I would now like to describe for you the strategy that was used to identify the cystic fibrosis gene, and to explain why this holds such promise for the identification of other disease genes. All of the basic hereditary information of living organisms is contained within DNA, which is the material that makes up the chromosomes inside each cell. We each inherit approximately half of our DNA from our father, and half from our mother. For a disease like cystic fibrosis, there are two copies of the gene, one inherited from each parent. If an individual has one normal copy and one defective copy, they are still entirely healthy. Such person is called a CF carrier. If the child of two carriers happens to inherit the abnormal gene from each parent, then that child will have cystic fibrosis.

DNA is not itself capable of carrying out functions inside the cell, but rather acts as a storehouse of information. The DNA is actually transcribed into another substance called RNA, and that RNA is then translated into protein. It is protein which performs most of the functions of the cell, and therefore mutations in the DNA sequence generally have their deleterious effects by leading to the production of an abnormal or absent protein which cannot carry out its job. For many diseases, the responsible gene has been identified (cloned) by first finding something wrong with the protein. For hemophilia A, for instance, a bleeding disorder inherited in a sex-linked fashion, the first stop in understanding was the identification of a defect in a clotting protein called Factor VIII. This protein was partially purified and some of its sequence was obtained. That allowed a deduction about the nature of the gene that encodes this protein, finally resulting in the cloning of the gene. Most disease genes that have been cloned up to his point have followed a similar strategy.

For cystic fibrosis, however, there was insufficient information about the protein to allow an approach based on this strategy. There was, to be sure, information that there was a problem in transport of chloride and water in cystic fibrosis cells, but it was not at all clear what the basis protein defect was that was responsible for that transport abnormality. Faced with this situation, most scientists as recently as ten years ago would have said that there was little or no chance of identifying the CF gene. The strategy that succeeded, and succeeded more rapidly than anyone could have predicted, was a new approach which I prefer to call "positional cloning", but which has also been called "reverse genetics". This strategy allows the cloning of disease genes without any information about their function, using only the fact that the disease is inherited in families. This information is used to map the gene to a specific chromosome, and this mapping is further and further refined until the area where the disease gene must be located has been narrowed to a very small segment. Eventually the gene itself is then identified by sifting through this interval.

The reason this is so difficult is basically a matter of scale. The human genome is made up of 24 different chromosomes and encodes approximately 100,000 different genes, each of which has a separate function. DNA is measured in basis pairs, and the total human genome is 3 billion based pairs in length. In searching for the cystic fibrosis gene, it is necessary not only to find the right gene, but to identify a specific abnormality in that gene, which may be as subtle as a single base pair. For sickle cell anemia, for instance, all of the ravages of this terrible disorder can be traced to the alteration of a single base pair out of 3 billion, located in a gene that codes for hemoglobin.

Thus, searching for the cystic fibrosis gene with no functional information is a problem of great difficulty. A useful comparison is to consider this analogous to trying to identify a single burned out light bulb in a house

somewhere in the United States without initially having any information about its geographic location. In this analogy, the house is the gene you're looking for, and the burned out light bulb is the abnormality in the gene that allows you to be certain that you found the right house. If you had to accomplish such a task, you would probably design some sort of searching strategy that allowed you to narrow down the proper location step by step, going from state, to county, to city, to city block, and eventually resorting to a house to house search.

The first step was to put the house in the right state, which in genetic terms was to place the gene on the correct chromosome. This was carried out by a process called linkage analysis. The principle is not new, but the advent of recombinant DNA technology has made it much more powerful over the last few years. Largely supported by the NIH, a large number of DNA "markers" (sometimes called RFLP's) have been mapped to specific chromosomes and are available for this purpose. What one does in such a linkage analysis is to collect a large number of families where the disease is occurring, and to analyze those families with this large panel of markers. Basically, one can look at several towns in each state as possible candidates for the approximate location for the gene. Even if a particular marker is not precisely on top of the gene, if it is in the right part of the right state, it will show a tendency to be inherited along with the disease in the families being analyzed. This strategy resulted in the successful mapping of the CF gene to chromosome 7 in 1985, which one can think of in our analogy as placing the gene in the state of Michigan, although the localization was quite fuzzy at that time. A great many additional markers from chromosome 7 were then quickly tested (analogous to checking out a lot of towns in the right part of Michigan). Two markers were found which were much closer to the CF gene than the original one. (Ironically, one of these was a cancer gene called met, whose cloning had been motivated by a desire to understand the mechanism of bone cancer. This is yet another example of how basic research in different areas can interact catalytically in unpredictable ways). These two markers allowed the placement of the CF gene in a somewhat more manageable interval, analogous to saying the gene was somewhere in Ann Arbor, Michigan.

This was still a very hard problem, however, because of the need to investigate many houses (genes) looking for a subtle abnormality. A new technique which considerably aided this search was a trick called chromosome jumping, developed in my laboratory in the middle 1980's. In fact, it was the development of this technique that brought me back to cystic fibrosis, almost ten years after initially puzzling over how the basic defect could possibly be approached. Chromosome jumping allows someone interested in a search of this sort to start at one edge of the town and leap into multiple city blocks with relatively little effort. The old way of searching (chromosome walking) required one to start at one edge of the town and methodically move from block to block until you got to the other end. If the house you were looking for happened to be at the far end of the town it would take you many years of fruitless searching until you got to the area of most interest. Jumping allowed this problem to be circumvented, and permitted the initiation of house to house searching at several locations simultaneously. In the context of this particular audience, I should perhaps point out that chromosome jumping as a concept was considered to be of high risk. The concept was developed while I was a postdoctoral fellow at Yale, but most of the work which led to progress in cystic fibrosis was carried out after I moved to the University of Michigan as a beginning Assistant Professor in 1984. In order to support this work, I submitted a grant application to the NIH in the spring of 1984, and was successful in obtaining funding. Had the NIH system not responded by supporting this high risk endeavor, or had the number of grants available been a bit lower so that I missed the cut off, I would have

been forced to work on something more traditional. The effects on CF research are likely to have been significant.

The house to house search was still a labor intensive effort, and for this purpose my group linked up with researchers at the Hospital for Sick Children in Toronto, led by Drs. Lap Chee Tsui and Jack Riordan. This international collaboration was highly successful and productive, and we basically pooled our research groups in order to work towards this common goal. This kind of collaboration between scientists, where each group brings different expertise to a problem, is more common than most people realize. Perhaps at times the public has the idea that scientists are people with large egos who have trouble getting along with their peers. While as a group we are not completely immune to such behavior, I would certainly state that from my own experience the drive to gain new knowledge and accomplish a difficult goal supersedes personal considerations, and is one reason why American science has been so consistently successful.

After about a year and a half of the house to house search, we uncovered a house that seemed to have some of the right characteristics: it represented a gene which seemed to be of considerable importance in the lung, the pancreas, and sweat glands, all organs which are affected in patients with cystic fibrosis. However, the real proof that this was the right gene demanded the identification of the burned out light bulb, which in this case turned out to be a deletion of only three base pairs of DNA in the middle of the gene. This was a very subtle abnormality which would have been easy to miss. In fact, when we initially found this, we wondered whether it could actually be the cause of such a devastating disorder. However, after surveying a large number of DNA samples, it became clear that this abnormality was present in about 70% of cystic fibrosis chromosomes, and was never found on a normal chromosome, indicating that this mutation must in fact be the most common cause of the disease. Other cystic fibrosis chromosomes turn out to have other less common mutations in this very same gene.

Once we were sure we had the right gene, the question turned to what its function would be. From determining the sequence of the DNA, one can predict precisely the sequence of the protein, as these are related through the genetic code. When the protein sequence was worked out and compared to all other proteins that have been studied, a striking result was found: the protein product of this gene, which is called CFTR for cystic fibrosis transmembrane conductance regulator, had dramatic similarities to a large family of proteins occurring in organisms as diverse as bacteria, yeast, fruit flies, and man. All of these proteins are involved in transporting small molecules, either into the cell or out of the cell. The ability to discover this similarity, which is done by a computer search requiring only a few hours, is made possible by the long term support by the NIH of databases of DNA and protein sequence, which are taking on increasing importance as the amount of information grows. It is now often the case that, just as for CF, a new gene finds partial matches in this database that make profound predictions about the function of the gene and direct future steps in research.

This is then the story of the cloning of the cystic fibrosis gene. There are several immediate outcomes. Knowing the common mutation, it is now possible to screen individuals to find out whether or not they are carriers for the cystic fibrosis gene, which is the case for approximately 1 in 25 Caucasian individuals. There are some complexities, since not every carrier has the same burned out bulb, but screening for the common mutation successfully picks up 70 percent of carriers, and looking for three or four other common mutations raises this to 85 percent. About 70 percent of couples at risk for having a child with cystic fibrosis can now be detected prior to

their beginning a pregnancy. While this is a complex issue, many individuals feel that it is appropriate to investigate the possibility of general population screening for cystic fibrosis, in order to give couples at risk that information and allow them to choose between various options about child bearing. Those options would include foregoing having children, adoption, artificial insemination, prenatal diagnosis, or proceeding with childbearing and accepting the one in four chance that the child will have CF. Much attention will need to be paid to the educational side of such a screening program, as there is no point in screening individuals if the information they are given is not clearly understood.

Even more exciting, however, is the possibility of using the cloned gene to develop new and better treatments, and perhaps even a cure. The first step in gene therapy for cystic fibrosis was in fact already accomplished last fall by three different groups who inserted the normal cystic fibrosis gene into CF cells growing in laboratory culture. The chloride transport defect in these CF cells was found to be corrected when the normal gene was inserted, indicating that this transfer is capable of correcting the disease. A major challenge of the future, towards which much research is now being directed, is to optimize this process in the airway of a living CF patient. The study of the gene and its protein product may also lead to better ideas about drug therapy for the disease, in that it may be possible to design a drug which will compensate for the defective protein, once we are able to obtain detailed information about its structure and function.

Basically, cloning the CF gene can be thought of as passing through a severe bottle-neck in scientific and medical progress. With the gene in hand, a vast array of experimental approaches are now possible. This has been reflected by an enormous increase in the number of investigators doing research on this disorder. It is clear that the cloning of the CF gene is only a start, and that the real challenge for the future is to understand its function and use this to develop therapies.

So what is the relevance of this story to the present and future condition of U.S. bimedical research? There are several lessons that can be deduced. First of all, the positional cloning strategy can be spectacularly successful, even in a situation like cystic fibrosis where no additional helpful clues exist to guide the search for the right house. The positional cloning strategy has in fact now been successful for a total of seven genes (including the muscular dystrophy gene), and several others will follow in the relatively near future. This is a genuine revolution in human genetics and medicine; it opens a new window into the ability to find and characterize genes responsible for disease which had previously been inaccessible.

A second more sobering lesson from CF is that this research is expensive. Various estimates have been made that indicate that the entire search for cystic fibrosis gene cost somewhere on the order of $50,000,000, with much of that having been supplied by the NIH and the Cystic Fibrosis Foundation. I have told you only a small part of the story. In most parts of this endeavor, we stood on the shoulders of a wide variety of other researchers, whose painstaking efforts over the last 20 or 30 years were essential for the success of the strategy.

The third lesson, and the most important one for this caucus, is the crucial role of consistent and vigorous support of basic biomedical research. In the CF story, advances often came from arenas where one could not have predicted them. The concept of linkage analysis, originally an obscure area of human genetics, has now emerged as a fundamental paradigm for the identification of disease genes. Painstaking studies of chloride channel behavior, first in normal cells, and only much later in CF cells, have played

a crucial role. I have already alluded to the benefits that now derive from the availability of databases for comparison of DNA and protein sequences, and to my own gratitude in being supported for chromosome jumping research when few people would have predicted that it would benefit CF. This is not an atypical story. Much of the success of U.S. research can be traced to the wide range of projects being pursued. Too much targeting can be counterproductive.

A fourth lesson is the need for a better map of the human genome if this kind of activity is to continue, and especially if it is to be successfully applied to more difficult problems where the inheritance pattern is not so simple, such as hypertension, breast cancer, diabetes, alcoholism, Alzheimer's disease, and schizophrenia. If we had at the outset possessed a detailed map of all of the states with the location of all of the towns and all of the houses, it would have enormously facilitated our effort to find the CF gene and taken several years off of the process. For diseases where the inheritance is less simple, the ability to identify the right town will be more limited, and it may be necessary to search through many towns simultaneously in order to find the right house and light bulb. This kind of labor-intensive activity will really only be possible and affordable if more information is available about the basic map of the human genome. This is one of the principle reasons that I am an enthusiastic supporter of the human genome project. This project, which will efficiently obtain complete maps of all the human chromosomes over the next five years, and the entire sequence of the human genome at the end of fifteen years, has recently begun funding through the NIH and the Department of Energy, and will fill a crucial need which will allow the generalization of this positional cloning approach to a much larger list of human diseases. This ability to identify genetic predispositions will allow medicine to move from its current state of treating diseases that are already underway to a more preventive one in the next century. There are many ethical and legal dilemmas which this set of advances presents, but the human genome project has accepted this challenge as a major part of their agenda. For example, discussions about policy changes that may be necessary to protect individuals from genetic discrimination are already intensively underway. The genome project deserves the continuing enthusiasm of the Congress as it ramps up to full strength over the next few years.

The fifth and final lesson is the need for improvement in scientific education. This sort of research is complex, and requires scientists with an in-depth understanding of a wide variety of fields. I am deeply concerned that the number of college and medical school graduates choosing careers in biomedical research is decreasing. Fears about lack of funding, especially over the last year or two, have certainly contributed to this trend. It is also clear that few high school students are currently exposed to the excitement and intellectual elegance of modern scientific research. To my mind this needs to be a major agenda item if we are to maintain our preeminence in the United States as the leader in this field.

In conclusion, the cloning of the CF gene represents a landmark, but it is only the start of what most of us hope will be a series of advances in ending the ravages of this devastating disease. With the gene in hand, a much broader array of approaches are now possible. We all look forward to the time, hopefully in the next decade, when this disease can be cured once and for all.

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Remarks by GEKAS (R-PA)

Meeting Summary

Workshop on Clinical Studies of Cystic Fibrosis Carrier Testing
January 31, 1991

On behalf of the NIH Director's Office, the National Center for Human Genome Research hosted a workshop on January 31, 1991, to discuss the NIH's role in supporting clinical studies of CF carrier testing. The meeting occurred from 1:00 pm to 5:00 pm in room B1N30B of Building 38A, and involved the external consultants, NIH staff and observers listed on the attached roster.

The purpose of the meeting was to gather information and advice on how NIH might best proceed in helping to assess ways to provide genetic education, testing, and counseling services for the cystic fibrosis gene. The attached material was provided to the participants as background for the meeting. The discussion yielded the following recommendations:

Role of Clinical Studies

The consultants concurred with earlier statements from the American Society for Human Genetics and two 1990 NIH workshops that clinical evaluations of alternative approaches to genetic education, testing and counseling are needed in order to establish the professional practices that should govern the provision of DNA-based testing for CF carrier status. Recent experience with the widespread introduction of other genetic tests, such as MSAFP screening, attest to the value of such studies in helping to establish practices that would improve professional interpretation and patient understanding of CF testing and test results.

Moreover, the pace of advances in applied human genetics suggest that whatever professional practices develop for CF testing will provide important precedents for the clinical introduction of subsequent DNA-based genetic tests over the next decades. Thus, the consultants stressed the need for clinical studies that use CF carrier testing to develop a generic model for the long-range integration of genetic services into health care.

High Priority Research Questions

The goal of these studies would be to identify clinical practices that best increase patient understanding of disease-gene carrier testing and test results, and best protect patients from test-related psychological harm, stigmatization, and discrimination. In all cases, questions of relative cost, relative effectiveness, and ability to meet the demand for services need to be evaluated.

In making such assessments, several questions become important to investigate:

1. What are the levels of understanding of and interest in CF carrier testing among different patient populations?

   The purpose of CF carrier testing is to better inform interested people of their reproductive health risks. In order to develop services effectively, it will be important to assess knowledge about and interest in this service in patient populations of different family risk status, reproductive status (i.e., pre- and post-conception), socio-economic strata, and possibly age and ethnic groups. Different approaches may be needed for patients in different groups.

2. What are the optimum forms and levels of pre-test education for different patient populations?

   Four variables need to be tested here for their effectiveness with different populations: alternative educational methods (print materials, videos, live discussions); alternative teaching personnel (genetic counselors, primary care physicians, nurses, lay counselors, etc); alternative settings (one-on-one vs. group sessions); and varying levels of content depth and detail.

3. What are the accuracy and cost effectiveness of various types of tests?

   A variety of testing methods and matrices are emerging for CF carrier testing. A comparative assessment of their clinical efficiency and reliability is needed, particularly with an eye towards their ability to accommodate tests for multiple genetic conditions. Multi-phasic genetic testing is likely to be the common mode in the future.

4. What are the best approaches to post-test counseling, in terms of patient understanding and psychological health?

   Variables to be evaluated here include: alternative counseling personnel (genetic counselors, primary care physicians, obstetricians, nurse-geneticists, lay counselors, etc.) and alternative counseling strategies (family vs. individual sessions).

5. What are the optimum settings for providing CF carrier testing services?

   Traditionally, such services have been provided by medical genetics programs. How well can they be accommodated in other settings, such as primary care physician's offices, HMO's, or community-based sites like work-place programs.

6. What record-keeping and reporting policies best protect against breaches of confidentiality, stigmatization and discrimination?

Studies of different policies and practices with respect to the confidentiality of test results may be useful in developing protections against social stigmatization and discrimination as a result of carrier testing.

Research Design

In order to adequately evaluate the several variables involved in assessing the delivery of CF carrier detection services in a timely way, the consultants recommended that NIH develop a consortium of multiple studies, each addressing some subset of the overall agenda in coordination with the rest. In addition to increasing the scope and pace of the research, such an arrangement would allow some features of the research, such as evaluation measures and tools, cost accounting, laboratory quality control and human subjects protections to be standardized across the participating investigations, making reliable comparisons between studies possible.

The consultants also recommended that support be provided to underwrite the current laboratory costs of testing during these clinical studies, to improve access to the studies by all interested patients and to anticipate the availability of less expensive commercial testing in the future.

Cost estimates drawn from NIH applications submitted to date suggest that five two-year studies could be supported for a total cost of 2.5 million dollars.

Workshop on Pilot Studies of Cystic Fibrosis Carrier Testing
January 31, 1990
Bethesda, MD

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AGENDA

Workshop on Pilot Studies of Cystic Fibrosis Carrier Testing
January 31, 1990

1:00 p.m. Introductory remarks:
Dr. Elke Jordan

1:15 p.m. Research needs with respect to CF carrier testing:
Participants' roundtable discussion

3:15 p.m. Break

3:30 p.m. Discussion: Methods for addressing research needs

5:00 p.m. Adjournment