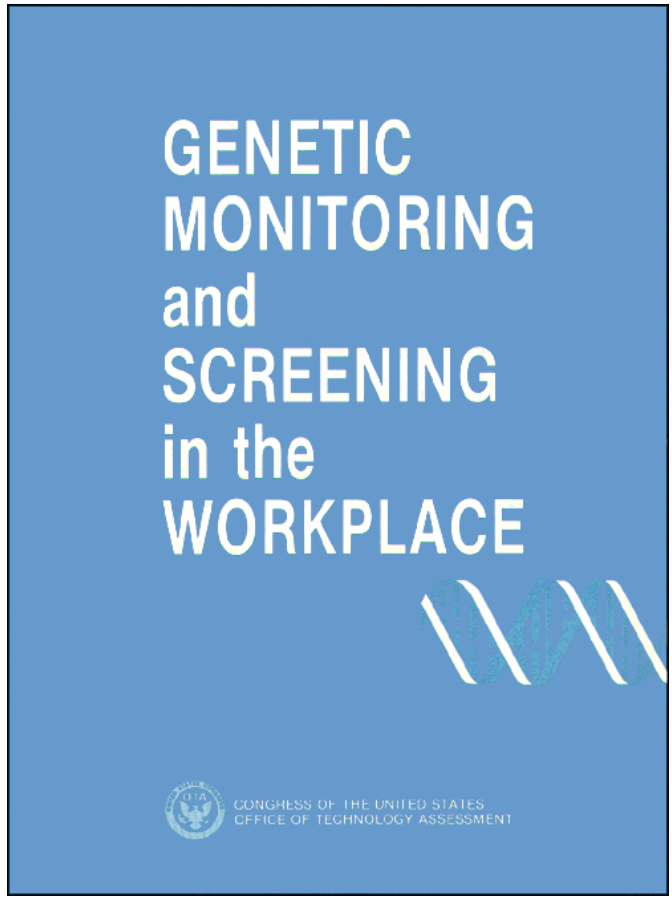
Genetic Monitoring and Screening in the Workplace

October 1990

OTA-BA-455
NTIS order #PB91-105940





Recommended Citation:

U.S. Congress, Office of Technology Assessment, *Genetic Monitoring and Screening in the Workplace, OTA-BA-455* (Washington, DC: U.S. Government Printing Office, October 1990).

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Foreword

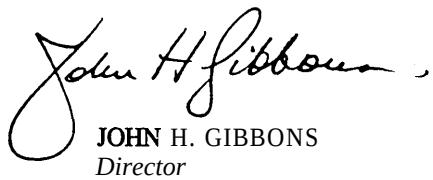
Genetic monitoring and screening have the potential to significantly change the workplace by detecting both occupational and nonoccupational diseases. These tests can identify genetic abnormalities that maybe associated with inherited diseases, susceptibilities, and traits in otherwise healthy, asymptomatic individuals. The ability to diagnose latent conditions (both occupational and nonoccupational) through genetic monitoring and screening raises policy questions about the proper use of such technologies. This report describes the issues associated with genetic monitoring and screening in the workplace. It examines the technologies used, analyzes the legal framework for the use of such tests, assesses the ethical issues inherent in the use of these tools in the workplace setting, describes how genetic information is conveyed by a genetic counselor, and, based on an OTA survey of 1,500 U.S. companies and the largest unions, evaluates the current and future use of genetic monitoring and screening in the workplace.

Genetic Monitoring and Screening in the Workplace was requested by the Senate Committee on Commerce, Science, and Transportation; House Committee on Energy and Commerce; and the House Committee on Science, Space, and Technology. It was also endorsed by the Senate Committee on Labor and Human Resources. It illustrates a range of options for action by the U.S. Congress on two central issues:

. the appropriate role of the Federal Government in the regulation, oversight, or promotion of genetic monitoring and screening; and
. the adequacy of federally sponsored research on the relationships between genes and the environment.

OTA was assisted in preparing this study by a panel of advisors and reviewers selected for their expertise and diverse points of view on the issues covered in the assessment. Advisory panelists and reviewers were drawn from industry, academia, labor organizations, legal experts, scientific and professional organizations, research organizations, and Federal agencies.

OTA gratefully acknowledges the contribution of each of these individuals. As with all OTA assessments, however, responsibility for the content is OTA's alone.



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NOTE: OTA appreciates and 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.

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Chapter 1

Summary, Policy Issues, and Options for Congressional Action

During the past three decades, our understanding of genetics has advanced remarkably as new methods for identifying, manipulating, and analyzing deoxyribonucleic acid (DNA) have developed. Less well understood, however, is the interaction between the environment and heredity, and the roles each plays in sickness and health. It has long been recognized that genetic risks are associated with certain workplace environments, such as exposure to radiation or certain chemicals. Recognition of genetic factors in disease presents new opportunities for detection, prevention, and treatment. This concept has provoked debate in recent years about whether genetic monitoring and screening of workers to identify outwardly healthy individuals (or populations) at risk for or susceptible to a variety of work-related conditions is appropriate or even feasible.

Genetic monitoring and screening have the potential to significantly change the workplace by detecting both occupational and nonoccupational diseases. They can identify genetic abnormalities which may be associated with inherited diseases, susceptibilities, and traits in otherwise healthy, asymptomatic individuals. The ability to diagnose latent conditions (both occupationally and nonoccupationally related) through genetic monitoring and screening raises policy questions about the proper use of such technologies.

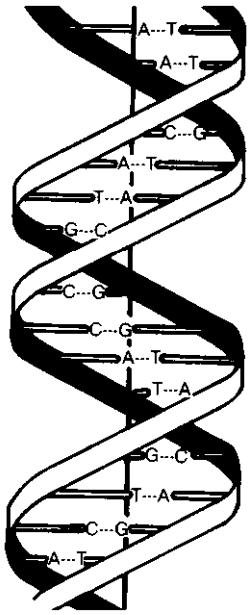
This report examines the potential applications and limitations of genetic monitoring and screening in the workplace. In response to requests from the Senate Committee on Commerce, Science, and Transportation, the House Committee on Energy and Commerce, and the House Committee on Science, Space, and Technology, this assessment presents the scientific, legal, ethical, and social issues surrounding the use of genetic monitoring and screening in the workplace. It also evaluates the results of a 1989 Office of Technology Assessment (OTA) survey on genetic monitoring and screening in the workplace of 1,500 U.S. companies, the 50 largest utilities, and the 33 largest unions. These survey results will also be interpreted in the context of a 1982 OTA survey on genetic monitoring and screening (part of a 1983 OTA assessment of genetic monitoring and screening).

DEFINING GENETIC TESTING

Genetic testing includes a number of technologies to detect genetic traits, changes in chromosomes, or changes in DNA. DNA is the chemical bearer of genetic information, which takes the structural form of a double-stranded helix (figure l-l). It is composed, in part, of four chemical subunits called bases. These four bases—guanine (G), adenine (A), thymine (T), and cytosine (C)---are the coding units of genetic information that form the DNA double helix structure (figure 1-2).

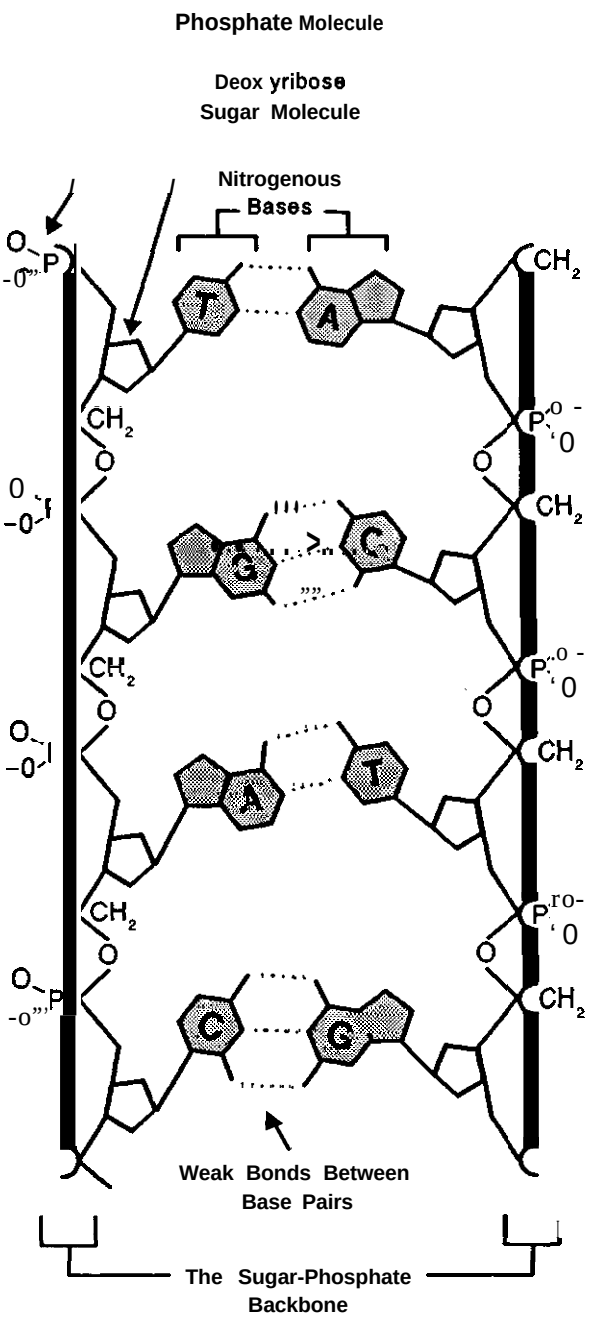
As used in the workplace, genetic testing encompasses two activities: genetic monitoring and genetic screening. Thus, genetic testing of employee populations involves both examining persons for evidence of induced change in their genetic material (monitoring) and identifying individuals with particular inherited traits or disorders (screening). The general term “genetic testing” is not used in this report; rather the more specific terms “genetic monitoring” and “genetic screening” are used (figure 1-3).

Figure l-l—The Structure of DNA



SOURCE: Office of Technology Assessment, 1990.

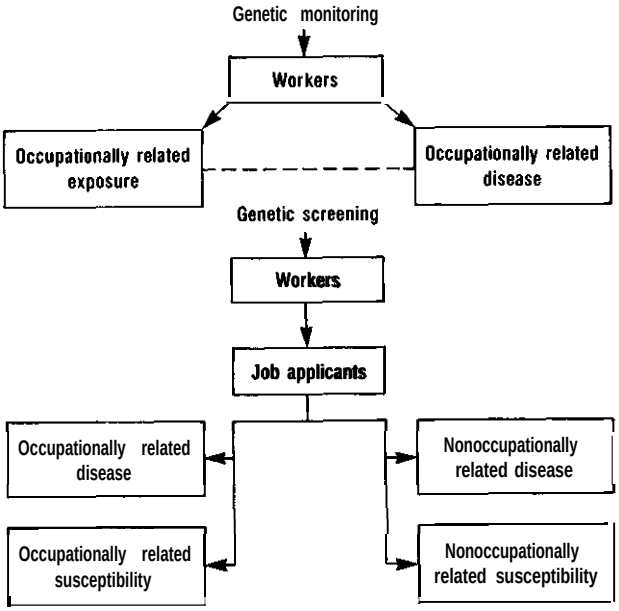
Figure 1-2—DNA Base Pairing



The four nitrogenous bases, adenine (A), guanine (G), cytosine (C), and thymine (T), form the four letters in the alphabet of the genetic code. The pairing of the four bases is A with T and G with C. The sequence of the bases along the sugar-phosphate backbone encodes the genetic information.

SOURCE: Office of Technology Assessment, 1990.

Figure 1-3-Components of Genetic Testing in the Workplace



SOURCE: Office of Technology Assessment, 1990.

What is Genetic Monitoring?

Genetic monitoring involves periodically examining employees to evaluate modifications of their genetic material--e.g., chromosomal damage or evidence of increased occurrence of molecular mutations—that might have evolved in the course of employment. The putative cause is workplace exposure to hazardous substances. The premise is that such changes could indicate increased risk of future illness.

Because ambient exposures, personal habits and lifestyle decisions (e.g., tobacco use, etc.), and age can also induce changes in genetic material, genetic monitoring could detect changes that arise from exposures outside of the workplace. In short, genetic monitoring ascertains whether the genetic material of a group of individuals has altered over time. In general, current techniques are not exposure-specific, but serve merely as an indicator of recent exposure.

Genetic monitoring could be performed on groups of employees to identify the risk for the exposed group as a whole, to target work areas for increased safety and health precautions, and to indicate a need to lower exposure levels for a group exposed to a previously unknown hazard.

What is Genetic Screening?

Genetic screening involves assays to examine the genetic makeup of employees or job applicants for certain inherited characteristics. (Employees could be screened on different occasions for different traits or with improved technology, but generally only once per characteristic.) Genetic screening can be used in two distinct ways. First, employees or job applicants could be screened for the presence of genetically determined traits that render them susceptible to a pathological effect if exposed to specific agents. For example, an employee or a job applicant could be tested to identify a genetic predisposition to an occupationally related disease. Second, employees or job applicants could be screened to detect general heritable conditions, not just conditions associated with occupational illness. Reasons for using the different classes of tests vary. In either case, whether screening for an occupationally related trait or one unrelated to job exposure, genetic screening tests involve examinations for inherited traits where a single measure is usually sufficient because these inherited characteristics, as a rule, do not change.

Genetic screening for occupationally related traits could be performed to ensure appropriate worksite placement of employees susceptible to certain occupational diseases, and ensure that employers place those workers most susceptible to a specific risk in the least hazardous environments. Both genetic screening for occupationally related traits and for nonoccupationally related traits could be performed to: improve employee productivity and lower workers' compensation costs through better worker health; promote and encourage general health awareness; and improve employers' health care cost-containment efforts, especially for health insurance. This could be done through exclusion (i.e., not hiring those with deleterious genes because of the potential drain on health insurance).

Genetic screening differs significantly from genetic monitoring. With screening, a one-time test to detect a single trait in a worker or job applicant is usually sufficient, while monitoring generally involves multiple tests of a worker over time. Most importantly, genetic screening focuses on the preexisting genetic makeup that workers or job applicants bring to the job. This is distinct from genetic monitoring which focuses on hazardous workplace exposures that induce changes in the genetic material in an exposed population as a whole.

DIFFERENCES BETWEEN GENETIC MONITORING AND SCREENING

From a policy standpoint, these differences—genetic monitoring v. genetic screening and occupational illness v. nonoccupational illness or general health--could be significant. Some criticize all types of genetic monitoring and screening in the workplace as paternalistic and discriminatory, while others advocate that, properly implemented, genetic monitoring and screening programs benefit both workers and industry. Others, however, maintain that it is one thing to monitor or screen workers because they are at increased risk for occupational illness induced by the workplace, but quite another to screen persons because they or their offspring—who could be covered on an employee's health plan—are at high risk for a disease unrelated to occupational exposure. Finally, some argue that genetic screening *per se*, even if to reduce occupational illness, is unfair because it ***a priori*** measures heritable conditions beyond an individual's control. Genetic monitoring is perceived by others as less threatening because it mirrors other forms of successful biological monitoring (e.g., benzene or lead exposure) performed on body fluids or tissue samples. The use of either technology, however, raises serious legal and ethical questions.

Screening for nonoccupationally related diseases-e. g., Huntington's disease or neurofibromatosis—raises new issues for containing health care expenses, for both the employer and employee. Increasingly, costs to U.S. employers of health-related benefits have skyrocketed. In particular, to avoid rising health care costs, many large companies are adopting self-insurance plans, which are not subject to State insurance regulation. Self-insurance refers to the practice of employers, particularly large employers, assuming the risks for the health care expenses of their employees instead of purchasing health insurance through insurance companies. Companies concerned about health insurance costs could be interested in screening workers and job applicants who are likely to develop genetically based diseases and could impose high costs on a company's self-insured health program. Similarly, companies could engage in genetic monitoring—

again, to safeguard workers' health while simultaneously reducing the burden of occupational illness on their health care costs. Corporate "wellness" programs, or other company-sponsored health promotion programs (box l-A) that emphasize prevention and encourage employees to adopt healthier lifestyles, are one way companies can limit their health care expenses.

In addition to the obvious and significant benefits from preventing serious illnesses, genetic monitoring and screening for occupationally related disease could provide indirect benefits, such as a reduction in the costs associated with occupational illnesses for employees and their families, employers, the insurance industry, and society. Workplace health risks can produce financial costs to the worker in the form of medical bills, changes in insurance status, lost wages, ill health, and, in some cases, premature death. When a worker incurs an occupational illness, the employer experiences lower productivity levels, higher insurance premiums, workers' compensation claims, and potential lawsuits. Insurance companies either sustain a loss or raise others' premiums. And, society pays for the care and compensation of some with occupational illnesses through Federal health programs. The magnitude and distribution among the sectors of society of the benefits and costs of genetic monitoring and screening will help determine the desirability of this approach to improving occupational health.

HISTORY OF GENETIC MONITORING AND SCREENING

The concept of genetic monitoring and screening surfaced before the discovery of DNA by Watson and Crick in 1953. As early as 1938, noted geneticist J.B.S. Haldane introduced the idea of sorting workers according to their susceptibilities. One of the first cases of an individual's genetic condition reacting to either a chemical agent or drug was reported in the 1950s, when some American soldiers in Korea experienced hemolysis (the destruction of red blood cells). The hemolysis was attributed to their carrier status of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, which results in less of the enzyme G-6-PD in their red blood cells. It was later postulated that carriers of G-6-PD deficiency could also undergo hemolysis after exposure to certain chemicals. The possibility of conducting a preplacement examination to detect employees with the trait was considered.

In the 1970s, there was considerable public interest in nonoccupational screening programs for sickle cell anemia. These programs became the focus of controversy and criticism because proper genetic counseling was not always provided, and results were not always kept confidential. As a result, discrimination sometimes occurred in the workplace, and from insurance companies. (Federal and State legislation in this area is discussed in a later section.)

Incidents of industry involvement in genetic monitoring or screening since the 1960s have been reported. They have varied from research programs using genetic monitoring techniques for evaluating chromosomal damage to efforts in genetic screening to detect conditions such as G-6-PD deficiency or sickle cell trait.

GENETIC MONITORING AND SCREENING IN THE WORKPLACE: A HISTORY OF CONGRESSIONAL CONCERN

Congressional interest in human genetics, genetic diseases, and genetic technologies is not new. In 1972, Congress passed the National Sickle Cell Anemia Control Act (Public Law 92-294), amending it 4 years later to the National Sickle Cell Anemia, Cooley's Anemia, Tay-Sachs, and Genetic Diseases Act (Public Law 94-278). The goals of both pieces of legislation included increased levels of basic and applied research, training, testing, counseling, and public education in the area of screening for sickle cell anemia and other genetic diseases. More recently, congressional interest in human genetics has focused on the mapping and sequencing of the human genome.

The 1983 Office of Technology Assessment Report

In the late 1970s and early 1980s, reports surfacing about genetic monitoring and screening in occupational settings captured the interest of Congress. Concern about scientific and social issues of such testing prompted the House Committee on Science and Technology to hold hearings and request an OTA assessment of *The Role of Genetic Testing in the Prevention of Occupational Disease.*

Box 1-A+ancer Detection in the Workplace

Among the greatest fears of industrial workers is the risk of cancer from exposure to hazardous substances. Although employees are concerned about cancer risk, they are not always informed about the specific dangers of the chemicals with which they work. By increasing employee and employer involvement m cancer prevention and detection, both groups stand to benefit: employees with gains m personal health, and employers with higher worker morale and productivity and reduced health expenditures. Because cancer risks vary from worksite to worksite, worker perceptions of various job hazards related to cancer and chemical exposure are important. From 1978 through 1987, the National Cancer Institute (NCI) allocated $14 million to the Occupational Safety and Health Administration (CM-IA) for cancer prevention training and education of workers. In 1983, NCI awarded grants to five unions, that had participated in OSHA's education program, to evaluate the impact of the unions' cancer prevention and education programs.

A 1987 study by the International United Rubber, Cork, Linoleum, and Plastic Workers of America, ***one*** of the participating unions, questioned approximately 24,000 of its members about their knowledge of chemical hazards, the location of engineering controls, and the usc of daily safety procedures. Prior to the study, employees had participated in the industry's cancer control program, which included worker education.

Despite the fact that over 10,000 different chemicals, many hazardous, are used by these workers, the study found that 22 percent of workers were not sure whether they worked with dangerous chemicals, and only 6 percent felt they were very informed about chemical hazards. Percentages of employees saying they were well-informed varied widely from company to company, ranging from 16 percent at one company to 32 percent at another. Thus, for adequate cancer education, greater understanding of chemical-specific risks is needed.

In addition to worker perception and involvement, management health programs can play an important role. Currently, several companies offer employees cancer screening clinics and other cancer detection programs. One such program, offered by Pennzoil (in conjunction with the Kelsey -Seybold Foundation) to employees at a Texas facility, began in 1984 as a cancer awareness clinic for white-collar employees to discover cancers unrelated to worksite exposure. The Pennzoil program, strictly voluntary and confidential, has since been expanded to industrial petroleum workers and other locations in 22 States, where the cancer detection procedure can include workplace risks.

The Pennzoil program involves an initial lecture on cancer risk and detection, and a personal cancer examination for those requesting one. Corporate management strongly supports these meetings, and encourages employees to attend the lectures. As part of the program, employees also complete questionnaires about cancer risk behaviors and personal medical histories. Those employees showing an increased risk of cancer are offered followup counseling sessions with Kelsey-Seybold Foundation Cancer Prevention Center physicians and medical tests, if necessary, paid for by Pennzoil. AU employees also are offered yearly screening or followup examinations. Pennzoil receives only summary data on participation, cancer detection, and demographic information. Both increased employee morale and detection of potential tumors resulted Along with Pennzoil's expansion of the program, Exxon Chemical Americas has undertaken a similar project with the Kelsey-Seybold Foundation Cancer Prevention Center.

The experience of cancer screening in the workplace suggests that the cooperation of corporate management and private organizations, together with an accurate assessment of employee understanding of workplace risk can create a healthier, more productive working environment; one benefiting both employer and employee. At present, genetic monitoring detects genetic changes that could result in greater risk of cancer. Future advances in genetic technologies could result in increased cancer testing and education at worksites. As genetic technologies make detection of cancer or other health risks more accurate, programs such as those just described could seine as models. For genetic monitoring and screening in particular, implementing successful worker education will be crucial.

SOURCES: Office of Technology Assessment, 1990, based on M. Minkoff, Keky-Seybold Foundation Cancer Prevention Center, Houston, TX, personal communication, October 1988; A.P. Schenck, A.D. Kaluzny, G.M. Hochbaum, et al., "Worker Perceptions and Actions Toward Cancer Control in the Workplace: An Analysis of Baseline Data, " and L.. Zimmerman, G. G. Jackson, J. Hughes, et al., ''Cancer Education and Screening in the Workplace: The Corporate Perspective, Advances in *Cancer Control: The War on Cancer--l5 Years of Progress,* P.F. Engstrom, L.E. Mortenson, and P.N. Anderson (eds.) (New York, NY: Alan R. Liss, Inc., 1987).

As part of its study, OTA surveyed American industry and unions to determine the extent and nature of employer genetic monitoring and screening (the 1982 OTA survey results are compared to the 1989 survey results in a later section).

In the intervening years, several developments have led to renewed congressional interest in assessing the current extent of and issues surrounding genetic monitoring and screening in the workplace. Understanding of human molecular genetics and biotechnologies applicable to the field have expanded enormously. Both the technical capability to detect genetically based disorders and the number of applications of such technologies have increased. Finally, the use of other types of employee testing (e.g., acquired immunodeficiency syndrome (AIDS), drug, and polygraph) as well as the current efforts to map the human genome, also combined to stimulate congressional interest.

Impacts of the Human Genome Project

Efforts underway to map and sequence the human genome stand to have a significant impact on many aspects of biology, medicine, and health-including genetic monitoring and screening. To date, genome projects have accelerated the production of new technologies, research tools, and basic knowledge. At current or perhaps increased levels of effort, they may eventually make possible the control of many human diseases-first through more effective methods of predicting or detecting disease, and ultimately, in some cases, through development of effective therapies based on improved understanding of disease mechanisms. Although not a direct result of the genome project, advances in human genetics and molecular biology have already provided insight into the origins of such diseases as cystic fibrosis, hemophilia, sickle cell disease, and hypercholesterolemia.

The new technologies developed through human genome projects research will also be used to assess public health needs. Techniques for rapidly sequencing DNA, for example, may facilitate the detection of mutations following exposure to radiation or environmental agents. Susceptibilities to environmental and workplace toxicants might be identified as more detailed genetic linkage maps are developed. In addition, special methods of surveillance could be used to monitor individuals at risk.

However, possible applications of and access to these genetic data pose profound ethical questions. The complexity and urgency of these issues will increase in proportion to advances in mapping and sequencing. The human genome project will certainly accelerate diagnostic applications. Progress to date indicates that the ability to diagnose a genetic abnormality precedes the development of therapeutic interventions and that this gap may be growing. Access to this information by third-parties (e.g., insurance companies or employers) and how this information is used are important related issues. These questions are complex and are unlikely to be resolved in the near future. As a means to explore these issues a working group on ethics was established in January 1989 by the Program Advisory Committee on the Human Genome. Additionally, a percentage of the Federal genome budget will go toward studying the ethical issues associated with the genome research.

THE STATE-OF-THE-ART

In 1983, OTA found that none of the genetic tests evaluated met established scientific criteria for routine use in an occupational setting. However, OTA determined that enough suggestive evidence existed to merit further research. Since that time, rapid progress in both human molecular genetics and occupational medicine has increased understanding of causal relationships between disease and environmental factors, including workplace exposure to a variety of substances. This report reexamines the technologies available and evaluated by OTA in 1983 in light of new developments and knowledge in this area. In addition, this report more thoroughly evaluates the area of genetic screening for nonoccupationally related traits and diseases. Finally, it also examines novel techniques (e.g., restriction fragment length polymorphisms (RFLPs)) and tests (e.g., Huntington's disease).

Genetic Monitoring Technologies

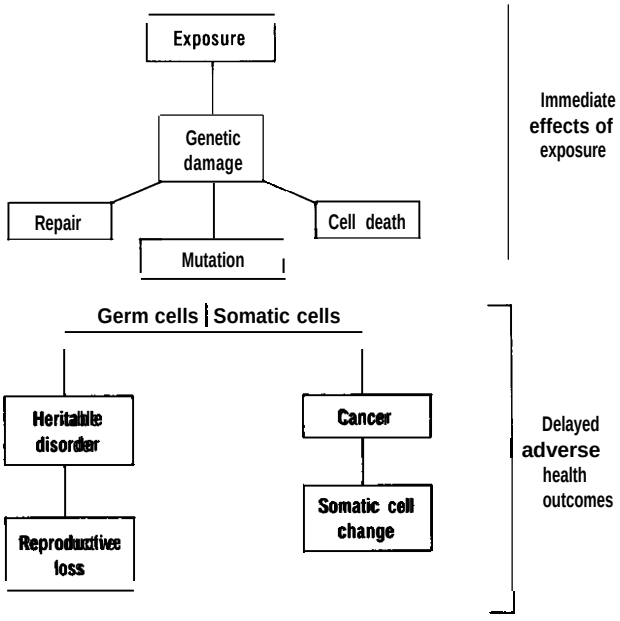
Genetic monitoring ascertains whether an individual's genetic material has altered over time. Workplace genetic monitoring is designed to detect the effects of a toxic substance or its byproducts, and to evaluate the genetic damage caused by such a substance. The objective of these techniques, ultimately, is to predict risk of disease due to genetic damage. When hazards are identified via genetic monitoring, prevention programs can be considered

that will reduce exposures to hazards. This is of particular concern for certain occupational groups that are exposed to such hazardous substances over many years at much higher concentrations than the general population.

It is well-documented that exposure to some chemical substances and to radiation at high doses causes cancer and genetic mutations (changes in genetic information). Not all mutations, however, cause disease (figure 1-4). The relationships between genes, mutations, and disease are becoming clearer with the development of molecular techniques. However, until the health effects of radiation and chemical exposures are better understood, genetic and biological monitoring of exposed populations can only provide a gross indication that genetic changes have occurred and that adverse health effects could follow. Changes in a cell's genetic material (DNA) can be detected at either the chromosomal level, using cytogenetic methods which detect major structural changes in chromosomes, or at the molecular level using noncytogenetic methods.

The application of cytogenetic tests to measure chromosomal damage is based on the concept that

Figure 1-4-Biological Consequences of Exposure to Mutagenic Agents



SOURCE: office of Technology Assessment, adapted from J.B. Ward, 'Issues in Monitoring Population Exposures," *Carcinogens and Mutagens in the Environment Volume //, The* Workplace, Hans F. Stich (cd.) (Boca Raton, FL: CRC Press, 19S5).



Photo credit: U.S. Council for Energy Awareness

A Nuclear Power Worker: Controversy continues regarding the carcinogenic effects of radiation in employees of the nuclear weapons and nuclear power industries.

damage to cells' genetic material represents initial events in a process that may eventually lead to disease. Cytogenetic methods can detect human exposures at biologically significant levels in populations, but the interpretation of findings for the individual remain uncertain. In some cases, detectable mutations result from gross changes in chromosome structure and can be visualized under the microscope. The disruptive effects of mutagens on chromosome structure, organization, and behavior have long been studied by geneticists. However, the connections between chromosomal damage and disease are unclear except in a small number of cancer cases. Most analysts agree that interpretation of cytogenetic results at the individual level is questionable and recommend that until the relationship between cytogenetic damage and disease is better understood, interpretation should be limited to the population level. In addition, cytogenetic monitoring of human populations is expensive and time-consuming. There can also be technical variations associated with both test limitations and interpretations.

Until recently, most tests for mutagenicity have been merely indicators of exposure, only providing evidence that exposure has occurred. This limitation is diminishing with the development of more techniques at the molecular level, thus refining the ability to document exposure and, in some cases, providing qualitative information. New molecular assays of mutagenicity, e.g., hypoxanthine-guanine phosphoribosyltransferase and oncogene protein detection, are providing greater specificity and will

augment tests already in use, e.g., the Ames test. New methods may provide better estimates of the health effects of low doses of some mutagens, as well as providing qualitative data on the nature of mutation. Detecting activated oncogenes and DNA adducts has the potential of predicting disease in asymptomatic individuals. As the nature of mutation becomes more clearly defined, the connection between mutation and disease will also become better understood.

A genetic monitoring or screening test must be proved valid and reliable before a decision can be made on its value. Validity is the probability that a test will correctly classify true "positive" and true ''negative' results. Tests of the same specimen must repeatedly give the same result whether performed by several different laboratories or by the same laboratory on several occasions to be reliable. If the tests are valid and reliable, establishing procedural safeguards and designing well-conceptualized test protocols can avert erroneous and misleading conclusions. The use of genetic monitoring methods in epidemiologic studies will continue to be plagued by problems associated with classical approaches to determining hazardous exposures in the workplace. Eliminating biases, obtaining controls, and keeping good records are procedural difficulties that may be encountered. The employment of more specific and sensitive tests, rather than the reliance on any one test for valid and reliable results, will lead us closer to understanding the relationships between exposure, mutation, and disease.

Genetic Screening Technologies

It has long been speculated that genetically determined variation in susceptibility may predispose some workers to occupational disease while others in the same environment seem to be unaffected. Genetic influences may be exaggerated or diminished by one's age, diet, or overall health status. Recognition of genetic factors in disease (both occupationally and nonoccupationally related disease) presents new opportunities for detection, prevention, and treatment.

In assessing the state-of-the-art in screening tests for use at worksites, three different questions must be discussed:

- What general techniques are presently available that could be used for genetic screening?
- What is known about the association among heritable traits, exposure to hazardous materials, and subsequent occupational illness?
- What genetic disorders unrelated to job exposures that are important to general health can be detected?

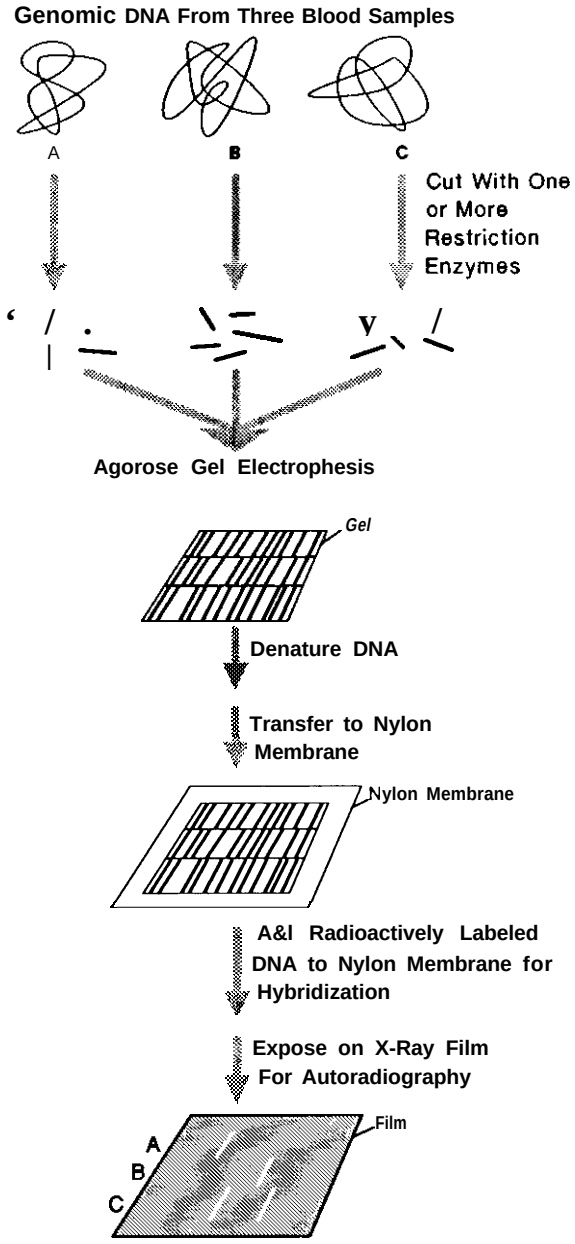
Since the 1983 OTA report, there have been several technical advances in genetic screening tests. In addition, several new susceptibilities to occupational disease have been identified, and progress in detecting some nonoccupationally related disorders has been made. These nonoccupationally related disorders, which are likely to affect large populations, might be of interest to an employer if they can be detected through preemployment screening.

Biochemical and molecular techniques for detecting genetic disease are discussed in this report. Biochemical genetics refers to the analysis of mutant genes on the basis of altered proteins or metabolizes. If diagnosed, some of these "inborn errors of metabolism" can be treated with enzyme replacement or dietary control. An example of such a biochemical disorder is phenylketonuria, which can be controlled by restricting dietary intake of the amino acid phenylalanine. In general, biochemical techniques for diagnosing genetic disease are often restricted to indirect analysis of gene products rather than diagnosis targeted at the gene itself.

Advances in DNA technology have greatly enhanced our ability to directly examine the genetic basis for disease and to predict and diagnose such diseases in larger populations. Until recently, most available tests for genetic conditions were not based on recombinant DNA techniques. Today, DNA-based tests encompass a variety of standard diagnostic techniques that allow examination of regions very near the genes (e.g., Huntington's disease) or direct examination of the genes themselves (e.g., sickle cell anemia and cystic fibrosis).

Two important tools, RFLPs, which serve as markers for the presence of a diseased gene, and cloned DNA probes, represent the major advances responsible for improved diagnosis of genetic disease (figure 1-5). Another technology, polymerase chain reaction (PCR) has also facilitated the ability to detect genetic disorders. PCR can be thought of as molecular photocopying (figure 1-6). PCR itself is not used directly to analyze DNA, but allows a scientist to take a sample that ordinarily would be insufficient to detect the characteristics of the DNA,

Figure 1-5-Detection of Restriction Fragment Length Polymorphisms Using Radioactively Labeled DNA Probes



Variations in DNA sequences at particular marker sites are observed as differences in numbers and sizes of DNA fragments among samples taken from different individuals (shown here as samples A, B, and C).
SOURCE: Office of Technology Assessment, 1990.

and reproduce it until enough DNA copies are available for examination by a number of technologies, including RFLP analysis. Chapter 5 discusses RFLP analysis and PCR in greater detail.

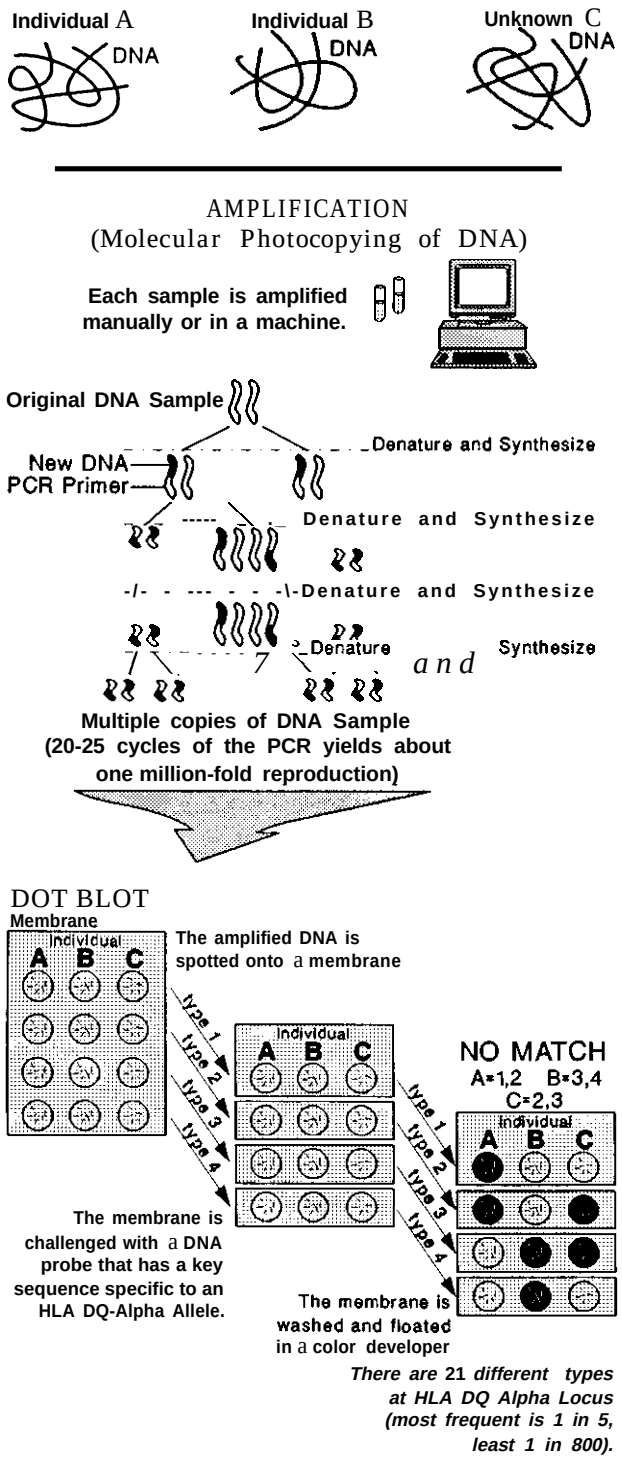
The obstacles to understanding associations between predisposition and disease are slowly eroding as the use of synthetic probes, PCR, and automated DNA-sequencing machines increase the efficiency and lower the cost of mass screening. However, before widespread screening of populations is begun, the validity of the tests should be determined. Also, quality control is likely to become a major issue as the volume of tests performed at laboratories grows. These are already issues in forensic applications of DNA-based tests.

At present, there are approximately 50 diseases that have the potential to enhance an individual's susceptibility to the toxic or carcinogenic effects of environmental agents. These occupationally related diseases include: G-6-PD deficiency, sickle cell trait, and the thalassemias (see table 1-1 for more examples).

Molecular biology has enhanced the traditional determination of "predisposition to disease' (previously based on physical examination, family history, and lifestyle habits) by seeking out and finding genes or markers associated with disease. Individuals found to have the gene or the marker can then be identified, sometimes with near certainty, to be candidates for disease. Often, predisposition only manifests in disease when there is an accompanying environmental insult, e.g. toxic substances, viruses, or other disease. The influence of the environment, however, remains the wild card in most cases, because possession of the genetic predisposition alone may be insufficient to cause disease. It is likely that for some time modern science will be more successful in identifying the genes and the markers than in identifying the environmental agent(s) necessary for activation of the predisposing genes.

Predispositions to certain cancers have been the focus of much research in the past few years. As the associations between carcinogenesis and genetics become clearer, the boundaries between occupational and genetic disease may become more blurred. (Box 1-B describes some of the connections between genetic damage and cancer.) Research on the predispositions to atherosclerosis, diabetes, mental illness, and chemical addiction has also progressed in recent years. In addition, research is providing insight into possible genetic predispositions to such common ailments as lower back injuries, obesity, allergies, and arthritis. While

Figure 1-6-The Polymerase Chain Reaction



SOURCE: Office of Technology Assessment, 1990.

predictive tests are not immediately foreseeable in any of those areas, as more populations are studied and more linkage maps prepared, it is possible that screening tests will be developed.

With accelerating interest in tests to detect abroad range of genetic disorders and increasing investment in biotechnology industries, the market demand for tests, especially DNA-probe tests, is expected to expand. While the population affected by genetic conditions for which tests are available is still somewhat small, the potential future test population for multifactorial diseases is enormous (see table 1-2).

WHAT LEGAL CONSIDERATIONS ARE INVOLVED?

Existing legal concepts must strain to keep pace with the scientific advances of genetic monitoring and screening. Only a limited body of law dealing directly with genetic monitoring and screening in the workplace exists. There is, however, a substantial body of law pertaining to the related practice of medical testing of workers, which may influence the legal issues associated with genetic monitoring and screening in the workplace.

Because an individual's genetic makeup is not chosen, legal questions of the most sensitive sort are raised in seeking to analyze these personal characteristics. Genetic monitoring and screening raise legal questions related to workplace safety and employee rights. Among the fundamental legal issues arising from genetic monitoring and screening in the workplace are:

- privacy from unwanted monitoring or screening;
- confidentiality of the information obtained;
- potential discrimination in employment opportunities; and
- ultimately, the health of the subject.

OTA examined common and statutory law—both of which have a bearing on genetic monitoring and screening in the workplace. Changes in the common law relating to workplace genetic monitoring and screening have been incremental over recent years. An increasing body of case law is developing, however, over employer screening for drug use and AIDS.

Table I-I-Identification and Quantification of Genetic Factors Affecting Susceptibility to Environmental Agents

High-risk groups	Estimated occurrence	Environmental agents to which group is (may be) at increased risk
RBC conditions		
G-6-PD deficiency	American Black males 16%; Mediterranean Jewish males 119'.; Greeks 17.-2%; Sardinians 1%-8%	Environmental oxidants such as ozone, nitrogen dioxide, and chlorite
Sickle cell trait	7Y0-13Y0 of American Blacks are heterozygotes	Aromatic amino and nitro compounds; carbon monoxide, cyanide
The thalassemias	Alpha: 4%-5% in Americans of Italian and Greek descent; Beta: 2%-7% American Blacks and 2%-3% American Greeks	Lead; benzene
NADH dehydrogenase deficiency (MetHb reductase deficiency)	Estimated 1% of population are heterozygotes	MetHb-forming substances
Catalase Hypocatalasemia	About 2% of U.S. population based on Swiss gene frequency	Ozone; radiation
Acatalasemia	1/10,000-20,000 of U.S. population based on Swiss gene frequency	
Low SOD activity	Frequency of genetic variants in population 1 to 2/10,000; normal population exhibits unimodal distribution; persons at low end of distribution may beat increased risk	Wide variety of environmental oxidants; paraquat; radiation; ozone
ALA dehydratase deficiency	Unknown, but thought to be rare	Lead
Hb M	Unknown, but rare	Carbon monoxide
Erythrocyte potphyria	1.5/100,000 in Sweden, Denmark, Ireland, West Australia; 3/1 ,000 in South African Whites; rare in Blacks	Chloroquine; hexacholorobenzene; lead; various drugs, including barbiturates, sulfonamides, others
GHS-Px deficiency	Rare	Environmental oxidants
GSH deficiency	Rare	Environmental oxidants
Liver metabolism		
Defect in gluocuronidation		
Gilbert's syndrome	6% of normal, healthy adult population	Wide variety of xenobiotics including polychlorinated biphenyls
Crigler-Najjar syndrome	Few persons live to adulthood	
Defect in sulfation	Unknown	Wide variety of xenobiotics; best association is with tyramine-containing foods
Acetylation phenotype, slow v. fast	Slow: 50% Whites; 50% Blacks; 10% Japanese Fast: 50% Whites; 50% Blacks; 90% Japanese	Aromatic amine-induced cancer; numerous drugs, e.g., isoniazid and hepatitis
Gout	0.27%-0 .3%. prevalence in U.S. and Europe	Lead
Oxidation center defects	9% of British Whites; 8% of Nigerians; 6% Ghanians; 1%. Saudi and Egyptians are poor oxidizers	Numerous xenobiotics requiring oxidative metabolism for detoxification
OCT deficiency	Unknown, but thought to be rare	Insect repellant (DET)
Paraxonase variant	25%-30% of population	Parathion
Rhodanese variant	Unknown	Cyanide
Sulfite oxidase deficiency heterozygotes	Unknown	Sulfite, bisulfite, sulfur dioxide
Inadequate carbon disulfide metabolism	Upward Of 30%-40%	Carbon disulfide
Alcohol dehydrogenase variant	5%. English; 20% Swiss; 70% Japanese	Metabolize (e.g., ethanol) more quickly than normal
Wilson's disease	Homozygous 1/100,000 while the heterozygote may approach 1/500	Cooper, vanadium
Serum variants		
Albumin variants	Less than 1/1 ,000 in Europeans, much higher frequency in North American and Mexican Indians	Unknown
Pseudocholinesterase variants	Highly sensitive homozygous and heterozygous persons of European ancestry have combined frequency of about 1/1,250; moderately sensitive genotypic variants of European ancestry have frequen cy of 1/1 5,000	Organophosphate and carbamate insecticides; muscle relaxant drugs

* Abbreviations used are: G-6-PD, glucose-6-phosphate dehydrogenase; NADH, nicotinamide adenine dinucleotide (reduced form); SOD, superoxide dismutase; ALA, aminolevulinic acid: GSH, reduced glutathione; Px, peroxidase; OCT, ornithine carbamoyl transferase; IgA, immunoglobulin A; PKU, phenylketonuria; PTL, phenylthiourea; XP, xeroderma pigmentosum; AT, ataxia telangiectasia; FA, Fanconi's syndrome.

SOURCES: E.J. Calabrese, *Ecogenetics: Genetic Variation in Susceptibility to Environmental Agents* (New York, NY: Wiley Interscience, 1984); E.J. Calabrese, "Ecogenetics: Historical Foundation and Current Status," *Journal of Occupational Medicine,* 28(10):1096-1102, 1986.

Box 1-B--Genetics and Cancer

Cancer is a genetic disease arising from genetic damage of diverse sorts—recessive and dominant mutations, large rearrangements of DNA and point mutations--all leading to distortions of either the expression or biochemical function of genes. The growing field of cancer genetics aims to uncover the genetic alterations responsible for uncontrolled growth of cancer cells. Many types of human cancer occur in familial as well as sporadic forms. Discrete genetic changes have been associated with different types of neoplasm, and are thought to initiate or cause progression of cancer. Chromosome studies in more than 10,000 cases of neoplasm have reported specific anomalies. The identification of genetic changes, therefore, presents the major diagnostic challenge in cancer.

Both dominant and recessive forms of cancer have been found. The genetics of the common cancers--breast, colon, and lung-are beginning to fit a pattern, Approximately 5 percent of cancer cases constitute a hereditary cancer syndrome in which a dominant gene predisposes to cancers of the breast, ovary, brain, gastrointestinal system, and white blood cell precursors. These are referred to as "cancer families' (see ch. 5 for further discussion). Apart from these, each type of cancer appears to have a small group of cases that fits the pattern of a major predisposing gene and a much larger group that seems to be largely environmenta1 in origin.

In addition, examples such as xeroderma pigmentosa imply that there is a connection between susceptibility to cancer and impaired ability of cells to repair damaged DNA. It is a reasonable expectation that if cancer is related to alterations in somatic cell genes, then the rate at which those changes occur could serve as a barometer of changes in the gem-dine that may not be expressed for many generations to come.

Certain cancers, e.g., lung, laryngeal, bladder, and testicular, have repeatedly been linked to environmental exposures. The effects on chromosomes of such chemicals as arsenic, asbestos, chromium, nickel, and vinyl chloride are well-documented. Substances that cause chromosomal abnormalities are called ''clastogens. The reader is referred to the 1983 Office of Technology Assessment report for more detail on the specific effects of those agents. Chapter 5 describes recent advances in detecting predisposition to some common cancers.

SOURCES: Office of Technology Assessment, 1990, based on J.M. Bishop, "The Molecular Genetics of Cancer, " *Science* 235:305-311, 1987; F. Mitelman and J.D. **Rowley, "Genes,** Chromosomes and Cancer: A New Forum for Research in Cancer Genetics," Genes, *Chromosomes & Cancer* 1:1-2, 1989; J.J. Nora and F.C. Fraser, *Medical Genetics: Principles and Practice* (Philadelphia, PA: *Lea* & Febiger, 1989); R. Parshad, K.K. Sanford, *K.H. Kraemer,* et al., ' 'Carrier Detection in Xeroderma Pigmentosum," *The Journal of Clinical Investigation* 85: 135-138, 1990; U.S. Congress, Office of Technology Assessment, *The Role of Genetic Testing in the Prevention of Occupational Disease,* OTA-BA- 194 (Washington, DC: U.S. Government Printing office, April 1983).

Of particular interest in terms of common law developments is the apparent continuing expansion of the public policy exception to the employment at-will doctrine for dismissal from employment. This rule forms the basis for most employment relationships, absent an explicit contract between the parties, and gives the employer virtually unlimited authority to terminate the employment relationship at any time. It includes the right to refuse to hire an individual because of a perceived physical inability to perform the job and the right to terminate employment because of a belief that the employee is no longer able to perform adequately. With respect to genetic monitoring and screening, this would allow an employer to use either in any way, including personnel decisions. Even if test results were inaccurate or unreliable, the employer would be protected in basing employment actions on them. In recent years, however, courts have begun to erode the scope of the at-will doctrine by creating exceptions. While exceptions to employment-at-will have grown to cover different grounds for dismissal, they have not been applied to other kinds of employment actions. This trend may also play an important role in forming judicial attitudes toward employment decisions based on genetic monitoring and screening results.

Beyond the role of occupational health and safety regulation, common law decisions regarding confidentiality and privacy are relevant to genetic monitoring and screening in the workplace. An area of concern is the role of the occupational health physician in genetic monitoring and screening. Because the occupational health physician is hired by the employer, there can be some question whether legal precedents protecting confidentiality in the physician-patient relationship apply, Occupational health physicians must balance patient privacy and confidentiality on the one hand with employer need-to-know on the other.

Table 1-2—Genetic Tests Available and Total Americans Affected

Genetic condition	Total cases
Currently ***available:***	
Adult polycystic kidney disease	500,000
Fragile X Syndrome	100,000
Sickle cell anemia	65,000
Duchenne muscular dystrophy	32,000
Cystic fibrosis	30,000
Huntington's disease	25,000
Hemophilia	20,000
Phenylketonuria	16,000
Retinoblastoma	10,000
Total	798,000
Potential future tests:	
Hypertension	58,000,000
Dyslexia	15,000,000
Atherosclerosis	6,700,000
Cancer	5,000,000
Manic-depressive illness	2,000,000
Schizophrenia	1,500,000
Type 1 diabetes	1,000,000
Familial Alzheimer's	250,000
Multiple sclerosis	250,000
Myotonic muscular dystrophy	100,000
Total	89,800,000

SOURCE: *Medical World News,* p.58,Apr. II,1988.



Photo credit: Margaret Anderson

U.S. Department of Labor, Washington, DC: Headquarters of the Occupational Safety and Health Administration.

Federal Regulatory Framework

Federal legislation ranging from the Occupational Safety and Health Act (OSH Act) (Public Law 91-596), the Rehabilitation Act of 1973 (29 U.S.C. 791 et seq.), Title VII of the Civil Rights Act of 1964 (42 U.S.C. 2000e), the National Labor Relations Act (NLRA) (29U.S.C. 151 et seq.), and the Americans with Disabilities Act (ADA) (Public Law 101-336) provide some protections against abuses, particularly those relating to unilateral employer imposition of genetic monitoring and screening, discrimination based on monitoring and screening results, and breaches of confidentiality concerning results.

The OSH Act contains several federally imposed statutory duties related to occupational safety and health that must be carried out by the employer. The Occupational Safety and Health Administration (OSHA) has regulated some employer practices that could have a bearing on genetic monitoring and screening, including employee access to medical records and communications about hazards by employers to employees.

Title VII of the Civil Rights Act of 1964 prohibits discrimination in employment practices based on race, color, religion, sex, or national origin. In addition to intentionally discriminatory actions, neutral employment practices that have a disparate impact on a protected group may violate Title VII. A Supreme Court decision, *Wards Cove v. Atonio,* recently placed stringent standards on workers attempting to use statistics to prove discriminatory employment practices. This decision could make it more difficult for an employee to prove that an employer's employment practices are discriminatory. Many genetic screening procedures (e.g., sickle cell disease, G-6-PD deficiency) have a disparate impact that could fall under the protection of Title VII.

The Rehabilitation Act of 1973 bans discrimination against handicapped individuals by employers who are government contractors or recipients of Federal assistance. In order to fall under its protection, an employee must prove that his or her genetic trait is or is regarded as an impairment, and in addition, he or she must otherwise be qualified. Accordingly, an individual with a genetic predisposition for a disease may not be denied employment or promotion simply because of the predisposition so long as the individual is otherwise qualified for the position. In such a case, the



Photo credit: Earl Dotter

The use of protective clothing can help prevent occupational illness and injury.

employer would have to make reasonable accommodation for the person.

ADA, which was recently signed into law and whose enforcing regulations have yet to be drafted and approved, extends a clear and comprehensive prohibition of discrimination on the basis of disability to the private sector. It bans discrimination against individuals with disabilities in hiring, discharge, compensation, or any term, condition, or privilege of employment by an employer engaged in an industry affecting commerce. By 1994, this legislation will apply to all employers with 15 or more employees. Whether a genetic marker or a trait constitutes an 'impairment' under ADA is unclear. Preemployment medical examinations or inquiries are to be used only as a tool for determining the applicant's ability to do the job. Thus, genetic screening for nonoccupationally related conditions would seem to be prohibited. ADA language, however, does not specifically address genetic monitoring or screening.

NLRA governs the relationships of employees, labor organizations (unions), and employers engaged in businesses affecting interstate commerce. Safety and health matters, including fitness-for-duty physical examinations and medical testing are considered mandatory subjects of bargaining between these parties. Thus, genetic monitoring and screening could be considered mandatory subjects of collective bargaining. In this context however, preemployment screening of job applicants would not be covered. Additionally, not all employees are union members and therefore would not be covered under collective bargaining agreements.

The protections provided by current Federal legislation are somewhat disjointed, applying at times to applicants and at times to workers, or offering protections of which applicants and workers may be unaware. The exact role of each will depend on the nature of the tests that are developed and their application. While it is clear that many legal tools presently exist, it is probable that new ones will be needed as unexpected challenges arise.

On the whole, it appears that Federal regulatory law, as administered by OSHA, is likely to have the most immediate impact on the use of genetic monitoring and screening in the workplace. OSHA has dealt extensively with related practices of biological monitoring that could forma ready source of rules for genetic monitoring and screening. OSHA's rules on access to medical records and hazard communication are among the most directly applicable sources of existing law. Thus, OSHA is the most appropriate candidate for regulating in the area of genetic monitoring and screening in the workplace. It could call on the National Institute for Occupational Safety and Health (NIOSH) to provide research and recommendations for regulatory development. However, at this time the OSH Act neither prohibits nor requires genetic monitoring or screening.

State Responsibility

States have a role in a variety of areas concerning genetic monitoring and screening. One of these areas is workers' compensation programs which are designed to provide no-fault compensation to workers suffering harm as a result of their employment. A particular challenge is posed, however, by diseases with long latency periods between exposure to a causative agent and onset of illness. It is the compensation of such long latency conditions that presents the most likely opportunity for the application of genetic monitoring and screening. Many issues concerning genetic monitoring and screening and workers' compensation (e.g., the role of genetic

data as evidence and their admissibility, and the coverage of a susceptible employee) are unresolved.

Some States have directly addressed genetic discrimination. OTA found in 1983 that four States had passed statutes limiting the use of genetic information in employment decisions. In three of these States—Florida, Louisiana, and North Carolina-the laws are specific to testing for sickle cell trait. In New Jersey, however, a fairly broad measure was passed banning employment discrimination based on genetic traits. If this measure becomes a model for other jurisdictions, the adverse impact, and perhaps benefits, of genetic monitoring and screening results on employees could be severely curtailed. The New Jersey experience will be interesting to observe as more genetic monitoring and screening tests become available.

WHAT ETHICAL ISSUES ARE INVOLVED?

Genetic monitoring and screening involve the acquisition of personal information in the workplace. Several important ethical issues arise when discussing the interests of employees, job applicants, employers, and society, including the potential for discrimination. Many of these issues express the same concerns as current laws: legal and ethical arguments often share common ground.

Yet, while legal and ethical issues can be similar, approaches to resolve dilemmas raised differ. Law does not reflect all moral values held by members of society, nor can it necessarily be used to resolve ethical dilemmas. Ethical arguments about the use of genetic monitoring and screening in the workplace often address obligations, rights, or values not explicitly covered by law. Awareness of the ethical issues surrounding new technology is essential for formulating and implementing policies that reflect the greatest possible regard for human values.

Although the ethical issues show little change since the 1983 OTA study, the emphasis placed on some concerns about genetic monitoring and screening has shifted. In 1983, OTA found that genetic monitoring and screening were not inherently unethical, and that if they were used to enhance worker health in a reamer consistent with ethical principles, they could be morally justified. Whether the tests were consistent with ethical principles depended on how they were done and how the resulting information was used. Since that time, there has been increased pessimism in public debate about the risks genetic screening for nonoccupationally related disease could have for employees' autonomy and privacy. Attention has shifted from the uncertain technical efficacy of genetic monitoring and screening in predicting or identifying illness to the potential abuses of genetic monitoring and screening in the workplace.

At least three parties play a role and have an interest in genetic monitoring and screening in the workplace--job applicants and workers, employers, and society. For these parties, three principal issues exist:

- the implementation of genetic monitoring and screening tests in the workplace and the use of the information they generate;
- the dissemination and storage of information gained from genetic monitoring and screening; and
- the role of genetic counseling for both employers and employees in genetic monitoring and screening programs.

Each of these issues is probably viewed differently by job applicants and employees, employers, and society, since each group has different interests to protect. In addition, the ethical issues associated with genetic monitoring and screening in the workplace vary according to whether the test performed is genetic monitoring for chromosomal damage, genetic screening for susceptibilities to occupational illness, or genetic screening for inherited conditions or traits unrelated to the workplace.

Employees and job applicants, for example, want to protect their autonomy and privacy. They could feel that all genetic information should remain confidential under any circumstance, especially if it might be used to deprive them of a job, health insurance, or other benefit (box l-C). Employers, in desiring to preserve their liberty to make their own hiring decisions, might want to be free to conduct monitoring or screening programs. They might also wish to establish the conditions for employee participation and consequences for those who refuse to participate. Such practice would be consistent with current preemployment medical testing practices. Society has an interest in promoting a safe workplace, and fair treatment of individuals, as well as economic efficiency.

Box 1-C-An International Survey of Attitudes of Medical Geneticists Toward Workplace Genetic Screening and Access to Results

A survey on mass genetic screening was sent to 1,053 medical geneticists in 18 nations, of whom 677 responded. Geneticists strongly preferred voluntary over mandatory workplace screening, by a 72 percent majority. In the United States, there was consensus (greater than 75 percent) that screening should be voluntary. Geneticists who thought screening should be voluntary cited the worker's autonomy or right to decide (74 percent), and the danger of stigmatization, discrimination in employment, or misuse of information by institutional third-parties (41 percent). Advocates of mandatory screening cited protecting the individual worker's health (64 percent), protecting public health (51 percent), and efficiency or cost-benefit arguments (22 percent). Nine percent of those who advocated voluntary screening and 12 percent of those who advocated mandatory screening based their responses in part on concern for economic interests of employers.

In advocating voluntary versus mandatory screening, a clear difference of opinion on whose welfare the respondent placed foremost was reported. Ninety-seven percent who advocated voluntary screening and 58 percent who advocated mandatory screening placed the worker's welfare as most important. Three percent who advocated voluntary screening and 37 percent who believed in mandatory screening placed societal interests first. Only 1 percent placed the employer's welfare first.

Advocates of voluntary screening were more likely than supporters of mandatory screening to describe a conflict of interest between worker and employer, 34 percent described such conflicts, as opposed to 13 percent who advocated mandatory screening. A majority of both groups, however, described no conflicts.

Ninety-eight percent of respondents said the worker should have access to test results, including 86 percent who said the worker should be told the results even if he or she did not ask for them. When asked whether the employer should have access to genetic screening results, 81 percent said employers should have no access without the worker's consent, including 22 percent who believed that employers should have no access at all.

Thirty percent of respondents who gave reasons for their choices about access believed it would be to the worker's benefit if the employer had some form of access, e.g., employers could shift susceptible workers to less dangerous jobs. Only 6 percent of respondents, however, thought that working conditions m general would be improved. Nineteen percent described potential economic disc rimination, stigmatization, or other misuse of test results by employers. Ten percent based their responses on the economic interests of the employer.

When asked whether government health departments should have access, 68 percent said there should be no access without worker consent. There was a strong consensus on this issue in six nations, including the United states.

These differences in perception indicate that geneticists-those in a position to conduct genetic screening tests-share concerns about how genetic screening might be used in the workplace. A large majority of geneticists ranked the interests of workers and society above those of employers in importance, but they disagree about how those interests can be best protected. Many geneticists believe that workplace screening should be voluntary and that workers should make autonomous decisions about whether to undergo genetic screening. Almost all geneticists believed workers should receive genetic screening results, but that employers' access should be restricted 'hey expressed concern that genetic screening results may be used to justify personnel actions that may stigmatize or discrimina te against some workers.

SOURCE: D.C. Wertz and J.C. Fletcher, "An International Survey of Attitudes of Medical Geneticists Toward Mass Screening and Access to Results," *Public Health Reports* 104(1):35-44, 1989.

A balance must be struck between promoting one party's autonomy and compromising that of another. If employers are free to implement and enforce genetic monitoring or screening policies, the autonomy of job applicants and employees will be limited. Conversely, giving the applicant or employee complete freedom to protect his or her own interests would restrict the freedom of the employer and, in some instances, present risk to co-workers or family.

Employer and employee interests can conflict at three points in the processes of genetic monitoring and screening:

- the decision to undergo genetic monitoring or screening;
- access to information gained from genetic monitoring or screening; and
- the communication and interpretation of genetic monitoring or screening results.

Certain broad guidelines for the use of genetic monitoring and screening could at least partially address the concerns of all parties. Such guidelines could produce maximal benefits to all parties—minimizing occupational illness without threatening privacy or confidentiality, denying equality of opportunity, or stigmatizing workers.

GENETIC COUNSELING FOR INDIVIDUAL USES OF GENETIC INFORMATION

The effects and results of genetic monitoring or screening transcend the workplace, and raise issues for the individual who is tested-not just as a worker—but as a person and family member. As a result of new technical capabilities to diagnose and predict genetically based disease, pathways for informed decisionmaking about ourselves and our family's health have expanded. However, these capabilities often create moral, ethical, and psychological dilemmas for which no easy solutions exist. Receiving such personal information in the workplace setting differs from the way most people learn about their genetic identity, because the individual may not have sought to be tested. When tests are conducted in a medical setting, a context is provided in which certain assumptions and expectations can reasonably be held by the person being tested. These factors might be different when the workplace becomes the background for receiving genetic information.

For many individuals, even considering whether to undergo genetic monitoring or screening constitutes a life crisis because of the possible outcomes. If the results are positive, the crisis obviously is exacerbated. How the results will affect the individual has much to do with the individual's own frame of reference, but also with the implications of the condition and its prognosis. Psychological issues permeate every aspect of genetic consultation. In addition to the intrapsychic consequences of receiving genetic information, there are potential impacts on family. Genetic information affects not only the individual, but also the spouse, parents, grandparents, siblings, and children. Social and psychological stress, as well as future financial and emotional burdens, can strain family functioning. In addition to coping with their own uncertain future, individuals may experience guilt or grief if they find they have unknowingly passed a deleterious trait to their offspring.

Obviously, the psychological impact of a positive diagnosis varies with its severity and treatability, and the fact that different families will react uniquely to similar situations. Support, counseling, and followup are likely to assist individuals and their families in coping with positive test results. The knowledge and skills of a properly trained counselor can help the individual understand the diagnosis, recurrence risk, prognosis, relevant preventive and therapeutic measures, and also aid in communicating important information to other family members.

However, doubts can be introduced into the lives of those tested because genetic monitoring and screening tests often convey a probability, but not a certainty, that disease will appear. When it is not possible to give an accurate recurrence risk or more than a general diagnosis, the interactions between the test subject and the test administrator are even more complex. In the case of genetic monitoring, it is likely that nonspecificity of diagnosis and prognosis will predominate. Further complicating the use of monitoring and screening tests is the fact that for most genetic diseases, effective



Photo credit: Diane Baker

A genetic counselor showing a chromosome chart to a client. Genetic counseling may assist individuals and families cope with positive test results.

Box 1-D--Huntington's Disease

Huntington's disease is **a chronic, progressive, degenerative disorder, beginning usually between the ages of** 30 and 50 years. It is characterized by uncontrollable, spasmodic movements in the face and extremities, as well as gradual loss of mental faculties, ending in dementia. The disease is lethal and incurable; death usually occurs on average 15 to 17 years after disease onset. The disease is transmitted as an autosomal dominant trait; offspring of an affected individual have a 50 percent chance **of developing the disease. The test for the Huntington's** gene is **most** often performed on an asymtomatic individual. If someone has the gene, that person will definitely **develop the disease. Symptoms for the disease usually begin past the typical childbearing years, between ages *35 to*** 45.

The test provokes considerable anxiety among those at risk who elect to take it. Not all of those at risk choose to be tested, even though there is a 50 percent chance that they will receive good news Prior to the availability of a predictive teat for Huntington's disease, surveys indicated that between 56 and 85 percent of those at risk would avail themselves of the test. In a survey conducted after the test became available, less than 14 percent of the sample population at risk elected to take the test.

In another survey, 66 percent of the sample population at risk said they wanted the test. Of that group, 15 percent said they might **commit suicide if the test were positive. Of the group that chose not** to be tested, 30 percent feared **they might be suicidal and therefore did not want their fears confirmed. For some people, uncertainty appears to be preferable to certainty.**

A recent study on the psychological reaction of people being tested for the disease found no clear increase in psychiatric illness among people who tested positive for the Huntington's gene. People's reactions to their test results ranged from "extreme joy and relief to disappointment, sadness and demoralization." This study suggests that **people cope well with this type of information if they are carefully screend, counseled, and provided followup care. In addition, it suggests that those who test positive should be given appropriate long-term monitoring.**

SOURCES: Office of Technology assessment, 1990; based on C. Mastromauro, R.H. Myers, and B. Berkman, "Attitudes Toward Presymtomatic Testing in Huntington's Disease," American Journal of Medical Genetics 26:271-282, 1987; K. A. Quaid, J. Brandt, and S.E. Folstein, "The Decision To Be Tested for Huntington's Disease," Journal of the ***American Medical Association*** **257:3362 (letter),** 1987; B. Teltacher and S. Polgar, "Objective Knowledge About Huntington's Disease and Attitudes Toward Predictive Tests of Persons at Risk," *Journal of Medical Genetics* 18:31-39, 1981; A. *Tyler* and P.S. Harper, "Attitudes of Subjects at Risk and Their Relatives *Toward Genetic Counseling in Huntington's Chorea,"* **Journal of Genetics 20:179-188, 1983.**

interventions are not yet feasible (box l-D). Employers undertaking genetic monitoring and screening programs should anticipate the complexity of interpretation and communication of test results.

The workplace is an atypical setting for receiving information of such personal importance. It should not be overlooked that when genetic monitoring or screening are used in the workplace, the focus of the tests--the person—is being provided with information that could have a significant impact on decisions unrelated to employment: marriage, procreation, and lifestyle. The absence of referrals to trained professionals and reimbursement for the costs of additional tests or counseling may be prohibitive factors influencing an individual's ability to obtain additional information. Genetic counseling and appropriate referrals for those at risk should accompany the use of either genetic monitoring or screening.

SURVEY OF THE USE OF GENETIC MONITORING AND SCREENING

To assess the current practice of genetic monitoring and screening by U.S. employers, a survey was conducted for OTA from March 24 to July 15, **1989,** by Schulman, Ronca, & Bucuvalas, Inc. This effort is a followup to a **1982 survey that was part of the 1983** OTA report. As with the earlier survey, the core remained a national survey of the ***500*** largest U.S. industries (Fortune **500), 50 largest utilities, and 33 major unions. The 1989 survey was designed** to provide comparability to the earlier survey in terms of populations sampled and the questionnaire content. The **1989 survey, however, did not exactly duplicate the 1982 questionnaire. Rather, it was designed to remove ambiguities that might have been present in the initial survey, but could be detected only in hindsight. It also was designed to include a representative sample of all other compa-**

Table 1-3-Summary of Methodology

Samples	
Fortune 500 companies . .	Sampled in 1989 and 1982.
50 largest utilities	Sampled in 1989 and 1982.
Unions	33 unions in 1989 and 11 unions in 1982.
Companies with 1,000+ employees	1,000 sampled in 1989. Not sampled in 1982.
Designated respondent	
Private companies:	
Chief health officer	Designated respondent in 1989 and 1982. Received version of questionnaire for health officers.
Chief personnel officer. .	Designated respondent in 1989 only. Received different questionnaire version for personnel officers.
Unions:	
Union president	Designated respondent in 1989 and 1982.
Followup methodology	
Reminder letters	Sent in 1989 and 1982.
Remailing questionnaires to nonresponders	Sent to all nonresponders in 1989 and 1982.
Telephone followup to nonresponders	All Fortune 500 and utilities in 1989. Only 200 largest companies in 1982.
Actual telephone interviews with nonresponders to mail survey	Done as a last resort in 1989 and 1982.

SOURCE: Office of Technology Assessment, 1990.

nies with 1,000 or more employees so that broader estimates could be made of the use and pattern of genetic monitoring and screening in the workplace. (See table 1-3 for a summary of the methodology of the 1989 and 1982 surveys.)

To flesh out the details of the data from the 1989 survey, OTA added questions that explored the use of genetic monitoring and screening in greater depth. Questions were asked about genetic monitoring and screening tests that might have been conducted as part of a voluntary wellness program, at the request of the employee, or for diagnosis. Including the results of the new questions produced a broader definition of genetic monitoring and screening for the 1989 survey. OTA believes the increased specificity attained an accurate measure of genetic monitoring and screening in 1989, established a firm base for future comparisons, and preserved general comparability to the 1982 study.

Table 1-4-Current Use of Genetic Monitoring by Fortune 500 Companies

Q.15. Is your company currently conducting *cytogenetic monitoring* of any employees or job applicants, for research or any other reason?

Q.18. Is your company currently conducting *direct-DNA monitoring* of any employees or job applicants, for research or any other reason?

(Base: Health officers)

	Number of companies currently conducting	
	Cytogenetic monitoring	Direct-DNA monitoring
Total	1	0
Type of business		
Electrical utility	0	0
Pharmaceutical	0	0
Other chemical	0	0
Petroleum.	1	0
Electronic	O	0
Other manufacturing	0	0
Nonmanufacturing	0	0
Number of employees		
Less than 5,000	O	0
5,000-9,999	0	0
10,000 or more	1	0

SOURCE: Office of Technology Assessment, 1990.

Table 1-5--Current Use of Genetic Screening by Fortune 500 Companies

Q.13. Is your company currently conducting *biochemical genetic screening of any* employees or job applicants, for research or any other reason?

Q.17. Is your company currently conducting *direct-DNA screening of* any employees or job applicants, for research or any other reason?

(Base: Health officers)

	Number of companies currently conducting	
	Biochemical genetic screening	Direct-DNA screening
Total	12	0
Type of business		
Electrical utility	0	0
Pharmaceutical	0	0
Other chemical	4	0
Petroleum	1	0
Electronic	O	0
Other manufacturing	2	0
Nonmanufacturing	5	0
Number of employees		
LOSS than 5,000	1	0
5,000-9,999	2	0
10,000 or more	9	0

SOURCE: Office of Technology Assessment, 1990.

Before presenting the trend data from 1982 to 1989, the current, past, and combined use of genetic monitoring and screening will be discussed. Following those sections, the overall use of genetic

Table 1-6-Past Use of Genetic Monitoring Tests by Fortune 500 Companies

Q.16. Has your company conducted any cytogenetic *monitoring* of any employees or job applicants, for research or any other reason in the past 19 years?
(Base: Health officers)

	Number of companies conduoced in past
	Cytogenic monitoring
Total	5
Type of business	
Electrical utility	0
Pharmaceutical	0
Other chemical	1
Petroleum	0
Electronic	0
Other manufacturing	1
Nonmanufacturing	3
Number of employees	
Less than 5,000	0
5,000-9,999	0
10,000 or more	5

SOURCE: Office of Technology Assessment, 1990.

Table 1-7—Past Use of Genetic Screening Tests by Fortune 500 Companies

Q.14. Has your company conducted any biochemical*genetic* screening of any employees or job applicants, for research or any other reason in the past 19 years?
(Base: Health officers)

	Number of companies conducted in past
	Biochemical genetic screening*
Total	8
Type of business	*o*
Electrical utility	
Pharmaceutical	0
Other chemical	4
Petroleum	0
Electronic	0
Other manufacturing	2
Nonmanufacturing	2
Number of employees	
Less than 5,000	0
5,000-9,999	1
10,000 or more	7

NOTE: Includes companies currently conducting genetic screening.
SOURCE: Office of Technology Assessment, 1990.

Table 1-8-Combined Testing: Current v. Past Monitoring and Screening by Fortune 500 Companies

(Base: Health officers)

	Number of companies
Conducted genetic monitoring or screening for research or any other reason, at present or in past 19 years	20
Currently conducting genetic monitoring or screening	12
Conducted monitoring or screening in past only	8
Conducted genetic screening for research or any other reason at present or in past 19 years	16
Currently conducting genetic screening	12
Conducted genetic screening in past only	4
Conducted cytogenetic monitoring for research or any other reason at present or in past 19 years	6
Currently conducting cytogenetic monitoring	1
Conducted cytogenetic monitoring in past only	5
Currently conducting direct-DNA screening for research or any other reason	0
Currently conducting direct-DNA monitoring for research or any other reason	0

SOURCE: Office of Technology Assessment, 1990.

monitoring and screening in 1989 and 1982 will be discussed.

In the 1982 survey, six health officers (1.6 percent) reported their companies currently conducted genetic monitoring or screening. In 1989, 12 health officers (5 percent) reported their companies currently conducted genetic monitoring or screening (1 of the companies used genetic monitoring and screening while 11 used only genetic screening) (see tables 1-4 and 1-5). (These numbers do not directly correlate because of different sized survey populations in 1982 and 1989.) The increase in the number of "current users' in 1989 could reflect slight differences in question wording between the 1989 and 1982 surveys.

The 1989 survey asked health officers whether their companies had conducted genetic monitoring tests in the past 19 years, for research or any other reason. Five health officers in Fortune 500 companies reported that their companies had conducted cytogenetic monitoring in the past 19 years of any employees or job applicants, for research or any other reason (table 1-6). All five companies that formerly conducted cytogenetic monitoring reported no current use of genetic monitoring or screening. A total of eight health officers in the Fortune 500 companies reported that their companies had conducted biochemical genetic screening of any employees or job applicants in the past 19 years (table 1-7). This included four health officers in Fortune 500 companies that reported they were currently conducting biochemical genetic screening.

A total of 20 health officers reported that their companies had conducted cytogenetic monitoring or

Table 1-9-Use of Genetic Monitoring or Screening: 1989 v. 1982 Survey Results

(Base: Health officers)

	Number of companies	
	1989	1982
Conducted genetic monitoring or screening for research or any other reason, at present or in the past*	*20*	*18*
Currently conducting genetic monitoring or screening	12	6
Conducted monitoring or screening in past only	8	12

● Defined as past 19 years in 1989 survey and past 12 years in 1982 survey.

SOURCE: Office of Technology Assessment, 1990.

Table I-10-Consideration To Conduct Genetic Monitoring and Screening in the Next Five Years: Health Officers

Q.33. Does your company anticipate conducting any *biochemical genetic screening,* for any reason, in the next 5 years?

Q.34. Does your company anticipate conducting any *cytogenetic monitoring,* for any reason, in the next 5 years?

Q.35. Does your company anticipate conducting any *direct-DNA screening,* for any reason, in the next 5 years?

Q.36. Does your company anticipate conducting any *direct-DNA monitoring,* for any reason, in the next 5 years?

(Base: Health officers)

	Percent			
	Yes	No	Not sure	No answer
Biochemical genetic screening	4	218	25	3
Cytogenetic monitoring	1	219	27	3
Direct-DNA screening	0	224	23	3
Direct-DNA monitoring	1	218	27	4

SOURCE: Office of Technology Assessment, 1990.

biochemical genetic screening, either currently or in the past 19 years. This includes 12 health officers who reported that genetic monitoring or screening was currently conducted, and 8 who reported that genetic monitoring or screening had been conducted in the past 19 years, but not currently (table 1-8). (In the 1982 OTA survey, past was defined as 12 years, and in the 1989 survey, as 19 years.)

Trend data on the use of genetic monitoring or screening can be obtained by tabulating comparable questions in the 1989 and 1982 surveys. These do not include the previously mentioned items added in 1989. Using this narrow definition, of the 330 companies (62.4 percent) responding to the 1989 survey, 20 health officers reported that their companies had conducted genetic monitoring or screening, either currently or in the past 19 years. In comparison, the 1982 survey found 18 health officers in the Fortune 500 sample who reported current or past use of genetic monitoring or screening (table 1-9). Thus, there has been little change between 1989 and 1982 in the number of companies that had used genetic monitoring or screening in the workplace.

In summary, the 1989 survey found 12 companies reporting current use of genetic monitoring or screening for research or any other reason. The ratio of current to past use of monitoring or screening was reversed in 1982, with 6 companies indicating current use of genetic monitoring or screening and 12 companies indicating past but not current use. Overall, OTA found that 20 companies had used genetic monitoring or screening in 1989, as compared to 18 companies in 1982.

If there has been little or no growth in the number of companies conducting genetic monitoring and screening in the workplace, what do companies foresee for the future? In 1982,, OTA found that 4 companies (1. 1 percent) anticipated using the tests in

the next 5 years, and 55 companies (15 percent) stated they would "possibly" use the tests in the next 5 years. The 1989 OTA survey provided the response categories "yes," "no," and "not sure" for the same questions to avoid classifying an indefinite answer as a positive response to future genetic monitoring or screening.

OTA found one Fortune 500 company that anticipated cytogenetic monitoring, one company that anticipated direct-DNA monitoring, and four companies that anticipated biochemical genetic screening. No company anticipated using direct-DNA screening in the next 5 years. Twenty-seven companies in 1989 indicated they were not sure whether they anticipated cytogenetic monitoring, and 27 were not sure whether they anticipated direct-DNA monitoring. For biochemical genetic screening, 25 companies were not sure whether they anticipated using it, and 23 were not sure about future direct-DNA screening (table 1-lO).[1] In 1982, 55 companies said they would possibly use such test in the next 5 years. Although this number cannot be directly compared to the current survey, the 1989 OTA survey appears to indicate fewer companies anticipate using genetic monitoring or screening.

POLICY ISSUES AND OPTIONS FOR CONGRESSIONAL ACTION

While technologies associated with genetic monitoring and screening in the workplace have continued to advance, OTA found no significant change in the use of these technologies since 1983. Thus, several of the policy issues and options for congressional action offered in the 1983 OTA report are still valid and remain unchanged.

Two central issues related to genetic monitoring and screening in the workplace were identified during the course of this assessment. They are:

- the appropriate role of the Federal Government in the regulation, oversight, or promotion of genetic tests (both monitoring and screening); and
- the adequacy of federally sponsored research on the relationships between genes and the environment.

Associated with each policy issue are several options for congressional action, ranging in each case from taking no specific steps to making major changes. Some of the options involve direct legislative action. Others involve the executive branch but with congressional oversight or direction. The order in which the options are presented does not imply their priority. Moreover, the options are not generally mutually exclusive; adopting one does not necessarily disqualify others that pertain to the same or other issues, although changes in one area could have repercussions in others. A careful combination of options might produce the most desirable effects.

ISSUE: Is there a role for the Federal Government in ***genetic monitoring*** in the workplace?

Option 1: Take no action.

Congress could take no action to prohibit, regulate, or promote the use of genetic monitoring in the workplace. This would allow employers, employees, and their representative trade groups and unions to regulate its use through negotiation, arbitration, and litigation.

Thus far, executive agencies involved in workplace health and safety have not regulated against the use of genetic monitoring in workplace settings. OSHA has regulated some employer practices that could affect the use of genetic monitoring, such as medical records access by the employee. Congress could take no action if it determines that present Federal regulation is adequate in this area. Under this scenario, constraints on the use of genetic monitoring would develop through court rulings in suits between pa-ties or by negotiations between companies and unions.

Option 2: Prohibit genetic monitoring in the workplace.

To prevent all possibilities for discrimination and breach of confidentiality, Congress could prohibit genetic monitoring in the workplace. In light of the many discrete changes needed in the OSH Act, NLRA, and Rehabilitation Act to achieve this degree of protection through regulation, Congress could decide to prohibit all genetic monitoring until further research into the methods is conducted. Such a

[1]These numbers cannot be added because of cross counting; nor do they directly correlate to the 55 companies because of question wording. In retrospect, those who chose "possibly' in 1982 might not have meant to indicate that genetic monitoring or screening was anticipated, they simply could not rule out the possibility they would use it in the future.

prohibition could shift the focus of the issue to levels of exposure in the workplace.

Prohibiting genetic monitoring, however, will delay the accumulation of data needed to make the judgment whether certain genetic monitoring tests are useful. By slowing the development of these data, prohibition might threaten efforts to identify workplace hazards, whether they are to be minimized through cleanup or worker selection. In addition, some workers who might have avoided dangerous exposures had they known of a susceptibility will sicken unnecessarily. Finally, this option clearly eliminates the possibility for mandatory worker protection under those discrete circumstances where overall worksite hazard reduction is not technologically or economically feasible.

Option 3: Promote genetic monitoring in the workplace.

Congress could decide that genetic monitoring in the workplace should be promoted because of its potential to improve the work environment and worker health conditions. This could be done by providing additional funding to those Federal agencies currently performing research into genetic monitoring methods, as well as basic research on the cause of occupational disease, in general, and the relationships between environmental exposures and health effects arising from genetic mutation. Such projects could identify useful occupational genetic monitoring tests and develop protocols for their use. However, many questions about the use of genetic monitoring remain unanswered. Because the interpretation of genetic monitoring is only considered to be reliable at the population level, rather than the individual level, the current usefulness of genetic monitoring in the workplace is questionable.

ISSUE: Is there a role for the Federal Government in ***genetic screening*** in the workplace?

Option 1: Take no action.

Congress could choose to take no action in the area of genetic screening in the workplace. As with genetic monitoring, any constraints on the use of genetic screening would develop through court rulings in lawsuits between employers and employees, or by negotiations between companies and unions. In support of this option is the viewpoint that congressional action is not currently warranted at this time. Use of genetic screening in the workplace has not changed greatly since the 1983 OTA report. However, there have been several newly recognized susceptibilities to occupational illness since that time. In addition, advances have been made in the area of molecular techniques for genetic screening for both occupationally and nonoccupationally related disease.

If Congress takes no action in this area, those identified as susceptible to *occupational illness* through genetic screening could be seen as unfit for work. In addition, those identified as being susceptible to a *nonoccupationally related disease* could be seen as a health insurance burden. Without proper restrictions, the use of genetic screening to detect either type of disease risk could make job discrimination a possibility.

Option 2: Prohibit genetic screening in the workplace.

The principal reason for prohibiting genetic screening in the workplace would be the concern over its potential misuse. Such potential for misuse probably would be greater for genetic screening than genetic monitoring because the former is targeted toward identifying *individuals* **at increased** risk while the latter focuses on *groups* at increased risk. The existing legal framework may offer protection in some circumstances, but many questions have not resolved.

A drawback to this option is that by prohibiting both types of genetic screening in the workplace, employers could not utilize screening for occupationally related disease. This type of screening offers some protection of the worker.

Option 3: Promote genetic screening in the workplace.

Congress could stimulate the research and development of genetic screening tools by providing funds for research into occupationally related disease, nonoccupationally related disease, or both. Useful screening tests for occupationally related disease could be developed which could have direct benefits for the individual worker and indirect benefits for the employer. In addition, more money could be provided in the area of research on occupationally related traits. NIOSH could be authorized to do research in this area, and to certify procedures for medical technologies that are of sufficient value to be used in an occupational setting. If such research were promoted, however, employers might be prone to use those screening tests to screen

out susceptible employees in lieu of cleaning up the workplace.

If research in the area of nonoccupationally related disease was promoted beyond current Federal research levels, employers might be prone to using such screening tests to discriminate against employees or job applicants who might increase the company health care costs.

ISSUE: Should the Federal Government regulate genetic monitoring or screening in the workplace?

If Congress determines that the current regulatory framework addressing genetic monitoring and screening is adequate, it could take no action and let the current regulatory framework stand. However, if Congress determines that the current regulatory framework is inadequate, it could pursue several avenues. A framework established by several major pieces of legislation exists on which to build: OSH Act; NLRA; Title VII of the Civil Rights Act of 1964; Rehabilitation Act of 1973; and ADA. The following options are discussed according to whether they apply to genetic monitoring, genetic screening, or both.

Genetic Monitoring and Screening

Option 1: Congress could amend Section 6(b)(7) of the OSH Act which states that OSHA standards shall prescribe the type and frequency of medical examinations or other tests to be made available, to specify whether genetic monitoring and screening tests are to be included.

To either prohibit or promote genetic monitoring and screening, Congress could amend this section's coverage with respect to genetic monitoring and screening. To contain abuses, Congress could include language directing OSHA to prescribe or recommend genetic monitoring or screening only when less intrusive medical tests will not provide information of substantially the same value. Thus, for example, tests for sickle cell anemia would not be permitted unless other tests of lung fiction and blood oxygenation were incapable of giving an employer the information needed to decide whether a particular worker could safely manage a particular task.

A principal drawback of this option is that performing genetic monitoring and screening tests on employees could be financially prohibitive for some employers. In addition, mandating genetic monitoring or screening tests could be burdensome for both the employer and the employee. Such an action could require the employer to hire new medical staff to perform them. Furthermore, the employee might not wish to undergo genetic monitoring or screening.

Option 2: Congress could amend the OSH Act to guarantee the confidentiality of genetic monitoring and screening results.

Congress could amend the OSH Act to specifically guarantee that genetic monitoring and screening results not be disseminated, except in nonidentifying, statistical forms for research purposes, to any third-party without specific authorization from the worker. Further, employers could receive only the conclusion of the occupational physician, i.e., whether the worker is fit for the job in question, without receiving details or results of the genetic monitoring or screening tests. The worker, on the other hand, would receive both the test results and the conclusions drawn from them by the examining physician. Several State statutes provide a model for such legislation.

Advantages of this option are the ability to shield workers from misuse of genetic information by immediate and potential employers, and the maintenance of adequate authority to provide statistical information needed for ongoing improvement of health and safety practices. As with the option just mentioned concerning recordkeeping, however, this amendment would logically be appropriate to all medical records, and not merely those concerning genetic monitoring and screening tests. Thus, evaluating this option requires a larger consideration of whether the OSH Act should guarantee the confidentiality of all medical testing in this fashion. If this option is adopted, consideration would also need to be given to remedies for breach of confidentiality and an examination of the role of the occupational physician employed by the company.

Option 3: Require full disclosure to employees and job applicants of the nature and purpose of all medical procedures performed on them.

Current law does not require employers to disclose the nature and purpose of medical procedures conducted on employees or job applicants, or how the results are to be used. Although employees are given access to their medical records, they may not

be able to interpret the data within the records, or challenge incorrect information. A congressionally mandated requirement that employers provide detailed information of what procedures were performed and why they were performed might serve as a deterrent to abuses. This would also protect the employees' autonomy by allowing them to be part of a decisionmaking process that affects their health and economic interests. If the test were genetic in nature, the assistance of a genetic counselor would be important to fully explain the procedure and the meaning of a positive result.

On the other hand, by requiring full disclosure, Congress would place requirements on employers that might be perceived as burdensome and expensive. Additionally, arguments might be made that such a requirement would intrude on the judgment of the occupational health physician.

Genetic Monitoring

Option 4: Congress could direct OSHA to clarify that genetic changes shall be included under the definition of occupational illness.

OSHA's definition of occupational illness now includes "abnormal condition,' but does not specifically cover genetic changes. Taking this action could ensure that data on worker exposures and subsequent genetic changes would be recorded in worksites where employers are using genetic monitoring. This would help with ongoing efforts to assess the effects of potentially hazardous substances, as well as offer the opportunity to more closely monitor the health of a particular worker.

Yet including genetic changes in the definition of occupational illness would implicitly equate all genetic changes with "illness." Many changes are likely to be without immediate symptomatic effect. Therefore, gathering and distributing this information might be unduly alarming, particularly to the workers in question. Also, all genetic change is not definitely a result of the workplace. Changes can be induced by personal habits and lifestyle decisions (e.g., smoking, diet) as well. Equating genetic changes with illness, may encourage employers to view such employees as somehow disabled or unfit for work, making job discrimination a distinct possibility.

Genetic Screening

Option 5: Congress could amend section 504 of the Rehabilitation Act to prohibit discrimination in hiring against otherwise qualified applicants because their genetic screening results reveal a proclivity toward certain diseases in the future.

Amending section 504 in this manner would address several potential concerns. First, it tackles the problem of discrimination against job applicants, a topic left largely untouched by the OSH Act and NLRA protections. Second, it addresses what is perhaps the most likely area of abuse for the use of genetic screening. Third, it focuses on one of the possible uses of genetic screening, i.e., identification of applicants who are qualified but likely in the future to suffer from a disease that will require full use of sick leave or even early retirement. Finally, amending section 504 also permits Congress to address the use of genetic screening in the workplace to detect nonoccupationally related illnesses.

By focusing on this section, rather than with section 503, Congress could avoid the problem of directing employers to include those with genetic variants that do not otherwise qualify them as "handicapped" under their affirmative action programs.

The disadvantage, however, is the uncertainty associated with section 504's requirement that employers provide a reasonable accommodation for handicapped workers. It may be clear what accommodation is necessary to make a job accessible to one who is deaf or blind, and in turn to make a judgment whether that accommodation is reasonable to require of an employer. It may be more difficult, however, to judge what is necessary for someone with a currently asymptomatic genetic illness or susceptibility.

Option 6: Congress could direct the National Labor Relations Board to make preemployment genetic screening a mandatory subject of bargaining, in order to increase the possibilities for workers to protect themselves against what they and their representatives perceive as abuses of genetic screening.

Fitness-for-duty physicals and medical tests are already regarded as mandatory subjects of bargaining between unions and employers when applied to current workers. Thus, extending the concept to preemployment physicals and genetic screening

would not require markedly different concerns to be placed on the bargaining table, and would provide some protection for job applicants.

A disadvantage to this option, however, is that unions do not represent the majority of American workers, so this action would not protect all affected persons. Additionally, in light of interest in "two-tiered" systems of compensation, it is possible that unions and employers may trade protections for current workers from potentially discriminatory genetic screening tests for the privilege of screening job applicants more stringently.

ISSUE: Is the current Federal research agenda addressing genetic monitoring and screening adequately?

The current Federal research framework for addressing genetic monitoring and screening is composed of extramural and intramural programs sponsored by several agencies, including the Department of Energy (DOE), NIOSH, National Institutes of Health (NlH), National Center for Toxicological Research, Center for Environmental Health and Injury Control, and Agency for Toxic Substances and Disease Registry. OTA found that, in general, Federal research programs do not adequately address genetic monitoring or screening technologies for use in the workplace.

Option J: Take no action.

In the absence of congressional directives encouraging more research on the relationships between environmental exposures and health, information on gene-environment interactions will continue to be gathered piecemeal by the Federal agencies involved in this area. Some of the research funded by the National Center for Human Genome Research at NIH will contribute to the development of more valid and reliable tests. Research agendas of the National Cancer Institute and the National Institute of Environmental Health Sciences include studies relevant to this report. Work being conducted internationally is also contributing to knowledge in this area. Congress could decide that existing research capabilities will provide an adequate and appropriate level of information in this area and that no additional action needs to be taken. If Congress, however, decides that it is important to determine these relationships in order to provide for a safe and healthy workplace, and that the cost of occupational illness warrants more extensive examination, taking no action will result in incremental and disjointed progress in reaching these goals.

Option 2: Encourage the appropriate agencies to pursue studies that will provide a better understanding of the link between mutagenesis and carcinogenesis through larger, better controlled epidemiologic studies.

Over the years, an increasing number of health effects have been attributed to mutations caused by toxicants. The diseases most often associated with genotoxic substances are various forms of cancer. Mutational changes such as point mutations and chromosomal rearrangements have been associated with early stage tumor development. However, not all mutations cause disease. Because the relationship between mutation and health effect is often indirect and not well understood, more research needs to be conducted in this area. Epidemiologic studies in an occupational setting can address this problem.

Option 3: Direct the Secretary of the DOE to report on past and current research efforts directed by DOE toward identifying the genetic risks of radiation exposure.

Open-ended data collection by DOE, and **prob**lems of access to data, have stalled an open discussion of the real risks of radiation exposure to American workers in high- and low-level environments. DOE has recognized this problem and could be encouraged to share data with interested investigators.

Option 4: Ensure that the Food and Drug Administration (FDA) and the relevant offices of NIH properly evaluate new genetic monitoring and screening tests for reliability and validity.

There is some concern that the unique nature of many genetic diseases-which may present heterogeneity, reduced penetrance, and variable expressivity-pose significantly different challenges to diagnostic tests. Tests made available to employers or physicians need not only to be safe and effective, but to clearly explain the limitations in careful labeling so as to avoid misuse and misinterpretation. As more tests become available for both occupationally and nonoccupationally related diseases, issues of quality control must be addressed. NIH and FDA could cosponsor a Consensus Development Conference(s) on genetic monitoring and screening that could evaluate the accuracy, safety, labeling, and potential misuses and abuses of new tests.

Chapter 2

Introduction

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Chapter 2
Introduction

Genetically determined individuality is a fact of life. Yet not long ago, the factors affecting heritability were, by today's standards, ill-defined and only partially known by scientists. During the past three decades our understanding of genetics has advanced remarkably as new methods for identifying, manipulating, and analyzing DNA have developed. Today, the secrets of inheritance are revealed by modern biology. At the same time, public awareness of the role that genetics play in daily lives is increasing.

Less well understood by both scientists and the public is interaction of the environment with genetics, and the role each plays in sickness and health. Nevertheless, it has long been recognized that genetic risks are posed by various workplace environments, such as exposure to radiation or certain chemicals. In an effort to reduce occupational illness, some have advocated genetic testing of workers to identify healthy individuals (or populations) at risk for, or susceptible to, a variety of work-related conditions. Such genetic testing has been heretofore viewed strictly as a tool to prevent occupational disease (23). However, recent progress in developing genetic tests to detect inborn conditions not obviously associated with worksite exposures--e.g., Huntington's disease or heart disease--and the advances expected to be made from the human genome project, has been coupled increasingly with the notion of using these tests in the workplace. A new dimension has been added to the debate surrounding genetic testing conducted at the workplace (1,2,3).

This report covers the scientific, ethical, legal, and social issues of genetic testing of workers. While the report is limited to issues central to use of genetic technologies, some discussion of other medical and biological testing of workers is presented to place genetic testing in context. What is excluded are job-associated injuries, nongenetic technologies to prevent occupational disease, and reproductive hazards in the workplace, which have all been assessed in previous Office of Technology Assessment (OTA) reports (21,22). Similarly, acquired immunodeficiency syndrome (AIDS) testing, the implications of genetic testing for health insurance, regulating carcinogens, technologies to detect heritable mutations, identifying and regulating neurotoxins, and nonmedical uses of genetic tests are topics of other OTA reports (9,10,1 1,13,20,24).

WHAT IS GENETIC TESTING?

Genetic testing includes a number of technologies to detect genetic traits, changes in chromosomes, or changes in DNA. As used in the workplace, it encompasses two activities: monitoring and screening. Thus, genetic testing of employee populations involves both examining persons for evidence of induced change in their genetic material (monitoring) and methods to identify individuals with particular inherited traits or disorders (screening). To avoid confusion, the general term "genetic testing" will not be used in the text, rather, the more specific terms genetic monitoring and screening will be used instead.

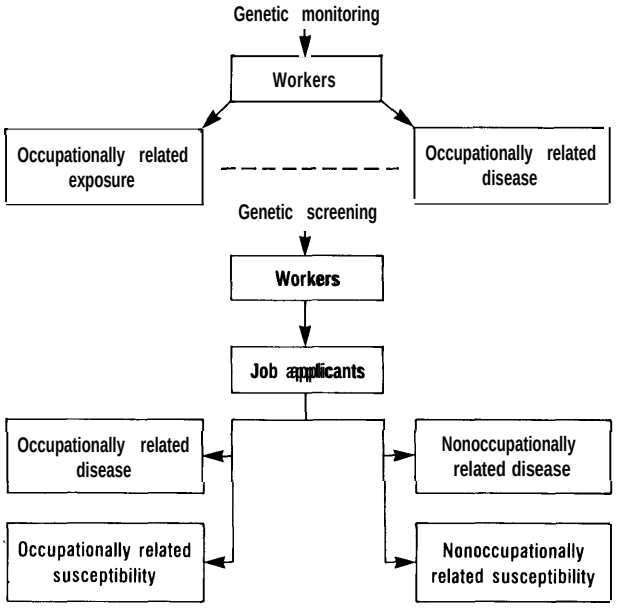
Genetic monitoring involves periodically examining employees to evaluate modifications of their genetic material-e. g., chromosomal damage or evidence of increased occurrence of molecular mutations—that may have evolved in the course of employment. The premise is that such changes could indicate increased risk of future illness. The putative cause is workplace exposure to hazardous substances. Because ambient exposures, personal habits and lifestyle decisions (e.g., tobacco use, etc.), and age can also induce changes in genetic material, genetic monitoring can be used to periodically monitor risk arising outside of the workplace. In short, genetic monitoring ascertains whether the genetic material of the group of individuals has altered over time. In general, current techniques are not exposure-specific but serve merely as an indicator of recent exposure.

Genetic screening is a process to examine the genetic makeup of employees or job applicants for certain inherited characteristics. (Employees could be screened on different occasions for different traits or with improved technology, but generally only once for each characteristic.) Genetic screening can be used in two distinct ways. First, employees could be screened for the presence of genetically determined traits that render them susceptible to a pathological effect if exposed to specific agents. An example of such genetic screening would be a test

for traits that might identify an employee with a genetic predisposition to an occupationally related disease. (Similarly, job applicants could be screened for a trait prior to being hired for a position where exposure could occur.) Second, employees or job applicants could be screened to detect general heritable conditions, not just conditions associated with occupational illness. Reasons for using the different classes of tests vary, and are discussed in the following section. In either case, whether screening for an occupationally related trait or one not related to job exposure, genetic screening tests involve examinations for inherited traits where a single measure is usually sufficient because generally these inherited characteristics do not change.

Genetic screening differs significantly from genetic monitoring. In most cases, screening requires a one-time test to detect a single trait in a worker or job applicant, while monitoring generally involves multiple tests of a worker over time. Most importantly, in genetic screening the focus is on the preexisting genetic makeup that workers or job applicants bring to the job. This is distinct from genetic monitoring, where the focus is on changes in the genetic material induced from hazardous exposures at the workplace (see figure 2-l).

Figure 2-l-Components of Genetic Testing in the Workplace



SOURCE: Office of Technology Assessment, 1990.

WHY USE GENETIC MONITORING AND SCREENING IN THE WORKPLACE?

As mentioned, genetic monitoring and screening tests are methods for identifying individuals or groups for evidence of alteration in the genetic material or with particular inherited traits. Detecting modifications or traits can inform individuals that they are potentially at increased risk for disease, or could pass a trait to their offspring. By applying genetic monitoring and screening tests to a group of apparently well persons and identifying those who have a greater probability of developing a disease, counseling, prevention, or early treatment (if available) become possible. The use of genetic monitoring and screening of selected individuals or groups at high risk through employers has not been a long-standing practice.

The recent development of tests for human genetic disorders (14) has fueled interest in genetic monitoring and screening of workers. To some extent, as interest in AIDS and drug testing of workers has increased, so has interest in genetic monitoring and screening by employers (4). Nevertheless, many aspects of genetic monitoring and screening in the workplace differ from other types of testing of workers and remain controversial. Many of the objections raised-scientific and social-are discussed in following chapters. In spite of objections, why consider using genetic monitoring and screening tests in the workplace? Genetic monitoring of employees could be performed on groups of employees to identify work areas for increased safety and health precautions, and to indicate a need to lower exposure levels for a group exposed to a previously unknown hazard. Genetic screening for occupationally related traits could be performed to ensure appropriate worksite placement of employees susceptible to certain occupational diseases, and ensure that employers place those workers most susceptible to a specific risk in the least hazardous environments. Both types of genetic screening (occupational and nonoccupational) could be performed to improve employee productivity and lower workers' compensation costs through better worker health; promote and encourage general health awareness; and improve employers' health care cost-containment efforts, especially for health insurance.

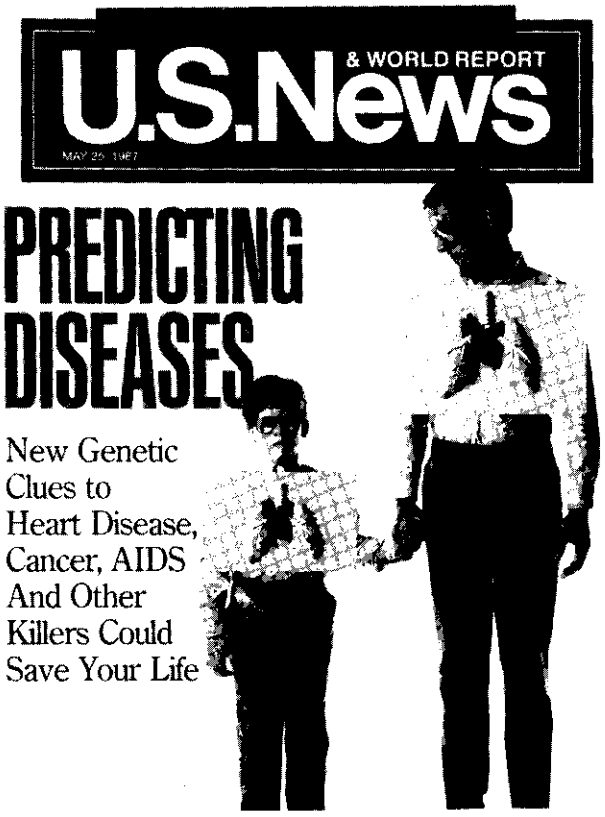


Photo credit: U.S. News & World Report, *May 25, 1987*

Media coverage of genetic monitoring and screening.

Worksite risks create costs to employers, who might be required to compensate individuals through workers' compensation for lost earnings, or workers' estates through tort liability claims for premature death. Genetic screening of workers or job applicants could be a tool to identify individuals with a particular genetic trait that indicates susceptibility to occupational illness if they are exposed to specific hazards, such as radiation or certain chemicals. Periodic genetic monitoring of employees could be used to detect induced genetic change that could indicate an increased risk for certain diseases, in particular cancer. Thus, genetic monitoring and screening could lead to improved worker health and payment of lower workers' compensation costs. On the other hand, without clear correlations between workplace hazards and occupational illnesses and without cost-effective tests, any expectations of money saved by genetic monitoring and screening for job-related conditions could be minor.

Increasingly, costs to U.S. employers of health-related benefits have skyrocketed. In particular, to avoid rising health care costs, many large companies are adopting self-insurance plans. Self-insurance plans are exempt from State mandates and other forms of State regulation (6). Business health spending between 1980 and 1987 almost doubled, from $68.1 billion to $134.6 billion (6). One company of 70 employees says that, in 16 years its health insurance premiums will exceed its payroll if both continue their present growth rates (5). Companies concerned about health insurance costs could be interested in screening workers and job applicants who are likely to develop genetically based diseases and could impose high costs on a company's self-insured health program. Similarly, companies could engage in genetic monitoring-again, to safeguard workers' health while simultaneously reducing the burden of occupational illness on their health costs.

In this respect, genetic monitoring and screening in the workplace differ. Genetic monitoring can be viewed as an extension of several types of biological monitoring in the workplace to detect changes or assess exposures that could be associated with increased exposure to occupational or nonoccupational risk. Genetic screening, on the other hand, can be used to detect both traits that indicate a predisposition to occupational disease, as well as traits not associated with workplace illness. Some argue from an economic standpoint that genetic monitoring and screening in the workplace to limit occupational illnesses could be less important in the long run than genetic screening by employers to limit general company health care expenses (2). A window on this development could be corporate "wellness" programs, or other company-sponsored health promotion programs (see box 2-A) that emphasize prevention and encourage employees to adopt healthier lifestyles (2).

From a policy standpoint, these differences—monitoring v. screening and occupational illness v. general health-could be significant. Some criticize all types of genetic monitoring and screening in the workplace as paternalistic and discriminatory, while others advocate that, properly implemented, genetic monitoring and screening (for both purposes) programs benefit both workers and employers. Others, however, maintain that it is one thing to monitor or screen workers because they are at increased risk for occupational illness induced by the workplace, but quite another to screen persons because they or their offspring-who could be covered on an employee's

Box 2-A--Cancer Detection in the Workplace

Among the greatest fears of industrial workers is the risk of cancer from exposure to hazardous substances. Although employees are concerned about cancer risk, they are not always informed about the specific dangers of the chemicals with which they work. By increasing employee and employer involvement in cancer prevention and detection, both groups stand to benefit: employees with gains in personal health, and employers with higher worker morale and productivity and reduced health expenditures. Because cancer risks vary from worksite to worksite, worker perceptions of various job hazards related to cancer and chemical exposure are important. From 1978 through 1987, the National Cancer Institute (NCI) allocated $14 million to the Occupational Safety and Health Administration (OSHA) for cancer prevention training and education of workers. In 1983, NCI awarded grants to five unions, that had participated in OSHA's education program, to evaluate the impact of the unions' cancer prevention and education programs.

A 1987 study by the International United Rubber, Cork, Linoleum, and Plastic Workers of America, one of the participating unions, questioned approximately 24,000 of its members about their knowledge of chemical hazards, the location of engineering controls, and the use of daily safety procedures. Prior to the study, employees had participated in the industry's cancer control program, which included worker education.

Despite the fact that over 10,000 different chemicals, many hazardous, are used by these workers, the study found that 22 percent of workers were not sure whether they worked with dangerous chemicals, and only 6 percent felt they were very informed about chemical hazards. Percentages of employees saying they were well-informed varied widely from company to company, ranging from 16 percent at one company to 32 percent at another. Thus, for adequate cancer education, greater understanding of chemical-specific risks is needed.

In addition to worker perception and involvement, management health programs can play an important role. Currently, several companies offer employees cancer screening clinics and other cancer detection programs. One such program, offered by Pennzoil (in conjunction with the Kelsey-Seybold Foundation) to employees at a Texas facility, began m 1984 as a cancer awareness clinic for white-collar employees to discover cancers unrelated to worksite exposure. The Pennzoil program, strictly voluntary and confidential, has since been expanded to industrial petroleum workers and other locations in 22 States, where the cancer detection procedure can include workplace risks.

The Pennzoil program involves an initial lecture on cancer risk and detection, and a personal cancer examination for those requesting one. Corporate management strongly supports these meetings, and encourages employees to attend the lectures. As part of the program, employees also complete questionnaires about cancer risk behaviors and personal medical histories. Those employees showing an increased risk of cancer are offered followup counseling sessions with Kelsey-Seybold Foundation Cancer Prevention Center physicians and medical tests, if necessary, paid for by Pennzoil. All employees also are offered yearly screening or followup examinations. Pennzoil receives only summary data on participation, cancer detection, and demographic information. Both increased employee morale and detection of potential tumors resulted. Along with Pennzoil's expansion of the program, Exxon Chemical Americas has undertaken a similar project with the Kelsey -Seybold Foundation Cancer prevention Center.

The experience of cancer screening in the workplace suggests that the cooperation of corporate management and private organizations, together with an accurate assessment of employee understanding of workplace risk, can create a healthier, more productive working environment one benefiting both employer and employee. At present, genetic monitoring detects genetic changes that could result m greater risk of cancer. Future advances in genetic technologies could result in increased cancer testing and education at worksites. As genetic technologies make detection of cancer or other health risks more accurate, programs such as those just described could serve as models. For genetic monitoring and screening, in particular, implementing successful worker education will be crucial.

SOURCES: Office of Technology Assessmcnt, 1990, based on M. Minkoff, Kelsey-Seybold Foundation Cancer prevention Center, Houston, TX, personal communication, October 1988; A.P. Schenck, A.D. Kaluzny, G.M. Hochbaum, et al., "Worker Perceptions and Actions Toward Cancer Control in the Workplace: An Analysis of Baseline Data"; and L. Zimmerman, G. Jackson, J. Hughes, et al., ''CanCer Education and Screening in the Workplace: The Corporate Perspective, " *Advances in Cancer Control: The War on Cancer—15 Years of Progress,* P.F. Engstrom, LE. Mortenson and P.N. Anderson (eds.) *(New* York, NY: Alan R. Liss, Inc., *1987).*

FORM (31 2602

PENNZOIL COMPANY
HEALTH RISK APPRAISAL

NAME		HOME ADDRESS	
SOCIAL SECURITY NUMBER	BIRTH DATE	COMPANY NUMBER	TODAY'S DATE

Health Risk Appraisal Is an educational tool. It shows you choices you can make to keep good health and avoid the most common causes of death for a person your age and sex. This Health Risk Appraisal Is not a substitute for a check-up or physical exam that you get from a doctor or nurse. It only gives you some ideas for lowering your risk of getting sick or injured In the future.

DIRECTIONS: To get the most accurate results answer as many questions as you can and as best you can. If you do not know the answer leave it blank, Questions with a • (star symbol) are important to your health, but are not used by the computer to calculate your risks. However, your answers may be helpful in planning your health and fitness program.

Please check or fill-in the appropriate numbers.

1. SEX		1 ☐ Male 2 ☐ Female
2. AGE		_____ Years
3. HEIGHT	(Without shoes) (No fractions)	_____ Feet _____ Inches
4. WEIGHT	(Without shoes) (No fractions)	_____ Pounds
5 Body frame size		1 ☐ Small 2 ☐ Medium 3 ☐ Large
6. Have you ever been told that you have diabetes (or sugar diabetes)?		1 ☐ Yes 2 ☐ No
7. Are you now taking medicine for high blood pressure?		1 ☐ Yes 2 ☐ No
8. What is your blood pressure now?		Systolic (High number) _____ | _____ Diastolic (Low number)
9. If you do not know the numbers, check the box that describes your blood pressure.		1 ☐ High 2 ☐ Normal or Low 3 ☐ Don't Know
10. What is your TOTAL cholesterol level (based on a blood test)?		_____ mg/dl
11. What is your HDL cholesterol (based on a blood test)?		_____ mg/dl
12. How many cigars do you usually smoke per day?		_____ cigars per day
13. How many pipes of tobacco do you usually smoke per day'?		_____ pipes per day
14. How many times per day do you usually use smokeless tobacco? (Chewing tobac co, snuff, pouches, etc.)		_____ times per day
15. **CIGARETTE SMOKING** - How would you describe your cigarette smoking habits?		1 ☐ Never smoked (go to question 18) 2 ☐ Used to smoke (go to question 17) 3 ☐ Still smoke (go to question 16)
16. STILL SMOKE. How many cigarettes a day do you smoke?		_____ cigarettes per day (go to question 18)
17. USED TO SMOKE -a. How many years has it been since you smoked cigarettes fairly regularly?		_____ years
b. What was the average number of cigarettes per day that you smoked in the 2years before you quit?		_____ cigarettes per day
18. In the next 12 months how many thousands of miles will you probably travel by each of the following? (NOTE: U.S. average = 10,000 miles)	a. Car, truck, or van:	_____ ,000 miles
	b. Motorcycle:	_____ ,000 miles
19. On a typical day how do you USUALLY travel? (Check one only)		1 ☐ Walk 5 ☐ Mid-size or full-size car 2 ☐ Bicycle 6 ☐ Truck or van 3 ☐ Motorcycle 7 ☐ Bus, subway, or train 4 ☐ Sub-compact or compact car 8 ☐ Mostly stay home

Photo credit: Pennzoil Co.

Health risk appraisal form from the Pennzoil program.

health plan—are at high risk for a disease not related to occupational exposure. Finally, some argue that screening per se, even if to reduce occupational illness, is unfair because it *a priori* measures heritable conditions beyond an individual's control, while genetic monitoring is similar to other forms of successful biological monitoring (e.g., benzene or lead exposure) that are performed from body fluids or tissue samples.

GENETICS IN THE WORKPLACE: A HISTORY OF CONGRESSIONAL CONCERN

Congressional interest in human genetics, genetic diseases, and genetic technologies is not new. In 1972, Congress passed the National Sickle Cell Anemia Control Act (Public Law 92-294), amending it 4 years later to the National Sickle Cell Anemia, Cooley's Anemia, Tay-Sachs, and Genetic Diseases Act (Public Law 94-278).

Beginning in the early 1980s, a public debate began about the feasibility of mapping, and perhaps sequencing, the human genome. Congress held several hearings on this issue and requested an OTA assessment on the subject (12). Two agencies, the National Institutes of Health and the Department of Energy, received funding to perform research for the human genome project (25). Much of the research done for the genome project will be important to the scientific advancement of genetic monitoring and screening techniques.

The 1983 OTA Report

In the late 1970s and early 1980s, reports surfacing about genetic monitoring and screening in occupational settings captured the interest of Congress. Concern about the scientific and social issues of such testing prompted the House Committee on Science and Technology to hold hearings and request an OTA assessment of the role of genetic testing in preventing occupational disease (7,8,23). As part of its study, OTA surveyed American industry and unions to determine the extent and nature of employer genetic monitoring and screening.

In the intervening years, understanding of human molecular genetics and biotechnologies applicable to the field have expanded enormously. Both the number of applications of such technologies and the technical capability to detect genetically based disorders have increased, linked to rapid scientific developments in recombinant DNA and cell culture techniques. This has heightened congressional concern about their applications (12,14,15,16,17,18, 19). Debates surrounding the changing climate of employee testing (e.g., AIDS, drugs, and polygraph) (4) and, as described in the following section, efforts to map the human genome, also combined to stimulate congressional interest in reassessing the extent of and issues surrounding genetic monitoring and screening in the workplace.

Impacts of the Human Genome Project

Efforts underway to map and sequence the human genome stand to have a significant impact on many aspects of biology, medicine, and health-including genetic monitoring and screening. (The history and debate surrounding mapping and sequencing the human genome have been analyzed in a separate OTA report (12).) To date, genome projects have accelerated the production of new technologies, research tools, and basic knowledge. At current or perhaps increased levels of effort, they may eventually make possible the control of many human diseases-first through more effective methods of predicting or detecting disease, then, in some cases, through development of effective therapies based on improved understanding of disease mechanisms. Although not a direct result of the genome project, advances in human genetics and molecular biology have already provided insight into the origins of such diseases as cystic fibrosis, hemophilia, sickle cell disease, and hypercholesterolemia.

The new technologies developed through human genome projects research will also be used to assess public health needs. Techniques for rapidly sequencing DNA, for example, may facilitate the detection of mutations following exposure to radiation or environmental agents. Susceptibilities to environmental and workplace toxicants might be identified as more detailed genetic linkage maps are developed, and special methods of surveillance could be used to monitor individuals at risk.

However, profound ethical questions are posed by possible applications of and access to these genetic data. The complexity and urgency of these issues will increase in proportion to advances in mapping and sequencing. There is no doubt that continuing scientific advances in mapping and sequencing the

human genome accelerate diagnostic applications. Progress to date indicates that the ability to diagnose a genetic abnormality precedes the development of therapeutic interventions and that this gap may be growing. An important related issue is that of access to this information by third-parties such as insurance companies or employers and how this information is used. These questions are complex and are not likely to be resolved in the near future. It will therefore be necessary to ensure that some means for explicitly addressing ethical issues accompanies such scientific research. A working group on ethics was established in January 1989 by the Program Advisory Committee on the Human Genome, and a percentage of the genome budget will go toward studying ethical issues associated with the genome research (25).

THIS OTA REPORT

Health and safety of the U.S. workforce involves many components. This report presents the technological, ethical, legal, and personal implications of employers using, *genetic* technologies. Where applicable, other types of medical testing are discussed to place genetic technologies in context. This report addresses two entirely different purposes of genetic monitoring and screening in the workplace: to prevent occupational disease and to detect nonoccupationally linked conditions related to general employee health. To place both genetics and worker health in context, historical perspectives of genetic monitoring and screening in this country are presented, as are perspectives on the evolution of occupational health.

With this report, OTA assesses the current practice of genetic monitoring and screening by U.S. employers, as determined by surveys of 1,500 companies, the 50 largest utilities, and 33 unions. Beyond determining the extent of genetic monitoring and screening, the report also examines the attitudes of employers toward using genetic procedures in the workplace. In addition, it examines the very notion of "genetic normality,' and explores what role both genetics and a person's job play in his or her identity-and how these two parameters could conflict.

For policymakers, this report presents a series of policy issues and options for congressional action aimed at addressing the concerns that arise when personal identity, corporate interests, and Federal regulation and oversight collide over genetic monitoring and screening in the workplace.

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Chapter 3

Occupational Health and Genetic Monitoring and Screening: An Overview

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Chapter 3
Occupational Health and Genetic Monitoring and Screening: An Overview

The concept of genetic monitoring and screening emerged prior to the discovery of the molecular structure of DNA by Watson and Crick in 1953. Although not always tied to the workplace, an examination of the evolution of genetic monitoring and screening can provide valuable insight to the procedures' current and potential employment applications. This chapter discusses the history of genetic monitoring and screening as they have been used in both workplace and nonoccupational settings. In addition, the economics of genetic monitoring and screening are examined by evaluating the costs of occupational illness to the employee, the employer, the insurance industry, and society. Finally, the Federal agencies either currently involved or potentially involved in the policy matters associated with genetic monitoring and screening in the workplace are introduced.

HISTORY OF GENETIC MONITORING AND SCREENING

As early as 1938, noted geneticist J.B.S. Haldane discussed "sorting out workers according to their susceptibility to occupational hazards" (7). He suggested, for example, screening out potters who had "constitutions" that could make them susceptible to bronchitis. Haldane went onto suggest that the entry into the workplace of those with the hereditary trait for bronchitis could be regulated.

One of the frost cases of an individual's genetic condition reacting to either a chemical agent or drug was reported in the 1950s. During the Korean conflict, some American soldiers taking the antimalarial drug, primaquine, experienced hemolysis (the destruction of red blood cells) (4). The hemolysis was attributed to their carrier status of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, which results in less of the enzyme G-6-PD in their red blood cells (see ch. 5 for further discussion). People with this trait are often found in malaria-ridden regions, and it is common among Blacks and those with Mediterranean origins. The trait protects people somewhat against contracting malaria, but also can result in hemolysis when triggered by eating fava beans or by taking certain drugs such as antimalarial medication. The soldiers in Korea who reacted to the antimalarial medication, as a result of G-6-PD deficiency, were characterized as "hypersusceptible.

It was believed by the early 1960s that carriers of G-6-PD deficiency could also undergo hemolysis after exposure to certain chemicals. Since then, some employers believe that those with G-6-PD deficiency should not handle aromatic nitro or amino compounds, industrial chemicals prevalent in dynamite factories. The concept of "hypersusceptibility" was being applied to the workplace. One idea considered was the use of a preplacement examination to detect susceptible employees (3 1). Once such employees were discovered, their susceptibility would be factored into their workplace assignment. By the early 1970s, performing "hypersusceptibility" screens had been proposed for five conditions, including G-6-PD deficiency, sickle cell disease, and alpha-1-antitrypsin deficiency (32). Approximately 50 human genetic diseases have been identified as having the potential to enhance an individual's susceptibility to toxic or carcinogenic effects of environmental agents (4) (see ch. 5). Genetic screening may be justified depending on the type and severity of the condition, as well as the difficulty or the expense of performing the genetic screening test (17).

Screening Programs for Sickle Cell Anemia and Trait

Sickle cell anemia in the United States was the subject of a great deal of public attention in the early 1970s. The Black community felt that it had become a' 'neglected disease' and that it had received little Federal research funding. As a result of public debate, considerable Federal interest developed in sickle cell anemia (22). President Nixon made an appeal for an effort to combat sickle cell anemia in his 1971 health address to Congress (9). Laws requiring sickle cell screening were eventually passed in at least 20 States (l). These laws targeted newborns, schoolchildren, marriage license applicants, and inmates of penal institutions (19,22).

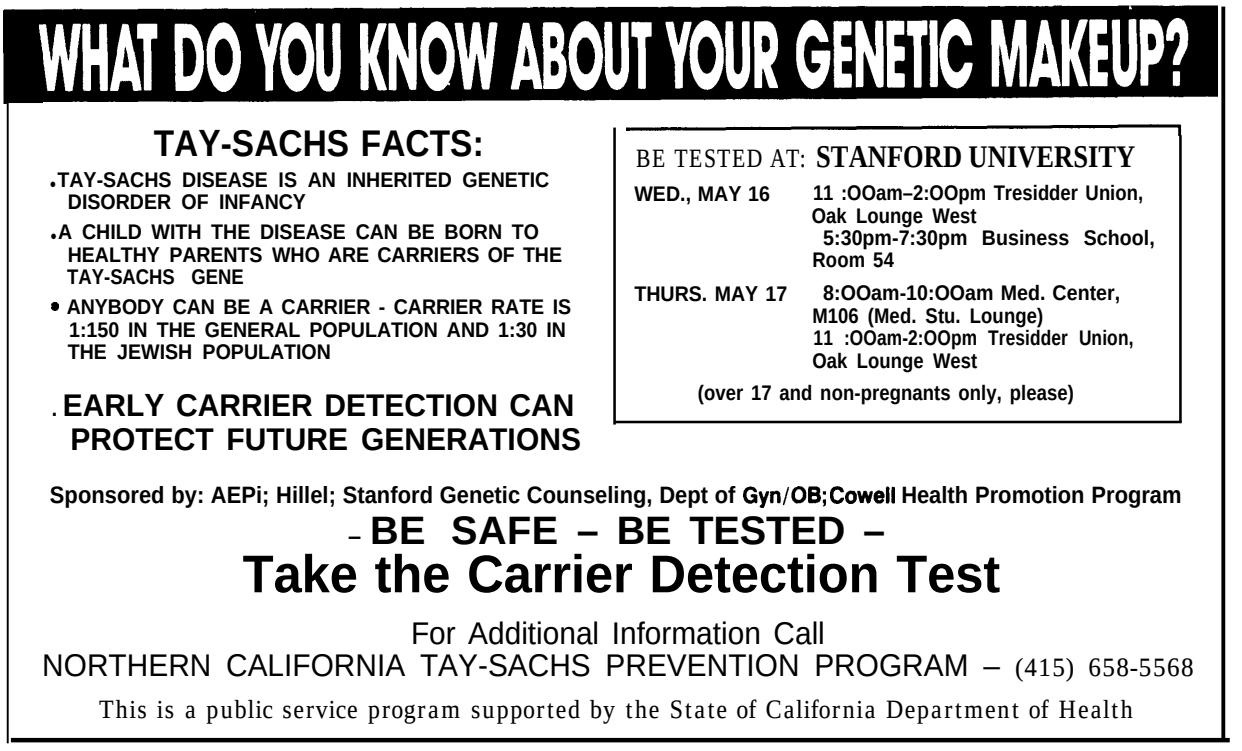


Photo credit: Alpha Epsilon *Pi*

An advertisement for Tay-Sachs screening.

Many who participated in screening programs found the resulting information difficult to interpret. A 1975 study by the National Academy of Sciences (NAS) reinforced this notion. The study found that many of the sickle cell screening programs initially established did not provide proper genetic counseling, and did not always keep the results confidential (19). For many, the difference between sickle cell anemia and sickle cell trait was not made clear in the screening program process. (Sickle cell anemia occurs when the patient inherits the gene for sickle hemoglobin from both parents; sickle cell trait occurs when the gene for sickle hemoglobin is passed on from only one parent.)

Some who participated in screening programs and were found to be carriers of sickle cell trait experienced discrimination at work and from insurance companies that raised their premiums (9). Apparently, discrimination in the workplace sometimes occurred because it was believed that those with sickle cell trait could experience the painful episodes characteristic of sickle cell disease (which occur when sickle-shaped red blood cells occlude the normal flow of blood) (2,24). The result for some job applicants was denial of employment based on their carrier status and removal for some who were already employed. In some cases, life insurance companies either raised premiums for carriers or denied coverage for applicants with sickle cell trait (9). At that time, laws were enacted in Florida, Louisiana, and North Carolina that prohibited such discrimination (26). Since the mid- 1970s, many of the State laws requiring mandatory sickle cell testing have been repealed. The sickle cell screening programs of the 1970s are often compared to Tay-Sachs disease screening programs (see box 3-A).

Controversy still exists over whether the carriers of sickle cell trait are at risk of having sickling episodes. A 1974 NAS report concluded “there was insufficient scientific information to forma basis for excluding carriers from the armed forces or for limiting their activities or duties” (20). However, it was not until 1981 that the U.S. Air Force Academy reversed its policy of excluding Blacks with sickle cell trait from pilot training, based on the belief that a low-oxygen environment (e.g., high-altitude exer-

Box 3-A-Community Screening for Tay-Sachs Disease

Tay-Sachs disease (TSD) screening programs were initiated in the early 1970s, around the same time the Nation's sickle cell screening programs began. While mass sickle cell screening eventually ended because of the belief that the information was sometimes used to the detriment of participants, TSD screening has been cited as a model in professional-community cooperation. TSD is a rare inherited, incurable, neurological disease most prevalent in Jews of Ashkenazi origin. It results in progressive necrologic deterioration and results in death within a child's first few years.

Many screening programs at the local level were initiated following the development of the blood test to detect TSD carrier status in 1970. Screening can determine whether one or both parents are carriers for TSD. If both are carriers, they have a risk of 1 in 4 in each pregnancy of having a child affected with TSD.

A mass screening program involving some 7,000 individuals was initiated in the Baltimore-Greater Washington, DC area in the early 1970s, Six to eight weeks prior to this program, the community received some education about TSD. Information was disseminated through the press, TV, radio, letters from religious, medical and community groups, medical presentations, and telephone contact. Eventually, similar screening programs were initiated in at least five countries.

In one survey, one-half of the TSD carriers were still uneasy with the information even though they had been informed of the meaning of carrier status through extensive educational efforts and genetic counseling. Current emphasis is on hospital- or physician-based screening for TSD with individual couples. Overall in the United States, TSD screening has reduced the incidence of TSD in the Jewish population by at least 70 percent.

SOURCES: Officee of Technology Assessment 1990, based on M.J. Goodman and L.E. Goodman, ''The Overselling of Genetic Anxiety, *The Hastings Center Report*, October 1982; R.H. Kenen and R.M. Schmidt "Stigmatization of carrier *status: social replications of* Heterozygote Genetic Screening Program, " *American Journal of Public Health 68:1116-1120, 1978.*

tion or flights, or deep-water activity) would cause a carrier to undergo a sickling episode (8,14).

While States were passing sickle cell screening laws, Congress passed the National Sickle Cell Anemia Control Act (Public Law **92-294) in 1972. Only States that met the requirements of the act were** eligible for Federal funds. To receive funds, a State program had to be voluntary, a requirement designed to defuse the controversy over mandatory screening programs. Although the intent of the law was to reduce stigmatization of and discrimination against the carriers of sickle cell trait, many saw these concerns as continuing unabated (23).

The National Sickle Cell Anemia Control Act was updated in 1976 and renamed the National Sickle Cell Anemia, Cooley's Anemia, Tay-Sachs, and Genetic Diseases Act (Public Law 94-278; hereinafter, The National Genetic Disease Act). Much broader in scope, it authorized increased Federal funds to be awarded as grants and contracts by the Secretary of the Department of Health, Education, and Welfare. Goals of the National Genetic Disease Act included increased levels of basic and applied research, training, testing, counseling, and education programs on genetic disease. Again, the emphasis of this legislation was on voluntary participation in testing programs. It also emphasized using proper guidelines for confidentiality of results, and stressed the availability of genetic counseling for all participants (23).

Advances in the treatment of sickle cell anemia have prompted renewed interest in screening newborns. A certain percentage of infants with sickle cell anemia are at risk of overwhelming infection and sudden death in the first few years of life. If their sickle cell disease is identified early on, affected infants can be given prophylactic antibiotics that significantly reduce the risk of infection and lower the overall mortality rate from the disease in early life (6). A 1987 National Institutes of Health conference on newborn screening for sickle cell disease concluded that every child should be screened to prevent the potentially fatal complications of sickle cell disease in infancy. In addition, for a program to be effective, proper followup capabilities should be in place prior to instituting a screening program. The services available to the patients and their families should include medical care, psychosocial support, and genetic counseling (35).

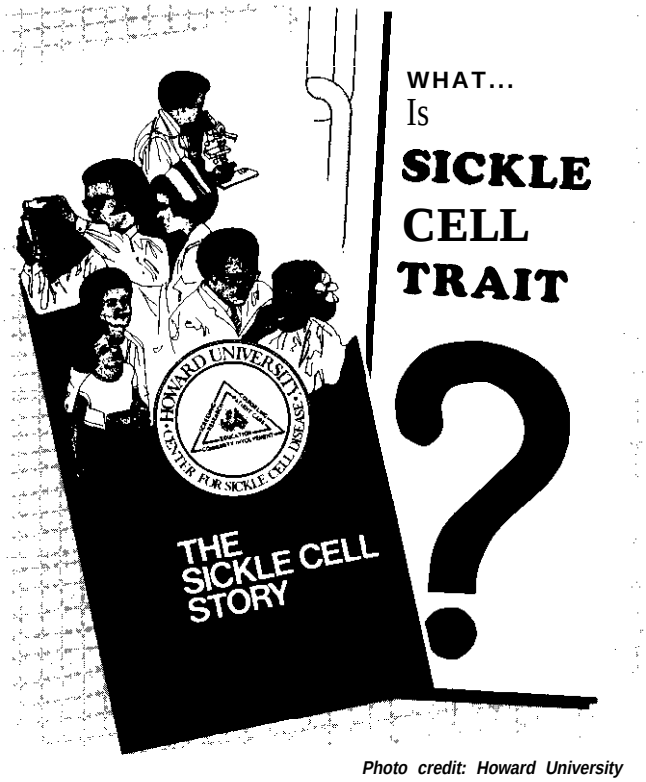


Photo credit: Howard University

Pamphlets describing sickle cell anemia and sickle cell trait.

Industry Involvement in Genetic Monitoring and Screening

Although the concept of screening out unhealthy workers has been around since the early part of this century, most screening technologies have only recently become available. Several incidents of industry involvement in genetic monitoring and screening since the 1960s have been reported. They have varied from research programs using genetic monitoring techniques for evaluating chromosomal damage to efforts in genetic screening to detect genetic conditions such as G-6-PD deficiency or sickle cell trait. Each use brings with it its own set of scientific, legal, and ethical issues.

An early pilot program of cytogenetic monitoring was initiated by Dow Chemical in 1964. (See ch. 4 for a discussion of cytogenetic monitoring.) Within 10 years, some 43,044 chromosomal profiles had been performed on 1,689 employees involved in the chemical production process. In addition, 25,104 chromosomal profiles were conducted on 1,302 applicants as part of a preemployment exam (13). These cytogenetic analyses and preemployment exams provided a baseline for future cytogenetic analyses of an individual. By comparing an employee's current data to that taken previously, the employee served as his or her own control. In 1977, Dow conducted an evaluation of workers exposed to both epichlorohydrin and benzene which, due to the ambiguity of the findings, gave rise to a controversy regarding use of cytogenetics for population monitoring (3).

Their efforts were criticized for several reasons, which included failure to take into account the effects of personal habits and lifestyle decisions (e.g., tobacco use, etc.), and age on chromosomal change. Also, the results of these profiles were given to those employees involved without properly explaining what the results meant in terms of their risk of cancer and genetic disease in their offspring (3,1 1). The program was terminated in 1977 by Dow Chemical in response to the questions about the validity and reliability of the results, and the interpretation of differences in results between employee groups.

Another corporation, Johnson & Johnson, conducted some cytogenetic monitoring research in 1980 to examine the effects of ethylene oxide, a sterilant gas, on workers (12). The project's intent was to determine whether workers exposed to ethylene oxide experienced any more chromosomal changes than those not exposed. This was done by analyzing sister chromatid exchanges and chromosomal aberrations in workers at three plants where three levels of exposure existed (see ch. 4). These groups were then compared to three control groups not exposed to ethylene oxide. After 6 months, the study found that employees working with the highest concentrations of ethylene oxide had a significantly greater incidence of sister chromatid exchange than the control group. This prompted Johnson & Johnson to discontinue the use of ethylene oxide at that particular plant (8).

A genetic screening program for sickle cell trait took place at the DuPont Corp. in the 1970s. According to company officials, the program was initiated at the request of a group of Black employees. The resulting information was not used for employment decisions, officials later stated. Rather it was for the "information and edification" of the employees (8). DuPont was criticized by some because, although there were many employees of

Mediterranean origin at the facility, only Blacks were given the sickle cell test. (People of Mediterranean origin as well as Blacks have a higher incidence of sickle cell anemia.)

Both the Dow cytogenetics program and DuPont's sickle cell screening program were later to become the focus of a great deal of controversy. A series of newspaper reports in 1980 argued that genetic monitoring and screening programs were widespread in industry and had been used in industrial settings for several years (29). Much was made over whether DuPont was actually using the information derived from the sickle cell screening program to make hiring or job placement decisions. The Federal response to genetic monitoring and screening was also examined. The newspaper series identified a section on medical surveillance found in the Code of Federal Regulations that stated that in a preassignment examination before exposure to certain carcinogens, a worker's personal history that included genetic and environmental factors could be taken. As mentioned in chapter 2, these events heightened congressional interest.

INTRODUCTION TO OCCUPATIONAL ILLNESS

It has long been recognized that there are substantial health risks posed by various workplace environments, risks often associated with exposure to harmful agents such as chemicals and radiation. These risks can produce costs to the workers in terms of loss of earnings, ill health, and even premature death. Such risks are costly to employers who may have to compensate workers through workers' compensation schemes for lost earnings and through health insurance schemes for the costs of the medical care they require, and who may have to compensate the workers' estates (through tort liability) for the premature death of the workers.

An occupational illness is defined by the Department of Labor's (DOL) Bureau of Labor Statistics (BLS) as any abnormal condition or disorder, other than one resulting from an occupational injury, caused by exposure to environmental factors associated with employment (37). This includes acute and chronic illnesses or disease that can be caused by inhalation, absorption, ingestion, or direct contact.

The prevalence of occupational illness is unknown. On the Federal level, BLS is responsible for collecting statistical data on occupational injury and illness. BLS statistics on occupational illness incidence rates represent only new cases that occur in a given year. Continuing conditions that were reported in previous BLS occupational injury and illness surveys are not reported (36). Gathering data on the incidence of occupational disease in the United States is extremely difficult for several reasons. Often the relationship between exposure to a health hazard and the risk of, or even onset of, disease is not well understood. Because occupational diseases may have long latency periods, it is difficult to gather the information necessary to link workers' employment history with their medical diagnostic records. Personal physicians are often not aware of their patients' prior chemical exposures or work environments, and therefore may not recognize and diagnose an occupational disease (5,10). It has been suggested that the BLS Annual Survey be modified to improve data collection and analyses (18).

Approximately 190,000 cases of occupational disease were reported in 1987 by BLS (37). This was a 39 percent increase over the 136,800 cases recorded in 1986, which represented a 9 percent increase over the 125,600 cases reported in 1985 (36). An explanation offered by BLS for the increase in illness rates was improved recordkeeping by industry as a result of new government guidelines, as well as an effort on the part of BLS to improve its statistics (41).

Costs of occupational illness affect several parties—the employee, the employer, the insurance industry, and society. The employee experiences physical pain and suffering, emotional costs, and financial costs in the form of medical bills, changes in insurance status, and loss of salary. When a member of the work force incurs an occupational disease, the employer experiences lower productivity levels, higher insurance premiums, workers' compensation claims, and potential legal fees and monetary damage assessed from any lawsuits (27). Insurance companies compensate occupational disease victims, and thereby either sustain a loss or raise others' premiums. Finally, society pays for a large portion of the care and compensation of occupational disease victims through Federal health programs.

Costs of Occupational Illness to the Employee

Costs of occupational illness for the individual employee can include loss of potential earnings (including those fringe benefits used for disability days); transfer to a lower paying job; early retirement; and direct medical expenses. In addition, the costs of such intangibles as premature death, pain and suffering, and family bereavement if an occupational illness victim dies cannot be estimated.

Costs of Occupational Illness to the Employer

An employer's costs associated with occupational illness include direct health care expenses, higher workers' compensation premiums, excess absenteeism, worker turnover, reduced productivity, and possible civil liability suits. Compensation for work-related illness can prove to be a contentious issue. Once an illness can be pinpointed to a particular employer, it is possible that employer can be sued by the employee affected even though workers' compensation is the "exclusive remedy' for such claims (28). Even within the employer's staff there may be disagreement as to the protocol for treating and compensating occupational illness cases. While occupational physicians and other employer-provided health professionals may be interested in the prevention and control of work-related disease from a purely medical standpoint, the employer may be interested in causality, and ultimately in compensation and liability from a legal standpoint. Thus, work-relatedness is defined as both a medical and a legal concept (40). Employers have a financial interest in using their resources efficiently; an interest that could be cited by members of industry as proper justification for monitoring and screening employees for genetic conditions or damage.

Costs of Occupational Illness to Insurance Industry

For the majority of Americans, access to health care, and the health insurance that makes such access possible, is provided through their jobs. Containment of ever-increasing health care costs, whether or not they are related to occupational illness, is a high priority for employers. The increasing propensity of employers to self-insure their employees' health care expenses is a reflection of this. Because these plans are not regulated by the States, there are fewer restraints on them than on traditional health insurance plans.

Companies concerned about insurance costs may be more interested in genetic screening for workers who are likely to develop both occupational and nonoccupational diseases. Many argue that genetic monitoring and screening in the workplace to limit occupational illnesses may be less important to them in the long run than monitoring and screening in the workplace to limit company health insurance costs (21,26).

Costs of Occupational Illness to Society

Society absorbs costs of occupational illness from the private sector. These include: transfer payments and services to disabled individuals and families (e.g., social security benefits and public assistance); health care costs not paid by the individual or the company which are then passed onto Medicare and Medicaid; and the administrative costs of related government programs.

FEDERAL AGENCIES INVOLVED IN OCCUPATIONAL SAFETY AND HEALTH

Although the principal Federal organization responsible for the occupational safety and health regulatory process is DOL's Occupational Safety and Health Administration (OSHA), there are several other agencies involved. In this section, the activities of OSHA, the National Institute for Occupational Safety and Health (NIOSH), the Environmental Protection Agency (EPA), and the National Labor Relations Board (NLRB) are discussed as they relate to both general occupational safety and health and genetic monitoring and screening in the workplace.

Occupational Safety and Health Administration

In 1970, Congress passed the Occupational Safety and Health Act (Public Law 91-596) (OSH Act) "to assure as far as possible every working man and woman in the Nation safe and healthful working conditions and to preserve our human resources. Within the OSH Act there are several federally imposed statutory duties that must be undertaken by the employer.



Photo credit: Margaret Anderson

U.S. Department of Labor, Washington, DC: Headquarters of the Occupational Safety and Health Administration.

Coverage under the OSH Act does not include State and local government employees, or those covered under other occupational health and safety legislation. Prior to the passage of the OSH Act, States were responsible for regulating occupational safety and health. Little uniformity among safety codes or enforcement practices existed, with no standardized reporting and recordkeeping system for occupational illnesses and injuries (25). In addition to Federal enforcement, OSHA now oversees 23 State OSHA programs. If a State plan is approved by OSHA, the State may receive up to 50 percent of its operating costs from OSHA. OSHA will only grant this approval if it can assure that the State performance will be as effective as its own (33).

Contained in the OSH Act was a provision to create OSHA within DOL headed by a presidentially appointed Assistant Secretary of Labor. OSHA is responsible for setting health and safety standards for workplaces, inspecting worksites to ensure proper compliance with those standards, issuing citations for violations of the standards, providing educational and consultation services and programs, and monitoring State programs. Perhaps the two most important OSHA duties are standard-setting and the enforcement of these standards. Effective March 1989, OSHA adopted new exposure standards for over 350 substances (15). Compliance with these standards is expected to reduce the number of workplace fatalities, illnesses, and lost workdays caused by work-related illnesses (38). Prior to this action, the bulk of OSHA's existing health standards were adopted when it was first formed.

At this time, OSHA does not have a formal policy on the use of genetic monitoring and screening in the workplace. Some argue that the OSH Act already provides statutory authority for the evaluation of the accuracy of genetic tests and could implement such genetic monitoring and screening programs, by having NIOSH formulate the criteria for acceptability of genetic monitoring tools and screening tests. Critics of using genetic monitoring and screening in workplace settings maintain, however, that if OSHA adopted a standard mandating genetic monitoring or screening, employers would exclude workers, rather than make the workplace safe for all.

National Institute for Occupational Safety and Health

NIOSH is a research agency of the Centers for Disease Control of the U.S. Public Health Service, which is within the Department of Health and Human Services. It was created under the OSH Act to conduct research designed to identify and evaluate workplace hazards, research concerning measurement techniques and control technologies, and education of occupational health and safety professionals. NIOSH also assists OSHA by developing criteria and recommendations to be used by OSHA in setting standards, and conducting Health Hazard Evaluations. (See box 3-B for information on an international agency similar to NIOSH.)

Congress deliberately separated the research and regulatory functions of the OSH Act to protect the neutrality of the science. However, some say the result has been less than ideal and point to lack of coordination between OSHA and NIOSH. In setting standards, OSHA is not required to follow NIOSH scientific recommendations; OSHA also considers other nonscientific factors, such as economic, social, and political factors, in its regulatory decisions (28).

Some NIOSH research requires on-site workplace investigations to gather testimony from both employers and employees, and to conduct medical examinations and tests to detect exposure to hazard-

Box 3-B--Occupational Safety and Health in Finland

In 1987, Finland's Parliament passed the Labour Protection Act which specifically directs employers to consider "possible risk for the genetic material" of the employee. Prior to the passage of this legislation, Finland's Institute of Occupational Health (101-1) was pursuing research opportunities in genetic monitoring. IOH oversees a register of employees who have been occupationally exposed to chemicals listed as potential cancer-causing agents. This enables researchers to monitor those workers for cancer. Another Federal organization, the National Institute of Radiation Protection and Safety, is conducting a longitudinal study to determine whether workers m four Finnish nuclear powerplants have suffered any chromosomal damage.

The main emphasis of IOH research is on prevention of occupational disease and injury. Projects are designed to be "multidisciplinary, problem-oriented and aimed at solving national problems." Research areas include: epidemiology, medicine, physiology, ergonomics, psychology, occupational safety, industrial hygiene, and toxicology. Most of the research in genetic monitoring and screening is performed within the Department of Industrial Hygiene and Toxicology through a wide range of toxicological, epidemiological, and medical studies. Scientists currently are using various methods of genetic monitoring techniques such as chromosomal aberrations, sister chromatid exchange, micronuclei detection and adduct formation in proteins, ribonucleic acid, and DNA, In addition, some "susceptibility assessments" have been conducted using genetic screening methods.

Scientists at IOH conduct some research and informational exchange with the international scientific community. This can be done through formal bilateral agreements with international research institutions or agencies, as NIOSH, or through international organizations as the World Health Organization. An example of a collaborative project currently underway with the other Nordic nations is a study to assess the health significance of somatic chromosome damage. Utilizing a cohort of 3,000 individuals, the project is aimed at determining g worker exposure to genotoxins, and whether or not this predisposes them to ill health, particularly cancer.

SOURCES: Office of Technology Assessment, 1990 based on A. Brogger, L. Hagmar, I.L. Hansteen, et al., "An Inter-Nordic Prospective Study on Cytogenetic Endpoints and Cancer Risk," ***Cancer Genetics and*** Cytogenetics 45:85-92, 1990 Finnish Institute of Occupational Health, Annual Report 1987 (Helsinki Finland: 1988); Finnish Institute of Occupational Health, Institute of Occupational Health (Helsinki, Finland 1988); Finland's Parliament "The Labor Protection Act of 1987," n. 27/87.

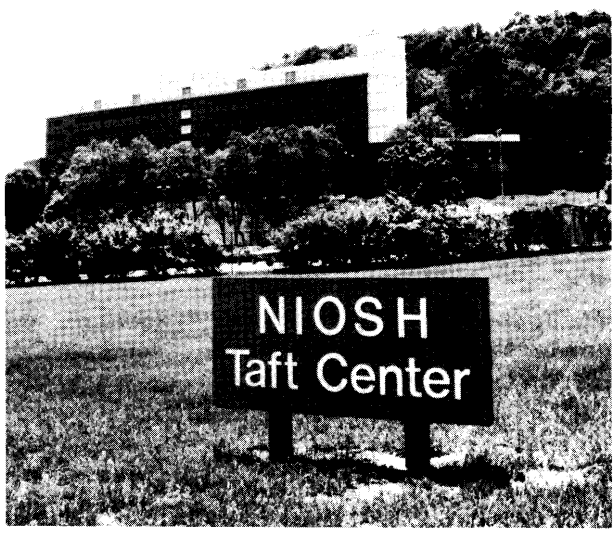


Photo credit: Kathy Goldberg

U.S. Department **of Health and Human Services, National Institute for Occupational Safety and Health, Robert A. Taft Laboratories, Cincinnati, OH.**

ous agents (see box ***3-C).*** Employees can contact NIOSH to request that the agency conduct worksite investigations.

At this time, because NIOSH is a research and not a regulatory agency, it cannot require usage of genetic monitoring or screening in the workplace. However, it currently conducts some research in this area (see app. D). NIOSH could be requested to formulate the criteria necessary for determining the acceptability of genetic monitoring or screening tests for use in the workplace setting ***(39).***

National Labor Relations Board

One of the central pieces of legislation regulating labor-management relations is the National Labor Relations Act (NLRA) of ***1935 (29*** U.S.C. 151 *et seq.).* It encouraged the practice of collective bargaining, and offered protection to workers of full freedom of association, self-organization, and designation of representatives. Amendments to the law in 1947, 1959, and 1974 clarified NLRB organization and procedures, and increased the protection of workers and enhanced their right not to participate in union activity (16).

Box 3-C-NIOSH Surveys of the Workplace

NIOSH conducted the National Occupational Hazard Survey of 4,636 facilities in 67 metropolitan areas from 1972 to 1974. The purpose was to survey American workplaces to determine to what occupational hazards the Nation's workers were being exposed, and to examine companies' health and safety programs. NIOSH conducted a similar survey, the National Occupational Exposure Survey (NOES) from 1981 to 1983. The NOES surveyed 4,490 facilities in 98 geographic areas. A facility site visit included completion of a standardized survey questionnaire by the facility management, and a walk-through survey taken by a NIOSH employee to inventory chemical and physical agents present in that particular work environment.

Among the issues the NOES attempted to answer were: what occupational groups are exposed to what types of potential health hazards in the United States? In what types of industries are these hazards found? What control technologies are present to prevent work-related disease in terms of plant operation and occupational safety and health practice? W are the exposures by intensity, duration, and type of control? And what trade name products were present?

Both surveys gathered a representative sample from all of the nonagricultural, nonmining, and nongovernmental businesses, with eight or more employees, that were covered under the OSH Act. One difficulty of the survey has been that it has taken several years to analyze the data. This has been due, in part, to the length of time it has taken to track down the components of trade name products seen on the walk-through surveys. During the NOES walk-through investigations, NIOSH representatives saw more than 10,000 different potential exposure agents and over 100,000 trade name products. Comparisons to the data collected from 1972 to 1974 will provide NIOSH with a valuable database that can be used to identify areas for further occupational health and safety research.

By comparing the data from both surveys, NIOSH has been able to analyze some of the trends in worker access to health care in the United States. NIOSH found two related events occurring simultaneously. First, facilities are increasingly substituting other health care professionals, primarily nurses and allied medical personnel, for on-site occupational physicians. Health units staffed only by paramedics or nurses are becoming increasingly common. If physician care is needed, the worker is often sent to an off-site medical facility through contractual agreements between the employer and the medical care provider. In comparing the figures from the two NIOSH surveys, the percentage of physician care offered off-site increased from 19.1 to 57.8 percent. Worker access to health care is increasing but much of it is being offered off-site.

The NOES also gathered data concerning some screening tests, preemployment exams, and the recording of health information. The screening tests used were: ophthalmology, audiology, blood urine, and pulmonary function tests, and chest x-rays. Overall, worker access to one or more screening tests increased slightly. This increase would have been greater, except that the number of immunizations given by employers decreased. Data on recording of health information showed a decrease in recording by employers because of the increased use of off-site medical facilities. This responsibility is being left to the off-site physician. This analysis suggests that while worker access to health care is increasing, the delivery mechanism is changing from on-site to off-site, a circumstance that could have implications for the field of occupational medicine.

SOURCES: Office of Technology *Assessment,* 1990; based on D.H. Pedersen and W.K. Sieber, Jr., "Some Trends in Worker Access to Health Care in the United States (1974- 1983), "Journal of Industrial Medicine 15(2): 151-165, 1989; U.S. Departmcntof Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Hcalth, National Occupational Exposure Survey: *Volume 1 Survey Manual,* J. Seta, D. Sundin, and D. Pedersen(eds.), DHHS Pub. No. (PHS) 88-106 (Washington, DC: 1988).

Under NLRA, NLRB administers the law and acts as an intermediary between workers and management. NLRB is responsible for preventing and remedying unfair labor practices, and conducting secret ballot elections to determine whether employees wish to be represented by a union. NLRB's Office of the General Counsel is charged with the responsibility of investigating and prosecuting unfair labor practices.

Although the law was enacted to assist the organization of unions, some members of the labor community have said that they would be better off if the law were repealed. Much of the criticism stems from what some see as the Board's lack of remedies to deal with unfair labor practices, as well as its backlog of pending cases (28,30). It is also argued by labor groups that they feel inadequately protected by NLRB when they confront management. In order for

an employer to have a duty to deal with a union to bargain over the issue of genetic monitoring or screening, it would have to be considered a mandatory subject of bargaining (39). Because health and safety issues are considered to be mandatory subjects of bargaining, it has been argued that health and safety includes genetic monitoring and screening (39). The extent to which unions and employers could bargain and come up with solutions to the many questions that would arise over the use of genetic monitoring or screening depends on answers to a variety of questions. These questions include issues such as the accuracy and predictive value of the tests, clinical significance of the results, access to results, how the tests are used, and who will pay for them.

Environmental Protection Agency

Established in 1970, EPA was created to protect and enhance the environment. EPA administers several environmental health statutes that include broad mandates to protect the public from environmental hazards (34) (see ch. 6). EPA has pollution abatement and control programs in the areas of air, water, solid waste, hazardous wastes, pesticides, radiation, and toxic substances. In addition, it reinforces other Federal agencies' efforts with respect to their operations' impact on the environment. EPA performs research in the area of genetic monitoring (see app. D).

SUMMARY AND CONCLUSIONS

The concept of genetic monitoring and screening is not new. Over 50 years ago, the idea of sorting workers according to their individual susceptibilities to occupational hazards was discussed. The idea of factoring "hypersusceptibility" into workplace assignments was again discussed in the early 1970s, and screens for five conditions, including G-6-PD deficiency, sickle cell disease, and alpha-1-antitrypsin deficiency were proposed.

Controversy over the negative impacts that could result from genetic screening arose following the introduction of a national sickle cell screening program in the early 1970s. The resulting information caused some carriers of the trait to be confused about their health status, as well as to be discriminated against by employers and insurance companies. As a result of this experience, some have concluded that widespread genetic monitoring and screening in the absence of clear guidelines on how the screening results will be interpreted and used has the potential for great abuse. At the same time, legislation concerning sickle cell anemia and other genetic diseases was passed at the Federal level authorizing funds for research, training, testing, counseling, and education.

In addition to mass screening programs, there have been reported cases where genetic monitoring or screening have been used to smaller extents in the workplace. The use of these technologies in the workplace brings with it its own set of scientific, legal, and ethical issues. Discussions concerning the use by employers of genetic monitoring and screening are being heard again, partly in response to the soaring costs of health insurance and also because of new scientific discoveries in genetics that could be applied to the practice of occupational medicine and public health. Because occupational illnesses are costly to all parties involved, there is increasing interest in using genetic screening methods to detect genetic traits that would make a worker susceptible to certain illnesses. Currently there are at least four Federal agencies involved in occupational safety and health, and perhaps genetic monitoring and screening in the workplace.

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Chapter 4

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Chapter 4
The State-of-the-Art of Genetic Monitoring

With the advent of molecular biology, the field of human genetics has undergone an extraordinary metamorphosis. Progress in molecular biology and human genetics clearly has transformed society on many levels—medical, social, economic, legal, and ethical. Because biotechniques are having such profound and practical impacts on daily living, it is important to appreciate the nature of the technologies in order to understand potential applications, such as genetic monitoring and screening by employers. The techniques used in genetic monitoring v. genetic screening for the most part are distinct, although the two areas tend to merge in the detection and diagnosis of cancer.

The term "genetic disease" is used broadly in this and the following chapter, referring to those conditions for which the major causative factor is genetic. There are over 3,000 diseases known to be caused by a single-gene defect and chromosomal anomalies are found in over 1 in 700 live births (44). In addition, research has demonstrated that genetic viability affects many aspects of health, ranging from heart disease to cancer (2,19). It has long been speculated that genetically determined variation in susceptibility may predispose some workers to occupational disease while others in the same environment seem to be unaffected (26,52,65). Additionally, certain environmental agents are known to mutate previously normal somatic cells that could, in some cases, cause disease.

Recognition of genetic factors in disease presents new opportunities for detection, prevention, and treatment. Because of uncertainties about the exact nature of the relationship between genes and environment, genetic monitoring and screening of otherwise healthy populations remain problematic.

Medical screening in the workplace involves evaluating employees before they begin work. It can range from a cursory questionnaire to an oral history to a full preemployment physical. (See chs. 3 and 9 for industry practice.) Genetic screening is a process that considers attributes or indices of altered DNA that may put an employee at high risk for developing disease, whether work-related or not. An extensive discussion of the state-of-the-art in genetic screening for inherited disorders appears in chapter 5. Monitoring, on the other hand, involves the periodic evaluation of employees for either the effects of a toxic substance or its byproducts (60). Genetic monitoring evaluates the genetic damage caused by such substances. In short, genetic monitoring ascertains whether an individual's genetic material has altered over time. Basic human genetics information necessary to understanding this chapter is contained in appendix A. Several documents have presented background material on human genetics and the techniques often used in this field (68,69,70,71, 72,73). The state-of-the-art in genetic monitoring, methodological and reliability issues in monitoring, and the interpretive value of monitoring are also discussed.

MUTATION AND HEALTH EFFECTS

Over the past 15 years an increasing number of health effects have been attributed to mutations caused by toxic agents (26). These mutational effects occur at a rate significantly above the normal background rate found in human cells. The relationships between genes, mutations, and disease are becoming clearer with the development of molecular techniques that enhance both the quantitative and qualitative evaluation of mutation.

The diseases most associated with genotoxic substances are various forms of cancer. Several types of mutational changes (i.e., point mutations, chromosomal rearrangements) have been associated with the early stage of tumor development, as well as with the following steps of tumor promotion and progression (36).

The emphasis on the relationships between genotoxins and cancer may be due to the fact that most studies have focused on somatic cell changes and because germline effects may take generations to appear. Genetic effects on human germ cells are imprecise. More research is needed. Most validation efforts undertaken in genetic monitoring have been designed to quantify the correlation of mutagenesis with carcinogenesis (46). Thus, genetic monitoring involves, for the most part, search for mutations in the somatic cells.

There are two classes of genotoxic agents commonly found in the workplace--chemicals and radiation. The differences between these agents are described below.

Mutagenic Effects of Radiation v. Chemicals

It has been documented for over 40 years that radiation at high doses causes significant carcinogenic and genetic effects. Less clear and certainly more controversial are the effects of low-level doses. The effects of radiation on chromosomes are described in the 1983 Office of Technology Assessment (OTA) report (72) and will not be discussed again here. However, two new topics are worth examination. The first is the extent to which research findings have affected the setting of limits for exposure for chemicals v. radiation. Second is the continuing debate about the effects of low-level radiation.

The finding that ionizing radiation induces chromosomal aberrations (CAs) may help elucidate the means by which certain chemicals alter DNA. Radiation-induced damage can be observed in cells within a few hours following exposure. In general, chemically induced lesions, however, are not converted into aberrations until the cells containing them undergo DNA replication (19). Meanwhile, some chemically induced damage may be repaired long before replication. Because of the lack of good baseline information on chromosomal damage as an effect of chemical mutagens, enthusiasm differs on recommending cytogenetic surveillance for exposed individuals. This has led some to assert that chemical exposures should be evaluated differently from radiation exposures (24).

For example, groups such as the International Commission on Radiological Protection use different rationales in setting limits for exposures to radiation than does the American Conference of Governmental Industrial Hygienists, which sets standards for chemical exposures. There are basic scientific and philosophical differences underlying these discrepancies (24).

External radiation dosimetry can be done on a continuous basis, providing a cumulative dose reading as well as the possibility of periodic readings. Dosimeters of this type are not available for chemical exposures. Thus, relation of dose to genetic monitoring results is much more difficult with chemicals (39).

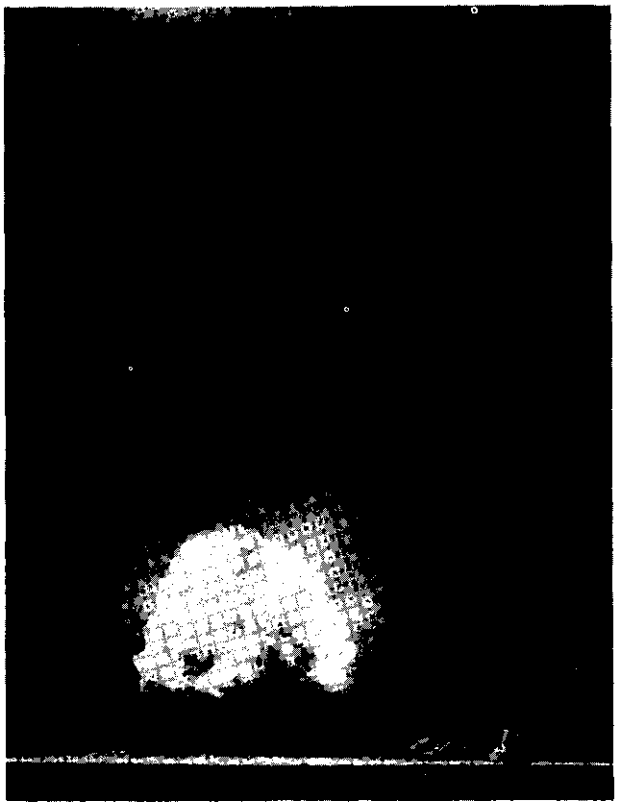
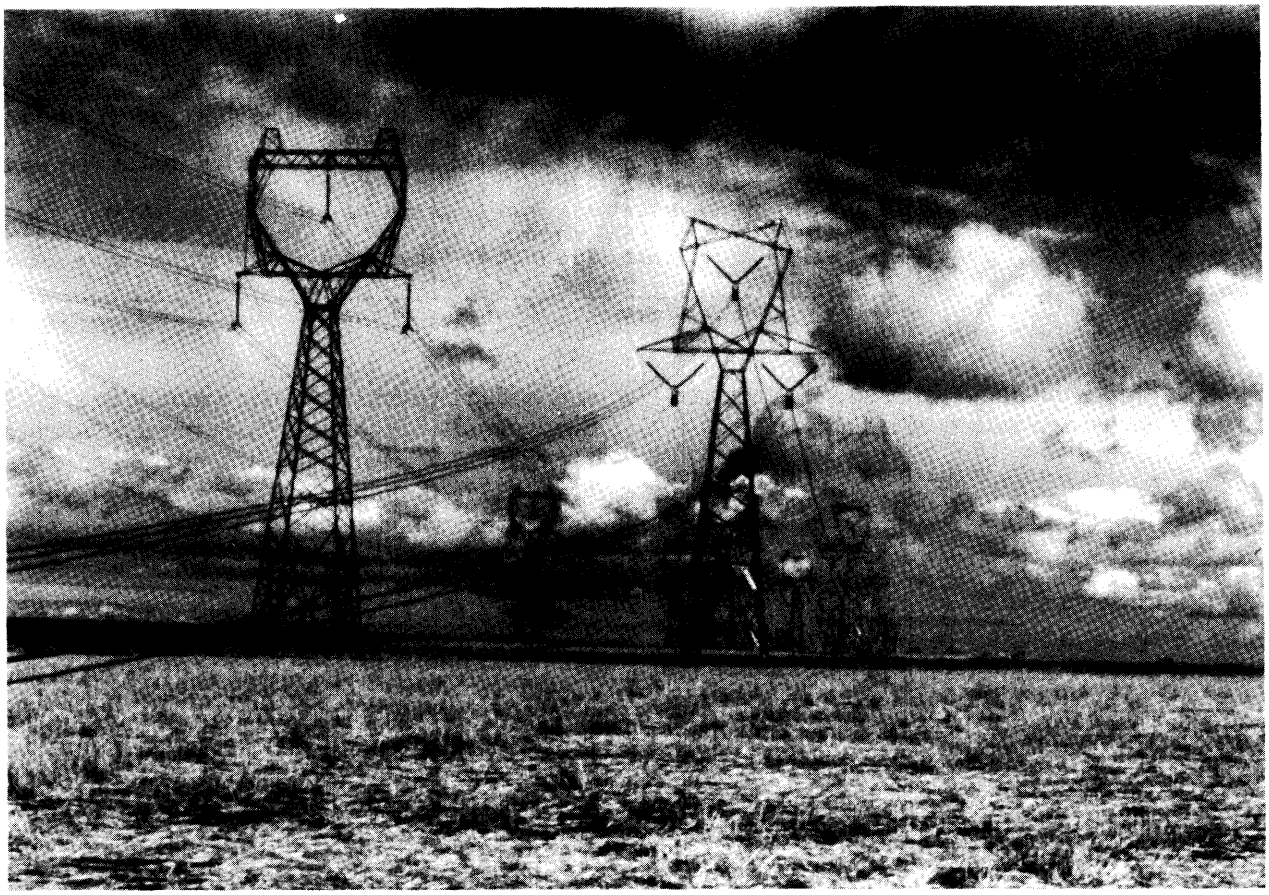


Photo credit: Los Alamos National Laboratory Records Center/Archives

The first atomic bomb detonation—July 16, 1945.

More data exist on the genetic and health effects of radiation, based largely on studies of Japanese atomic bomb survivors, as well as biological experimentation. The data on radiation have been collected over several generations and have led to the consideration of radiation as a somatic and germinal genotoxic agent. Chemical standards, on the other hand, are based on far fewer data, and tend to consider acute, rather than long-term and germinal effects of exposures. Such analysis has led, in many cases, to differences in evaluating exposures.

Internal biological doses are often determined for workers exposed to radiation whereas most limits for workplace chemicals are established in terms of airborne concentration or external exposures (24). Finally, radiation standards assume that biological damage caused by low doses of radiation is cumulative and is not repaired as rapidly as damage caused by chemicals, whereas standards set for chemical exposure are based on the assumption that biological damage caused by exposures to low doses is not cumulative and is frequently repaired. While the



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effects of low-level, long-term exposure to chemicals are hardly understood, the debate in this area relative to ionizing radiation still rages.

Until the health effects of radiation and chemical exposures are better understood, genetic and biological monitoring of exposed populations can only provide a gross indication of health risks. Health effects may not appear for as many as 30 years following initial exposure.

Low-Level Radiation

In the past few years, science has offered sharply conflicting opinions about the dangers of low levels of radioactivity. This divergence is due, in part, to the different assessments of radiation doses received by those studied, and to insufficient understanding about how small doses of radiation increase cancer risk (55).

The debate has been rekindled, in part, because of the nuclear accidents at Three Mile Island and Chernobyl, and current concerns about the effects of radon (74). Concern about the carcinogenic effects of radiation in employees of the nuclear weapons and nuclear power industries has also fueled the debate (14,55). And, most recently, an association between low-dose exposure to radiation and leukemia in the offspring of men employed in a nuclear facility was reported (20).

In a study of mortality among workers at a nuclear fuels production facility, the rate of cancer was found to be normal or below normal except for leukemia (16). This, and similar studies, have led some to the conclusion that very low doses of ionizing radiation are not harmful after all, or might even have net benefits, a phenomenon called "hormesis" (57). This net benefit is attributed to an overprotective response involving enhanced DNA

Table 4-1—Major DNA Lesions Produced by Chemical Interaction and Their Genotoxic Consequences

Primary lesion	Description	Consequence
Alkylation	Covalent adduct formed, involving the genotoxic agent and a DNA base or phosphodiester bridge	Alteration of base pairing, loss of the base, stimulation of error-prone repair
Intercalation	Noncovalent stacking of the genotoxic agent between adjacent base pairs in the DNA helix	Alteration of DNA transcription, replication, or repair
Cross-linkage	Formation of two covalent bonds between bases within (intrastrand) or between (interstrand) DNA strands	Dimer formation, alteration of replication
Breakage	Scission of either a single or both strands of the DNA helix	DNA rearrangements forming chromosomal aberrations after mitotic cell division

SOURCE: R.W. Hart and D. Brusick, "Assessment of the Hazard of Genetic Toxicity," *Toxic Substances and Human Risk,* R.G. Tardiff and J.V. Rodricks (eds.) (New York, NY: Plenum Press, 1987).

repair of arising mutations that more than compensates for the harmful effects of radiation.

Critics of this theory argue that radiation-induced mutations have not been proven to be beneficial (in fact, the preponderance of evidence is quite the opposite (79)). Although an adaptive response was detected after exposure to very low doses of ionizing radiation, the protective effects remain to be determined (35). Also, studies reporting no increase in cancer after radiation exposure have not waited long enough before drawing conclusions. Leukemias typically start to appear about 2 years after a dose of radiation, compared with about 15 years for other cancers. Forty years after Hiroshima and Nagasaki, most cases of leukemia have already occurred, whereas other cancers are still being reported (55). Thus, studies that report "only" an increase in leukemias could be reporting the beginning of the trend toward more cancer reporting years away.

In late 1989, a panel of the National Research Council (NRC) concluded that exposure to low levels of radiation, such as that from x-rays or radon, is at least three to four times more likely to cause fatal cancer than is commonly believed. This dramatic about-face from previous NRC reports is due to a reevaluation of dose data from atomic bomb populations. Reconstructions of the original bomb designs revealed much lower radiation doses than originally thought. Also, as the surviving population has aged, more fatal cancers have developed than expected, including cancers of the breast, lung, stomach, ovary, throat, colon, and bladder, as well as leukemia, the standard "canary in the mine" (43).

The effect of the NRC conclusions is to at least quadruple estimates of the number of radiation deaths expected among workers in the nuclear power and nuclear weapons industries, those who frequently undergo radiation therapy and x-rays for diagnosis, and those who are routinely exposed to radioactive elements in certain natural gases, building materials, or tobacco. These revised estimates, however, do not change the difficulty or impossibility of doing definitive epidemiological studies of low-level radiation effects (63).

TECHNOLOGIES FOR GENETIC MONITORING

In simple terms, a mutagen is a substance capable of inducing a heritable change in the genetic material of cells. The changes can be detected at the molecular or chromosomal level through measurement of sister chromatid exchange (SCE), unscheduled DNA synthesis, point mutations, CAs, formation of DNA adducts, and oncogene activation, described in this section. Much progress has been made in measuring these endpoints and understanding the role of these processes in the induction of mutagenesis. Table 4-1 summarizes the major DNA lesions produced by genotoxic substances. In many cases, mutagens are also carcinogens, so at high exposure levels, the most common manifestation of genetic damage is in the form of cancer (75). Box 4-A describes some of the connections between genetic damage and cancer.

Exposure to genetically toxic agents initiates a process which is illustrated in figure 4-1. The damage will be resolved in one of three ways: cell death, successful DNA repair, or viable mutation. It is difficult to establish the causal relationships between the mutation and cancer because of the long latency of human cancer. Nonetheless, the rationale behind the use of genetic damage assays as indicators of exposure is that events observed initially and at high frequencies are the start of a process that may ultimately produce abnormal growth (neoplastic changes) in a smaller subset of cells.

Box 4-A--Genetics and Cancer

Cancer is a genetic disease arising from genetic damage of diverse sorts-recessive and dominant mutations, large rearrangements of DNA, and point mutations-all leading to distortions of either the expression or biochemical function of genes. The growing field of cancer genetics aims to uncover the genetic alterations responsible for uncontrolled growth of cancer cells. Many types of human cancer occur in familial as well as sporadic forms, Discrete genetic changes have been associated with different types of neoplasm, and are thought to initiate or cause progression of cancer. Chromosome studies in more than 10,000 cases of neoplasms have reported specific anomalies. The identification of genetic changes, therefore, presents the major diagnostic challenge in cancer.

Both dominant and recessive forms of cancer have been found. The genetics of the common cancers-breast, colon, and lung—are beginning to fit a pattern. Approximately 5 percent of cancer cases constitute a hereditary cancer syndrome in which a dominant gene predisposes to cancers of the breast, ovary, brain, gastrointestinal system, and white blood cell precursors. These are referred to as 'cancer families' (see ch. 5 for further discussion). Apart from these, each type of cancer appears to have a small group of cases that fits the pattern of a major predisposing gene and a much larger group that seems to be largely environmental in origin.

In addition, examples such as xeroderma pigmentosa imply that there is a connection between susceptibility to cancer and impaired ability of cells to repair damaged DNA. It is a reasonable expectation that if cancer is related to alterations in somatic cell genes, then the rate at which those changes occur could serve as a barometer of changes in the gem-dine that may not be expressed for many generations to come.

Certain cancers, e.g., lung, laryngeal, bladder, and testicular, have repeatedly been linked to environmental exposures. The effects on chromosomes of such chemicals as arsenic, asbestos, chromium, nickel, and vinyl chloride are well-documented. Substances that cause chromosomal abnormalities are called ''clastogens. The reader is referred to the 1983 Office of Technology Assessment report for more detail on the specific effects of those agents. Chapter 5 describes recent advances in detecting predisposition to some common cancers.

SOURCES: Office of Technology Assessment, 1990, based on J.M. Bishop, "he Molecular Genetics of Cancer," *Science* 235:305-311, 1987; F. Mitelman and J.D. Rowley, ''Genes, Chromosomes and Cancer: A New Forum for Research in Cancer Genetics," Genes, *Chromosomes & Cancer 1:1-2, 1989;* J.J. Nom and F.C. Fraser, *Medical Genetics: Principles and Practice* **(Philadelphia%** PA: Lea & Febiger, 1989); R. Parshad, K.K. Sanford,, K.H. Kraemer, et al., ''Carrier Detection in Xeroderma Pigmentosum," *The Journal of Clinical Investigation 85: 135-138,* 1990.

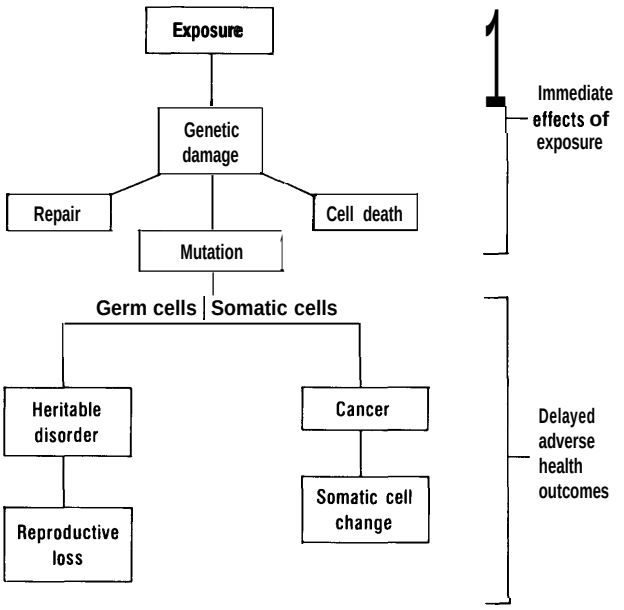
Thus, the purpose of monitoring tests is to detect biologically significant exposures **early,** even though the results are currently unsuitable as a basis of quantitative risk assessment. Advances in testing at the molecular level (discussed below) will most likely provide better predictors of neoplasia, as the relationships between mutation and neoplasia become better understood.

Environmental agents can increase the risk of genetic disease and cancer in exposed populations. Humans are exposed to over 25,000 toxic compounds that are potentially or demonstrably mutagenic in lower organisms (44). The fundamental problem of evaluating genetic risk from environmental exposures rests with the ability to identify a chemical as a somatic or germ cell mutagen in humans (67). Because this cannot be done ethically or legally in humans, most studies rely on animal models. Problems arise in trying to extrapolate from animal studies to human populations because of genetic differences and dose-response relationships. Yet, the whole process of making carcinogenic risk estimates is based on the assumption that there is a qualitative and quantitative correlation between the results of animal mutagenicity and carcinogenicity tests and expected effects in humans. Most Federal and State regulations are based on this premise (17): that is, if mutagenic activity is observed for a chemical, even in bacteria, it is possible that it or its metabolizes could be carcinogenic.

Reduction of risk requires, among other things, sensitive methods for detecting harmful agents. Mutagenesis can be measured in many ways, the most conventional methods are cytogenetic and biochemical. Molecular methods, however, are increasingly being developed and will shed further light on the nature of mutagenesis and its relationship to carcinogenesis (see also ch. 5).

A previous OTA report discusses in greater detail technologies for detecting heritable mutations (73). The reader is referred to that publication for elabora-

Figure 4-1—Biological Consequences of Exposure to Mutagenic Agents



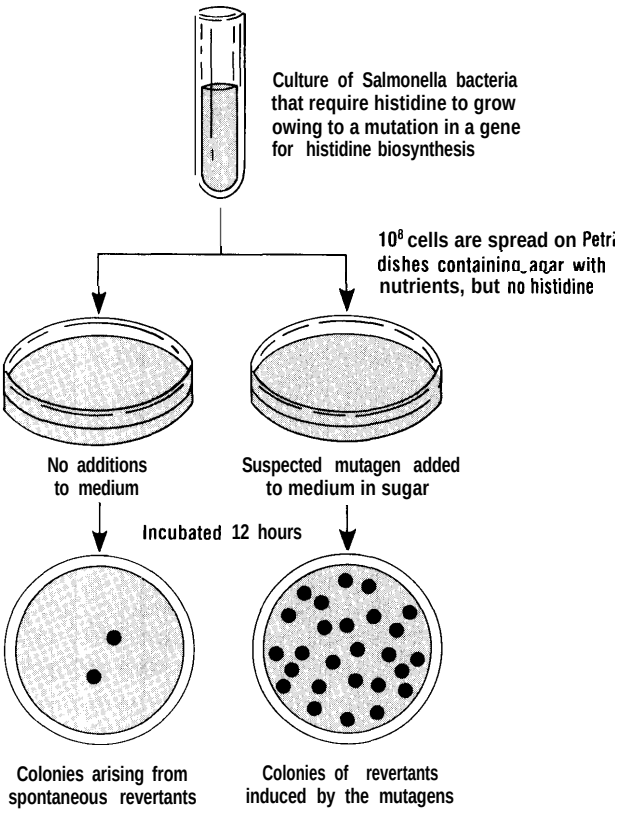
SOURCE: Office of Technology Assessment, adapted from J.B. Ward, "Issues in Monitoring Population Exposures," *Carcinogens and Mutagens in the Environment Volume II, The* Workplace, Hans F. Stich (cd.) (Boca Raton, FL: CRC Press, 19S5).

tion of techniques and methodological considerations relevant to tests for mutagenicity. Other than a brief discussion of biological monitoring, the remainder of this section will address tests used specifically for monitoring occupational populations for genotoxic effects. The focus is on detection of genetic changes, not just the presence of chemicals, in workers.

Tests of Mutagenicity

The more traditional approach to testing for exposure to mutagens has been to measure the chemical itself (or a byproduct) in blood, breath, and urine. Mutagenic activity in urine can be shown by using rapid screening tests developed for bacterial or in vitro cell culture systems. Standard analysis of body fluids for the presence of mutagens was discussed in greater detail in the 1983 OTA report and will not be covered further here. The most common short-term test for mutagenicity conducted on body fluids is the Ames/Salmonella test (see figure 4-2). Because the specificity of the procedure has come under fire in recent years it is discussed in detail in box 4-B.

Figure 4-2—The Ames Test



The Ames testis used to determine whether a chemical can cause mutations in bacteria Mutant bacteria that have lost the ability to synthesize the amino acid histidine and cannot grow in its absence are treated with the test chemical. Potent mutagens can cause mutations that reverse the hismutation, resulting in bacteria that can grow in the absence of histidine.

SOURCE: Office of Technology Assesment, 1990.

Testing for the presence of mutagens in blood and urine is more suited to occupational settings as a complement to ambient measurements, thereby providing an indicator of exposure and absorption. The presence of mutagens only serves as an indicator of recent exposure and provides no information regarding the health effect on the individual.

Biological monitoring, therefore, involves examining the worker for absorption of a toxic substance or its byproduct as an indicator of internal dose. Most work to date has focused on the relationship between internal dose and external exposure, rather than between internal dose and adverse effects (58). Detection of mutagens in urine has been reported in several types of workers including oncology nurses and pharmacists involved in preparing and administering cancer chemotherapeutic drugs (65).

Box 4-B—The Ames Test

Most current studies of **mutagenesis are** based on the pioneering work of Ames et al. The general procedure involves treating a bacterial cell population containing a designated genetic marker with a mutagen. The mutagen kills off a fraction of the cell population with survivors growing back into a larger population. Within this survivor population, a fraction of the cells will have lost the marker. This fraction, expressed as a percentage, is taken as a measure of the mutagenic action suffered by the original population. Since about ***85*** percent of compounds known to be carcinogenic in rodents arc also mutagenic in the Ames test, some have suggested that the Ames test is a belter indirect test of carcinogenicity than a direct test of mutagenicity. In fact, because of the correlation between mutagenicity and carcinogenicity, some statutes, such as the Toxic Substances Control Act (Public Law 94-469), require chemical manufacturers to demonstrate negative mutagenicity of a chemical via the Ames test as a substitute for long-term, more expensive bioassays for carcinogenicity.

The limitations of the Ames test, however, are many. First, only mutations in viable cells are scored. Those m cells killed by the agent are not measurable. While such mutations could be lethal in the particular chromosome containing the marker gene, similar mutations at loci on other chromosomes could produce viable but genetically damaged cells. Furthermore, mutants often possess reduced rates of cell multiplication. Thus, the fraction of mutated cells in the test population will be materially decreased from the original value.

The Ames test also fails to measure large mutations such as deletions, because such lesions have a high probability of extending into vital genes on the marker chromosome and causing the death of the cell. Large mutations are known to be extremely important in the activation of oncogenes and in the induction of genetic disease.

In addition, critics argue that the Ames testis not specific, as large doses of mutagenic agent are required before significant measurements can be made. The low specificity produces a high false positive rate and a less than desirable predictive value. Finally, in order to calculate mutagenic effects for low dosages, it is necessary to resort to extrapolation over a large dosage interval. Whether this extrapolation should be linear or based on a threshold region has been widely debated. So far, regulatory agencies have favored the threshold hypothesis which postulates that there are low dosages with no mutagenic effect.

Efforts have been made to correct for these deficiencies, including use of a plasmid unnecessary for reproduction as the carrier of the marker, use of several markers, and use of lower dosages on a more variable cell population. Some feel that the current reliance on the Ames test and its requisite extrapolation may underestimate the health effects of low doses of some mutagens.

A method by which to recover and analyze the mutated genes could facilitate the molecular analysis of mutagenesis in intact organisms as well as in cultured cells. This approach uses chromosomally integrated shuttle vector genes that are integrated into the mammalian cell's chromosomes and replicated in synchrony with the chromosomal DNA. Pure clones of mammalian cells containing the mutant genes can then be isolated, recovered, and sequenced.

SOURCES: Office of Technology **Assessment,** 1990, based on B.N. Ames, J. McCann, and E. Yamasaki, "Methods **for Detecting Carcinogens and Mutagens** *with the Salmonella/Mammalian-Microsome Mutagenicity* Test" Mutation *Research 31(6):347-364, 1975; RI...* Davidson and C.R. Ashman, "Chromosomally Integrated Shuttle Vectors and Molecular Analysis of **Mutagenesis in Mammalian Cells," Somatic Cell** *and Molecular Genetics 13(4):415-417, 1987;* J.J. Nom and F.C. Fraser, Medical Genetics: *Principles and Practice (Philadelphia, PA: Lea & Febiger,* **1989);** T.T. Puck and C.A. Waldren, "Mutation in *Mammalian* Cells: Theory and Implications,"Somatic Celland ***Molecular*** Genetics 13(4):405-409, 1987; R.W. Tennant, B.H. Margolin, M.D. *Shelby, et al.,* "*Prediction* **of Cbemical Carcinogenicity in Rodents From In** Vitro Genetic Toxicity Assays," Science 236:933-941, 1987; C.A. Waldren and T.T. Puck, "Steps Toward Experimental Measurement of Total Mutations Relevant to Human Disease,' Somatic Cell *and Molecular Genetics* **13(4):411-414, 1987.**

Biological monitoring techniques are frequently used for chemicals known to have adverse health effects, as well as mutagenic effects. For example, the recognition of the neurotoxic and narcotic properties of toluene--a product of crude oil used as a solvent in oils, resins, rubber, and paints, and as a basic material in many synthetic chemicals-has lead to the development of biological monitoring methods for assessing toluene uptake. Short-term exposure to high concentrations of toluene can cause drowsiness, dizziness, and headaches. Breath, blood, and urine tests can be used to check and control levels of exposures (11).

Studies of Effects on Sperm

Traditionally, most studies of chromosomal abnormalities are performed on cultured white blood cells. But to assess the effect of mutagens on reproduction, analysis must be done on germ cells. Knowledge about adverse effects of toxic exposures on reproduction is limited, but some credible associations have emerged.

The potential for occupational exposure to have an adverse effect on sperm was shown when workers exposed to dibromochloropropane had markedly reduced sperm counts and a decrease in number of offspring (34,78). Sperm count can be affected by a multitude of factors, so direct causal relationships between decreased counts and particular exposures are difficult to establish. Some studies, however, have shown that certain physical abnormalities of sperm are produced by environmental exposure, such as atypical shape, nondisjunction of the Y chromosome, and abnormal motility (54).

Abnormal sperm morphology has been associated with exposure to lead and carbaryl (32,80). Adriamycin, a cancer drug effective against a broad spectrum of neoplasias, has been shown to cause reduced sperm count and increased CAs in mouse germinal cells (3). Solvents such as ethylene glycol ethers, pesticides such as ethylene dibromide, metals such as mercury and arsenic, and alkylating agents such as ethylene oxide, have demonstrated spermatotoxic effects in animals (18).

Cytogenetic Indicators

Results from extensive animal and human studies show an empirical association between chromosomal damage and mutagenic-carcinogenic agents. CAs and SCEs are the principal cytogenetic indicators used to estimate exposures to carcinogens. The efficiency of these indicators can potentially be improved by the application of developing computer image analysis for the scoring of CAs (35). It has not been determined whether these indicators of exposure are predictors of disease risk except as a diagnostic tool for some tumors, so the clinical significance for individual workers is unclear.

Studies of some occupational exposures reveal associations between exposures and chromosomal effects (12,65). The results of cytogenetic techniques that use blood cultures to study the in vivo response of people exposed to mutagens are compelling but inconclusive. The main conceptual basis for the application of cytogenetic tests to measure chromosomal damage is that damage to the genetic material of cells represents initial events in a process that may eventually lead to disease. Cytogenetic methods can detect human exposures at biologically significant levels in populations, but the interpretation of findings for the individual remain uncertain.

Detectable mutations result from gross changes in chromosome structure and can be visualized under the microscope. The disruptive effects of mutagens on chromosome structure, organization, and behavior have long been studied by geneticists. The relationship between CAs, spontaneous abortions, and birth defects is well-documented. But, the connections between chromosomal damage and disease are unclear except in a small number of cancer cases. Again, cancer is the disease most commonly hypothesized to be associated with induced CAs because of their presence in lymphoproliferative disorders such as leukemia, and in solid tumors (62). Most analysts agree that interpretation of cytogenetic results at the individual level is questionable and recommend that until the relationship between cytogenetic damage and disease is better understood, interpretation should be maintained at the population level. In addition, cytogenetic monitoring of human populations is expensive and time-consuming (12).

Chromosomal Aberrations

One of the few direct methods for measuring gross changes in DNA involves visualization of the chromosomes through the light microscope. The viewer might see overt breakage and rearrangement of the chromosomes within the cell as well as more subtle changes involving the exchange of material between chromatics of a chromosome. The type of

alteration produced by physical and chemical agents depends on the lesions induced in the DNA and, therefore, on the chemical structure of the genotoxic substance (12).

CAs are usually induced by agents that can directly break the DNA duplex such as different types of radiation chemicals that imitate the effects of radiation. CAs therefore serve as a biological dosimeter in individuals exposed to ionizing radiation. The same is not true for cases of chemical exposure, however, since most chromosome-breaking (clastogenic) chemicals require metabolic activation and are dependent on a critical time in DNA replication. CAs have been demonstrated for a large number of chemicals in vitro, but relatively few chemicals have been convincingly shown to increase CAs in vivo (15). On the other hand, some investigators have reported that in vivo cytogenetic assay is a very accurate assay system to identify carcinogens from non-carcinogens (4).

For chemical exposures, chromosome analysis is, for the most part, a low sensitivity method. This stems from the low frequency of CAs, thereby requiring that large numbers of individuals and cells be studied to detect a statistically significant increase in CAs. Detecting effects at low exposure levels or in small groups is not informative (15). Application of this method to ionizing radiation, on the other hand, is well-established. It continues to be applied routinely to all suspected cases of radiation exposure in several countries, most notably by the National Radiological Protection Board in the United Kingdom (7).

Recently, two studies have demonstrated that cancer developed more frequently among individuals having CAs (22,64). These data suggest a direct relationships between CAs and development of disease.

Sister Chromatid Exchange

The study of SCEs is an indirect indicator of mutation, although the biological significance is unknown. Unlike CA measurements, SCE can be a sensitive marker for the measurement of DNA damage and repair (76). Sister chromatics are the two daughter strands of a duplicated chromosome. SCEs are events that occur when apparently equivalent sections of the sister chromatics of the same chromosome are exchanged during cell division (mitosis). SCEs occur in cells at a normal rate, but



Photo credit: U.S. Council for Energy Awareness

A Nuclear Power Worker: Controversy continues regarding the carcinogenic effects of radiation in employees of the nuclear weapons and nuclear power industries.

appear to be elevated when exposed to agents that damage DNA. Of importance from a practical standpoint, SCEs appear to result only as an effect of chemical mutagens, not radiation. They are most efficiently induced by substances that form covalent adducts to the DNA, distort the DNA helix, or interfere with DNA precursor metabolism or repair (33).

Detecting SCEs in peripheral blood lymphocytes is one way of monitoring chemically induced chromosomal damage and is less costly than tests of CAs because SCEs are easily scored. Because CA and SCE represent different types of genetic damage, however, it would be misleading to replace one assay with the other.

SCE analysis has the potential for being useful in both screening and monitoring, because in addition to the tendency toward increased SCE as a result of exposure to genotoxic chemicals, certain inherited conditions demonstrate increased SCE (13). On the other hand, caution must be taken to protect against confounding factors such as cigarette smoking, alcohol consumption, drug intake, chemotherapy, infections, and vaccination, as all have been shown to induce SCEs.

As mentioned previously, chemically induced lesions are often repaired and therefore would not show up in the SCE assay. The frequencies of SCEs, therefore, can fall off rapidly with time after an acute exposure, and the time at which the SCEs are scored becomes a confounding variable in interpretation. Nevertheless, elevated SCE frequencies may pro-

vide a good indication of prior exposure to chemical mutagens. Although, because the effect of chemicals on induction of SCEs varies, calibration curves have to be derived for each agent for SCEs to be quantitative predictors of mutation induction (13).

To date, many studies of the effects of occupational chemicals on SCE frequencies have been conducted; often with contradictory results (76). The contradictions could be due to unidentified confounding factors related to lifestyle of those tested. Some evidence also exists that SCE frequencies do not necessarily increase with level of exposure. At relatively low levels, certain chemicals, such as benzene, mainly affect DNA repair at the replication point, inhibiting, rather than inducing the formation of SCEs (76). Thus, without accounting accurately for exposure levels, separate studies could yield conflicting results. Finally, for a given exposure, it is not known whether higher or lower frequencies of SCEs is better, i.e., a sign of damage or a sign of repair (47).

At present, many known carcinogens produce SCEs, but no systematic sampling of chemical agents has been conducted to determine whether correlations for certain chemicals are truly predictive of health risk (66).

Micronuclei Assay

One consequence of the induction of CAs is the formation of micronuclei, which result from the exclusion of fragments of/or whole chromosomes from nuclei formed at mitosis. The presence of micronuclei can be taken as an indication of the previous existence of CAs. Micronuclei are far easier to score than CAs at metaphase (although less frequent) and provide a simple means for estimating induced genetic damage. In addition, micronuclei persist for varying lengths of time after their formation so they can be detected in nondividing descendants of cells. Early studies of the effects of ionizing radiation on mitosis showed that the frequency of micronuclei was dependent on radiation dose (19).

One of the most dramatic presentations of micronuclei has been demonstrated in worker populations exposed to cytostatic drugs such as cyclophosphamide, a chemotherapeutic agent. Increased numbers of micronuclei were observed in lymphocytes of groups of workers from industry and hospitals where the drug is processed and administered (81).

Table 4-2—Main Confounders and Limitations of Occupational Cytogenetic Studies and Ways To Control Them

	Control efforts
Confounders	
Exposure conditions:	
Identification of correct chemical exposure	Factory record checking
Estimate of dose of exposure	Industrial hygiene survey
Individual variations:	
Genetic factors	Unknown before analysis
Lifestyle factors	Match with controls
Health factors	Check medical records
Limitations	
Culture conditions:	
Culture time	CAs: First division metaphrases SCEs: Second division metaphases
Culture medium and chemicals	Keep constant
Time between sampling and culture	Keep constant
Persistence of mutagens in the blood sample	In vitro experimentation
Analysis and scoring:	
Scorer variation	Coded slides, one scorer
Interpretation of damage scored	Strict scoring criteria

SOURCE: M. Sorsa and J.W. Yager, "Cytogenetic Surveillance of Occupational Exposures," *Cytogenetics*, G, Obe and A. Basler (eds.) (Berlin, West Germany: Springer Verlag, 1987).

Limitations of Cytogenetic Tests

In cytogenetic studies, at least two major types of technical variations exist. The first includes factors associated with differences in slide reading, culture conditions, and concentrations of test chemicals. The second involves sampling times and differences in cell populations being tested (65).

Test Limitations

Scoring, or counting of the cells, is also an extremely important element in cytogenetic toxicology. Slides must be randomized and coded to avoid scorer bias. Accurate results depend on slides prepared at a specific time during the analysis to ensure that the proper time in the lifecycle of the cell is reached. Consistent scoring criteria and statistical analyses must be maintained to obtain reliable and valid results. Table 4-2 summarizes some of the major limitations and confounders of occupational cytogenetic studies.

Test Interpretation

Baseline data for the effects of various chemicals on SCEs and micronuclei formation are inadequate. In particular, quantitative data on the normal back-

ground frequencies of micronuclei are unavailable, making it difficult to set standards for exposed populations. Theoretically any increase detected between preemployment data and post-exposure data would suggest that exposures are too high.

Micronuclei are associated with increasing age and smoking (29). All measurements must establish a background level of alterations that is seldom, if ever, zero. The background incidence of all genetic events varies with time and between individuals. To date, there is no international standard for the conduct of human cytogenetic surveillance studies, although guidelines have been developed by the International Commission for Protection Against Environmental Mutagens and Carcinogens (31). The U.S. Environmental Protection Agency has also provided guidelines for cytogenetic evaluations (51).

Application of Cytogenetic Tests to Occupational Exposures

Elevated cytogenetic abnormalities of the three types previously described may be associated with occupational exposures to ionizing radiation or some chemicals, particularly where long-lived alterations are involved. The nature and longevity of the alterations vary from one agent to another. For some chemicals such as benzene, the alterations may persist for years and probably represent a cumulative exposure. For others, such as vinyl chloride, the alterations disappear quickly after reduction of exposure; thus cytogenetic assays can monitor exposure only over a short period of time.

Over 100 cytogenetic studies have been reported from various occupational exposure groups (65). Among the occupational chemicals with best documented positive cytogenetic tests are ethylene oxide, styrene, benzene, and alkylating anticancer agents. Occupational cytogenetic studies of arsenic, benzene, epichlorohydrin, ethylene oxide, lead, cadmium, zinc, and vinyl chloride were described in the 1983 OTA report. They are not discussed again here, but summaries of those findings appear in table 4-3, which lists the most common occupational exposures that induce cytogenetic abnormalities.

Since the 1983 OTA report, increased CAs have been reported in individuals exposed to phosphine, a common grain fumigant (21), and a range of pesticides, including organophosphorous, organochlorinated, and carbamate groups (56). Animal studies have demonstrated elevated SCE and CA frequencies in rat cells exposed to a common household insecticide known as DDVP (37).

Table 4-3-Occupational Hazards Reported To Increase the Frequency of Cytogenetic Abnormalities

Alkylating anticancer agents (CA, SCE)	DDT (CA)
Arsenic and arsenic compounds (CA)	Epichlorohydrin (CA)
Asbestos (CA, SCE)	Ethylene oxide (CA, SCE)
Benzene (CA)	Mineral oils (CA)
Benzidine (CA)	Nickel refining (CA)
Bis(chloromethyl)ether (CA)	Organophosphorous insecticides (CA, SCE)
Cadmium/lead/zinc (CA)	Pentachlorophenol (CA,SCE)
Chromium (CA, SCE)	Rubber industry (CA, SCE)
Coal gasification (CA)	Shale oils (SCE)
Coal tars (CA)	Styrene (CA)
Coke production (SCE)	Sulphite (wood pulp) (CA)
Diesel fumes (CA)	Trichloroethylene (CA, SCE)
Dimethylformamide (CA)	Vinyl chloride (CA, SCE)

KEY: CA = chromosomal aberrations; SCE = sister chromatid exchanges.
SOURCES: J. Ashby and C.R. Richardson, 'Tabulation and Assessment of 113 Human Surveillance Cytogenetic Studies Conducted Between 1965 and 1984," *Mutation* Research 154:1 11-133, 1985; M. Sorsa and J.W. Yager, "Cytogenetic Surveillance of Occupational Exposures," *Cytogenetics, G. Obe* and A. Basler (eds.) (Berlin, West Germany: Springer Verlag, 1987).

As mentioned previously, chemical agents are more likely to induce SCEs than CAs, which are more likely to be induced by ionizing radiation. A few notable exceptions exist. Workers exposed to vinyl chloride exhibit increased CAs and are at risk for developing hepatic angiosarcoma, a form of liver cancer. Workers exposed to benzene also show elevated CAs and are at increased risk for developing leukemia (7). Steelworkers with a history of coke oven exposure have an increased SCE frequency as well as significantly elevated CAs (8) and are at increased risk of developing lung cancer.

Frequently, both elevated SCE and CA frequencies are demonstrated for a particular genotoxic agent. In approximately 30 percent of studies conducted, however, there is disagreement between these two endpoints for the same chemical, indicating that the fundamental way in which a particular chemical interacts with the DNA to produce SCEs is likely to be different from the mechanism that produces CAs (72).

The conclusions of the 1983 OTA report pertaining to the appropriate use of cytogenetic assays for occupational testing still hold true and are summarized as follows:

- the appropriateness of cytogenetic tests for occupational monitoring needs to be considered on a case-by-case basis for each chemical;
- a monitoring program should be instituted when in vitro and animal tests have proved that the chemical in question is mutagenic or carcinogenic;
- no occupational studies, to date, directly relate cytogenetic abnormalities to increased individual risk for disease; and
- at the present time, cytogenetic monitoring is insufficient to predict health risks for an individual although it may have predictive value for a group.

For industrial practice this implies that when workers are in the vicinity of an established genotoxin, exposures should be reduced to a level that does not affect their chromosome morphology or DNA. In a sequence of cytogenetic studies on vinyl chloride exposed workers, a reduction of CAs was detected when the exposure level to the agent was decreased (l). To date, data on CAs are routinely used by regulatory agencies as contributing information for setting safe exposure standards. In view of the lack of a threshold level where there is zero risk, there is no safe level of exposure. Thus, this should apply to all workers, not just to those determined by some test to be susceptible (39).

It is likely that new populations of workers who have been exposed to significant levels of a genotoxin are yet to be discerned: data are now available for only 500 of the more than 100,000 major environmental and industrial chemicals (39). In the case of major synthetic genotoxins it is likely that improved hygiene measures will be undertaken before a surveillance study is begun, as was the case in vinyl chloride and ethylene oxide, where the greatest cytogenetic damage was observed at the early stages of surveillance before hygienic measures reduced exposure levels for later sample dates (2).

Analysis of Mutagenesis at the Molecular Level

Until recently, most tests for mutagenicity have been merely indicators of exposure, only providing evidence that exposure has occurred. This limitation is being removed as more techniques at the molecular level are being developed, refining the ability to document exposure and, in some cases, providing qualitative information about the nature of the mutation. As the nature of mutation becomes more clearly defined, the connection between mutation and disease will also become better understood. This section describes the more common molecular approaches to analysis of mutagenesis.

HPRT Lymphocyte Selection System

One method used for detecting gene mutations is a T-cell assay that uses the hypoxanthine-guanine phosphoribosyltransferase (HPRT) gene as a mutation indicator, because there is an easy selection method to distinguish those cells in which mutations have inactivated the HPRT gene. Thus, the assay determines the frequency of T-cells carrying the HPRT-inactivating mutations. Mutation frequencies are elevated in people exposed to such mutagens as chemotherapeutic drugs, cigarette smoke, and ionizing radiation (38). In fact, HPRT mutations inhuman T-cells can be detected in atomic bomb survivors 40 years after the presumed mutational event (23). The test is extremely sensitive, permitting study of effects of very low doses of environmental mutagens (40).

At the laboratory investigation level, individual mutant T-cells have been cloned and their HPRT genes analyzed to identify the specific sequence changes they have undergone. As a means to better understand mutagenesis, this approach is useful, but is obviously not practical for populations. A second laboratory approach involves electrophoresis to separate mutated strands of DNA, amplification of the mutated DNA through the polymerase chain reaction (PCR) (see ch. 5), and determination of their specific DNA sequence. This approach has lead to the establishment of an "HPRT Mutational Spectra Repository" that is collecting data on HPRT mutations together with information on types of environmental exposures experienced by the individuals whose cells manifested the mutations (38). The use of this technique requires that an individual's spontaneous mutation rate be determined as well as the rate of changes induced by environmental mutagens.

It is unclear whether HPRT mutations are related both to exposures and a subsequent cancer; HPRT may just be a sentinel event in a pathway not related to a specific cancer (59).

DNA Adducts

One type of DNA alteration involves the binding of exogenous and xenobiotic materials to DNA to form additional products, or adducts (42). Radiolabeling, immunochemical, and physical methods can detect adducts at extremely low concentrations. Adducts can form in many tissues but are not stable since they are easily removed by DNA repair systems. DNA adducts have special significance in view of their potential to force replication or repair errors and thus be chemical progenitors of genetic alterations that can be passed on to offspring (5).

The toxicological significance of adducts is unclear, but they can be used as markers of exposures to specific toxicants. Current evidence suggests an association between the onset of specific types of toxicity (e.g., mutation, cancer, developmental effects) and the concentration of DNA adducts (42). Recent studies have suggested that for DNA adduct formation, it may be more meaningful to relate tumor response to the target organ concentration of DNA adducts than to applied dose (6).

Adducts exist at variable background levels between individuals differing by age, race, sex, and interference factors. Adducts can be measured using blood, semen, urine, buccal mucosa, or skin biopsy specimens (42).

The relationship between DNA adducts and tumor initiation depends heavily on the nature of the chemical exposure. The use of DNA adducts as molecular dosimeters will provide better information about individual differences in absorption, distribution, biotransformation, cell proliferation, and DNA repair and detoxification between high- and low-dose exposures and between tissues (42). Further research must correlate specific toxic effects of specific DNA adducts with the induction of gene mutation or tumor formation before they will be useful beyond dosimetry studies. It may be simplistic to assume that specific adducts will ever be good predictors of tumor formation, since there are so many other intermediary steps and modifying factors between adduct formation and the development of a detectable tumor (63).

Most studies of DNA adducts in humans have been in populations where the exposure was to a ubiquitous compound producing delayed clinical effects, making the cumulative exposure unknown and the identification of unexposed control populations impossible.



Photo credit: American Cancer Society

DNA from lung cancer patients who smoke cigarettes shows a DNA adduct pattern that intensifies with the amount and duration of smoking.

However, certain cohorts reveal reliable dose relationships. Testicular and ovarian cancer patients receiving cisplatin, a platinum-based chemotherapeutic agent, show a dose-response relationship for adduct formation (50). Roofers and foundry workers have tested adduct positive for benzopyrene (25,61).

Lung cancer patients have tested positive for adducts, probably from a variety of hydrocarbons (49). In fact, DNA from cancer patients who smoke cigarettes shows an adduct pattern that intensifies with the amount and duration of smoking. Traces of this adduct pattern can persist for at least 14 years (53). Furthermore, while DNA from heart and lung tissue shows the highest adduct levels, the bladder, kidney, aorta, and liver of longtime smokers showed the same pattern of adducts, indicating widespread damage.

Results in most studies show individual rates of metabolic activation of carcinogens and repair capacities. The same chemical exposure, therefore, can produce wide variability in the numbers of adducts. More baseline data are needed before adducts will be a reliable form of risk assessment. In addition, there is an appreciable amount of background DNA adducts that needs to be more carefully assessed in all individuals.

Most of the assays for detecting adducts resulting from occupational exposures are sufficiently sensitive and will be improved by three methods currently

under investigation: tandem mass spectrometry, 32P-postlabeling, and accelerator mass spectrometry, which provide the additional advantage of detecting low levels of interactive genotoxic agents (63).

In general, protein adducts, as compared to DNA adducts, are stable for the lifetime of the protein and can be used as indicators for recent exposure. They can be found in the hemoglobin of red blood cells and in sperm. They are considered a form of biological monitoring rather than a test of mutagenicity because they allow for direct measurement of the relationship between external exposure and internal dose. The unique features of this approach are the sample size and the ease of obtaining red blood cells. As in other tests, however, there will be considerable differences between chemicals and their effect on adduct formation and data must be collected on each chemical.

Determination of DNA Repair

Determining DNA repair in lymphocytes can indirectly estimate some types of damage to genetic material. DNA repair systems probably arose as evolutionary consequences of DNA damage resulting from ultraviolet radiation and naturally occurring mutagens. The method detects damage susceptible to excision repair, but some other mutagenic lesions may not be detected. DNA repair is an ongoing normal cellular process; monitoring methods detect elevated levels of DNA repair activity. Increased DNA repair activity probably reflects recent exposure to a genotoxic compound.

Sensitivity of the DNA repair assay to detect abnormality from low-dose exposure has not been demonstrated. Since this assay as used routinely cannot determine whether the damage is correctly repaired or not, the biological significance of detectable induced repair cannot be determined (35).

DNA Quantification

Two cytometric methods to measure the DNA content of individual cells could provide a means for identifying workers who are at increased risk in occupational groups exposed to certain carcinogens. Most recently these methods-called simple filter microfluorometry and quantitative fluorescence image analysis-have been applied to groups exposed to bladder carcinogens (27). Collectively the methods are referred to as absolute nuclear fluorescence intensity, or ANFI. The value of ANFI is based on the finding that tumors contain cells with abnormal, elevated amounts of chromosomes, and therefore, DNA. These aneuploid cells may be cancerous or premalignant.



Photo credit: U.S. *Environmental Protection Agency*

Increased chromosomal aberrations have been reported in individuals exposed to phosphine, a common grain fumigant, and a range of pesticides.

In the ANFI technique, cellular DNA obtained from exposed populations is treated with a fluorescent stain. Quantitative spectrofluorometry is then used to detect excess DNA. The intensity of the fluorescence is proportional to the DNA content of the cell. Fluorescence in excess of a standard norm may be a useful diagnostic criterion. In fact, DNA changes have been observed in asymptomatic patients prior to biopsy-confined clinical disease (27).

The real power of the technique could likely be its ability to detect disease in asymptomatic individuals. If tumors can be detected while still noninvasive and nonmetastatic, then screening could become valuable for treatment success (77). In 1981, a study was conducted of 1,385 chemical production workers exposed to aromatic amines, primarily 2-naphthylamine, to assess the predictive value of this technique. Of a cohort of 67 individuals tested positive via ANFI, 33 have been diagnosed histologically positive for bladder cancer (48).

Serum Oncogene Proteins

Oncogenes, or cancer-causing genes, are discussed in greater detail in chapter 5 because of their importance in detecting early stages of cancer. Oncogene detection, however, may become in-

creasingly important in monitoring situations because of the effect of genotoxic agents on the induction of oncogene activity. Oncogenes can be activated by translocations, breaks, and deletions caused by clastogens. The presence of activated oncogenes can be identified by molecular methods such as restriction fragment length polymorphisms (see ch. 5) or by screening of serum for oncogene-related proteins in conjunction with PCR sequencing.

This approach was recently used in a study of workers exposed to polychlorinated biphenyls (PCBs) (9). PCBs are a group of chlorinated aromatic hydrocarbons found in the past in transformer and capacitor fluids, plastics, pump oils, hydraulic systems, printing ink, flame retardants, pesticides, and copy paper. They have well-documented acute and chronic health effects on skin, neurophysiology, and reproduction.

Municipal workers exposed to PCBs in cleaning of a transformer were tested for oncogene-related proteins in their serum. While the connection between exposure to PCBs and elevated serum oncogene proteins was not substantial, the relationship between cigarette smokers exposed to PCBs and elevated proteins was remarkable, indicating a strong effect of smoking on oncogene activity. Serum oncogene protein detection may offer a tool for early diagnosis of cancer.

METHODOLOGIC CONSIDERATIONS

Before a decision can be made on the value of any genetic test, it must be valid and reliable. In considering the application of genetic monitoring to detect job-related illness, the additional criteria of cause and effect between a particular trait (or genetic change) and occupational illness must be evaluated.

The 1983 OTA report presented a full discussion of the concepts of validity, reliability, predictive value, and relative risk (72). Because these fundamental criteria have not altered since that report, basic aspects are only summarized here. Similarly, general criteria for evaluating the acceptability of genetic tests linked to environmental exposure have been discussed elsewhere (41,72). Certain variables such as age, sex, race, and lifestyle will continue to confuse establishing causal linkages between exposures and subsequent disease. If the tests are valid and reliable, establishing procedural safeguards and designing well-conceptualized test protocols can avert erroneous and misleading conclusions. Table 4-4 presents some of the pitfalls encountered in any epidemiology study, whether genetic or not, attempting to identify hazardous agents in the workplace.

Table 4-4-Pitfalls of Classical Epidemiological Studies in Identifying Hazardous Chemicals in the Workplace

Difficulty identifying suitable study populations:
. inadequate size
. unreliability of death or birth medical records
● lack of reliable incidence data
Long latency period in onset of effects (excluding in utero exposure for major anomalies):
● complicates data collection
● prevents detection of effects of new exposures
. requires assessment of current risks based on much earlier exposures
Lack of sensitivity:
● normal incidence of specific diseases can obscure increased rates
. multiple exposures confound attempts to establish cause-effect relationship
. effects of ubiquitous exposure are difficult to detect
● large populations are required to detect common effects
Substantial population exposure to agent prior to detection:
● dilution of exposed population
● failure to consider power of study

SOURCE: M. Legator, University of Texas Medical Branch, Galveston, TX, written communication, August 1990.

Validity, Reliability, and Predictive Value

The validity of genetic testing (i.e., the probability that a test will correctly classify true susceptible and true nonsusceptible individuals) should be evaluated before any test is placed into routine use. Few tests are 100 percent valid because of the influences of variable test performance and genetic and environmental factors. Sensitivity and specificity are the two characteristics subsumed under validity. Sensitivity is the frequency with which the test will be positive when the genotype in question is present. Specificity is the frequency with which the test will be negative when the genotype in question is absent. Sensitivity and specificity are usually inversely related.

In addition to validity, reliability under conditions of routine use must also be demonstrated. That is, tests of the same specimen must repeatedly give the same result whether performed by several different laboratories or by the same laboratory on several occasions.

Predictive value of the test is determined by sensitivity and specificity, as well as the prevalence of the trait or genetic damage in the population. Prevalence is the percentage of the population that is affected with a particular disease at a given time. When the prevalence of a particular traitor genetic damage is low in the population, even a highly specific test will give a relatively large number of false positives because many persons being tested will not have the endpoint.

Procedural Safeguards and Difficulties

In undertaking any testing of exposed populations—whether cytogenetic, biochemical, or DNA-based tests—good sampling and data collection are essential. Individual factors that can affect test results include such confounding variables as sex, age, race, ethnic group, work history, diet, genotype, medication, alcohol and drug consumption, and smoking. These factors play a role in the induction of CAs and must be considered when drawing conclusions about the effects of genotoxic agents. For example, smoking and alcohol consumption have been shown to increase the frequency of CAs and SCEs (30,45). Thus, they must be controlled for any population study.

In all cases, certain precautions should be taken before employing these techniques in wide-scale population monitoring. They are:

- documentation of clastogenicity of the chemical in question in vitro and in vivo;
- determination of the duration and level of exposure;
- establishment of an appropriate matched control population;
- determination of the history and habits of the individuals to be tested (i.e., smoker, medication and drug use, other exposures, nutrition) (12); and
- determination of test variability and sample size requirements to detect a true difference (lo).

The greatest difficulties in monitoring may not be technical but procedural. Eliminating biases, obtaining suitable control groups, and obtaining good records may be the greatest obstacles, made especially difficult with chemical carcinogens because of the long latency period between exposure and resultant malignancy (a problem with retrospective cohort studies). Adequate protocols (enough subjects used and cells scored) must be used to ensure that the results are reliable.

Box 4-C-A Battery Approach To Determining Exposure-Disease Associations

The use of biological markers in a battery of tests over time allows for the resolution of more detail in exposure-disease associations. For instance, instead of waiting to identify a worker who has developed bladder cancer and had been exposed to benzidine, a researcher might: 1) ascertain the worker's predisposition by determining whether he or she is a slow or fast acetylator (see ch. 5); 2) determine early biologic effect by measuring the amount of the H-ras oncogene expression product, p-21 protein in the urine; 3) quantify the degree to which bladder cells are in a premalignant aneuploid state by using quantitative fluorescence image analysis; and 4) evaluate the prognosis of early tumors by measuring the glycosaminoglycans on bladder cell surfaces. Additionally, the current contribution of cigarette smoking, a confounder to the benzidine-bladder cancer association, can be assessed by evaluation of macromolecule adducts to a representative cigarette smoke component such as 4-aminobiphenyl. The implications of this example are that the exposure-disease association can now, in some cases, be resolved into detailed and quantifiable components. This resolution has implications for understanding basic mechanisms and for intervention.

SOURCE: P.A. Schulte, "Methodologic Issues in the Use of Biologic Markers in Epidemiologic Research" .4merican .Journal of *Epidemiology 126(6):1006-1016, 1987.*

The Battery Approach to Genetic Monitoring

The most sensible approach to genetic monitoring, if validated, would be to employ a battery of relevant and sensitive tests, rather than rely on any one test for valid and reliable information. Genetic monitoring is based on epiderniological methods, using the observation of immediate effects such as sperm morphology, urine mutagenicity, and cytogenetics. Immediate effects can be measured in tandem and more long-term health outcomes, such as appearance of neoplasia and reproductive effects, should follow in the study design. It should be borne in mind that the frequencies of immediate effects will always be higher than frequencies of adverse health outcomes (28).

In an ideal study, types and durations of external exposures should be determined as best possible. Mutagenicity assays, such as the Ames or HPRT tests, could be conducted to determine if mutagenic agents were present. Cytogenetic analysis examining overall CA rates and SCE or micronuclei frequencies could be conducted as indicators of mutation. Tests of sperm morphology could be done to estimate potential germline mutations. Molecular studies, such as DNA adduct formation, DNA quantification, or serum oncogene protein detection can serve as direct measures of mutagenicity and toxicity. Combined, these tests can provide a qualitative association between occupational exposure and abnormalities in endpoints. This approach is likely to be extremely costly.

If the tests are conducted in parallel, sensitivity increases while specificity decreases. If they are conducted in sequence, sensitivity decreases while specificity increases. The investigator would have to decide which characteristic was more desirable given the exposure and the circumstances.

The intelligent use of a combination of tests may yield a finer resolution of exposure-disease associations. Box 4-C gives an example of such an approach.

SUMMARY AND CONCLUSIONS

Occupational exposures to certain substances can alter genetic makeup through structural damage to both genes and chromosomes. Genetic damage, regardless of cause, appears as recessive and dominant mutations, large rearrangements of DNA, point mutations, and loss of genetic material, leading to distortions of either the expression or biochemical function of genes. But not all mutations cause disease. In addition, most occupational exposures are likely to cause principally nonheritable damage to somatic cells, rather than germline or heritable damage. The relationship between mutation and health effect is often indirect and not well understood. Cancer, a disease of somatic cells, is the most common class of genetic disease correlated with genotoxic substances.

Until the health effects of exposures are better understood, monitoring can only provide a gross indication that genetic changes have occurred and that adverse health effects could follow. The rationale behind the use of assays of genetic damage stems from historical evidence that events observed initially and at high frequency could be the start of a process that ultimately produces neoplasm in a smaller number of cells.

New molecular assays of mutagenicity, such as HPRT and oncogene protein detection, are providing greater specificity and will augment tests already in use, such as the Ames test. New methods may provide better estimates of the health effects of low doses of some mutagens, as well as providing qualitative data on the nature of mutation. Detecting activated oncogenes and DNA adducts has the potential of predicting disease in asymptomatic individuals. The use of genetic monitoring methods in epidemiologic studies will continue to be plagued by some of the pitfalls associated with classical approaches to determining hazardous exposures in the workplace. The greatest difficulties may not be technical but procedural-eliminating biases, obtaining controls, and keeping good records. Methods for determining types and levels of exposures must be improved, and certain methodological and procedural safeguards should be adhered to. In addition, the employment of more specific and sensitive tests, rather than relying on any one test for valid and reliable results, will lead us closer to understanding the relationships between exposure, mutation, and disease.

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Chapter 5

The State-of-the-Art in Genetic Screening

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Chapter 5
The State-of-the-Art in Genetic Screening

As mentioned in chapter 2, genetic screening in the workplace can be used in two distinct ways. First, genetic screening can detect traits that may indicate an increased susceptibility to occupational illness after exposure to specific agents. Second, screening tests can be used to identify genetic disorders not associated with specific job exposures. Thus, in assessing the state-of-the-art of screening tests for use at worksites, three different questions must be discussed. Namely, what general techniques are presently available that could be used for genetic screening? What is known about the association among heritable traits, exposure to hazardous materials, and subsequent occupational illness? And, what genetic disorders can be detected unrelated to job exposures that are important to general health?

The following sections address the recent technical advances in genetic screening tests, with an emphasis on recombinant DNA tests. Important background information on human genetics and disease can be found in appendix A. In evaluating the interaction of occupational exposure and genetic influences, the discussion focuses on traits evaluated in the 1983 Office of Technology Assessment (OTA) report (111), but also assesses several newly recognized susceptibilities to occupational disease. Finally, progress in detecting some nonoccupationally related disorders is presented. These disorders are presented because they are likely to affect large populations, screening tests for them are under investigation or being developed, and they might be of interest to an employer if available through preemployment screening.

BIOCHEMICAL TECHNIQUES FOR DETECTING GENETIC DISEASE

Biochemical genetics refers to the analysis of mutant genes on the basis of altered proteins or metabolizes. If diagnosed, some of these "inborn errors of metabolism" can be treated with enzyme replacement or dietary control.

Phenylketonuria is the classic example of an inborn error of metabolism, inherited as an autosomal recessive, that can be controlled by restricting dietary intake of phenylalanine. In this disease, the individual lacks the enzyme necessary to convert phenylalanine to tyrosine. Retardation and seizures are common symptoms. Carriers, or heterozygotes, for the disease tend to have the enzyme at a level about half that found in individuals who are homozygous for the normal gene. Affected individuals have almost none of the necessary enzyme. Most inborn errors of metabolism, for which the enzyme defect is known, lend themselves to biochemical tests for the detection of affected and carrier individuals.

Sickle cell disease is a form of chronic hemolytic anemia characterized by the presence of crescent-shaped (or sickled) red blood cells that cause peripheral oxygen deficit by blocking the terminal arterioles. It is a biochemical disorder of hemoglobin for which the mutant gene has been found. The disease has an extraordinarily high frequency in populations of West African origin, occurring in about 1 in 625 U.S. Blacks at birth (87). One in eight Blacks is a carrier for the disease, a condition referred to as "sickle cell trait. ' The trait can be detected biochemically by hemoglobin electrophoresis, or by testing for the gene itself, now that the gene has been cloned (see subsequent discussion of cloning) (66,99).

In general, biochemical techniques for diagnosing genetic disease are often restricted to indirect analysis. Only for fewer than 10 percent of monogenic disorders has the fundamental biochemical defect been elucidated (85). Advances in DNA technology (described below) have greatly advanced our ability to directly examine the genetic basis for disease and to predict and diagnose such diseases.

MOLECULAR TECHNIQUES FOR GENETIC SCREENING

Until recently, most available tests for genetic conditions were not based on recombinant DNA techniques. Traditionally, enzyme or other protein-based assays that identified abnormal gene products (or the consequences of abnormal gene function) are more commonly performed. For example, in the case of Tay-Sachs disease, reduced activity of a particular enzyme signals the carrier state, and absence, the



Photo credit: Lawrence Livermore National Laboratory, Livermore, CA

Direct image of chemically unaltered strand of DNA obtained using a scanning tunneling microscope. (Light microscopes magnify objects up to about 1,000 times; electron microscopes about 300,000 times. Scanning tunneling microscopes can magnify images up to 1 million times.)

disease state. Today, DNA-based tests encompass a variety of standard diagnostic techniques that allow examination of regions very near the genes (e.g., Huntington's disease) or direct examination of the genes themselves (e.g., sickle cell anemia and cystic fibrosis).

DNA can be extracted from any tissue containing nucleated cells, including blood. Once extracted, the DNA is stable and can be stored indefinitely so that samples from people with genetic disorders can be collected and saved for investigations to diagnose future family members.

The remainder of this section describes the types of techniques that can be used for genetic screening, with emphasis on molecular methods developed since the 1983 OTA report, including restriction fragment length polymorphisms (RFLPs), allele-specific oligonucleotide (ASO) probes, polymerase chain reaction (PCR), and automation of these and other technologies useful to DNA-based genetic diagnostics.

Two major tools, recognition of RFLPs and development of cloned DNA probes are the major advances responsible for improved diagnosis of genetic disease.

Restriction Fragment Length Polymorphisms

Variations in the DNA sequence of two individuals are likely to occur on average every 300 to 500 base pairs (49). These variations occur both within and outside of genes and usually do not lead to functional changes in the protein products of genes. In the 1970s, it was demonstrated that certain bacterial enzymes, called restriction endonucleases, could be used to map genes by cleaving DNA at specific sites. This discovery led researchers to propose that natural differences in DNA sequence (polymorphisms) might replace other chemical and morphological markers as a way to track chromosomes through a family (linkage analysis) (50).

Because of the naturally occurring variation in the DNA sequences of individuals, the lengths of DNA resulting from cuts by the endonucleases will differ. This phenomenon is referred to as RFLP. RFLP analysis is a relatively straightforward process, and over 3,000 RFLP loci have been identified, including more than 100 highly polymorphic loci at which many alleles exist in the population. Some of these loci are located so close to a gene of interest that they are nearly always inherited with the gene. So even when a gene associated with disease has not been identified and even when a disease gene's locus is not precisely known, the inheritance of an associated RFLP can be used as an indicator of inheritance of the gene.

Briefly, the method involves cutting the DNA with a restriction enzyme, and sorting out various fragments by electrophoresis in a gel in which the DNA fragments will migrate according to length. The double-stranded fragments are then converted into single strands and transferred onto a nylon membrane, to which the fragments adhere. This technique is referredtoasa"Southern blot' after its inventor, E.M. Southern (96). The membrane is then soaked in a solution containing a radiolabeled DNA probe which binds to the particular fragment containing its complementary sequence. The probe is obtained through cloning the gene of interest or by chemical synthesis. The nonspecifically bound probe is washed away and the falter is placed on a piece of x-ray film. The radioactively labeled bands expose the x-ray film and their locations indicate the

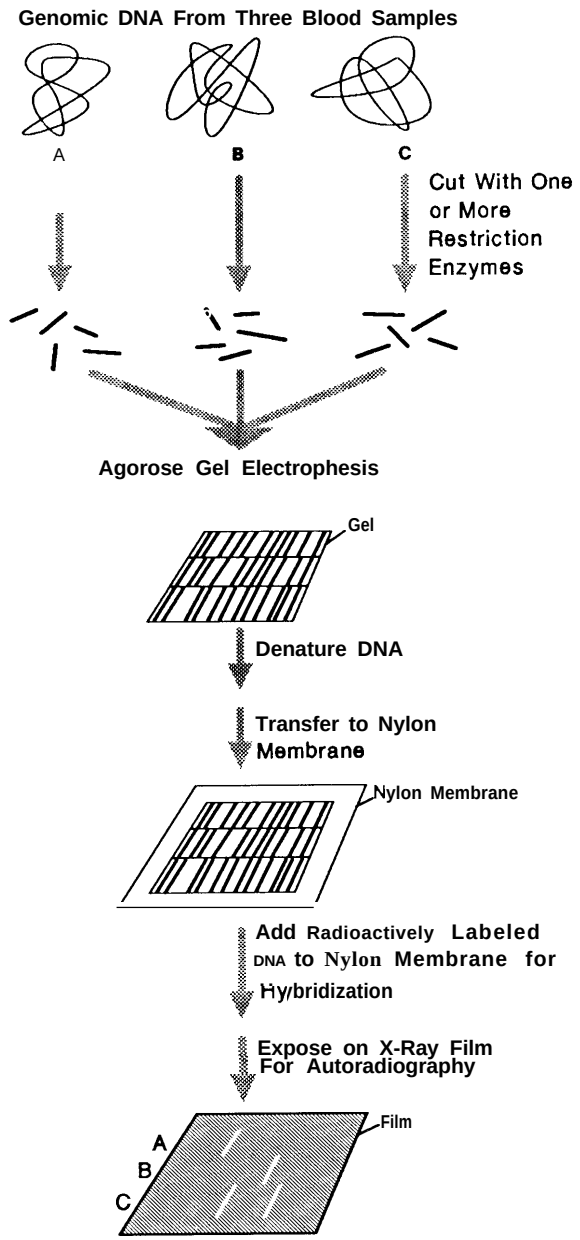
size of the fragments complementary to the gene probe under study (figure 5-l).

A new probe technology, using fluorescence rather than radioactivity, is expected to speed up the time it takes to make a diagnosis while simultaneously decreasing the incidence of false positives (37). Enzyme-linked dye methods are already available commercially (87). These methods do not necessarily improve accuracy, but provide greater safety in the laboratory.

As stated previously, the RFLP itself is not the cause of disease.[1] Rather, RFLPs serve as flags, or markers for the presence of the disease gene. The general location of many genes has been determined and located on or near a specific restriction fragment. The segregation pattern of the RFLP within a family is analyzed and the inheritance of specific alleles of the RFLP is then used to predict the inheritance of the disease gene. One of the first applications of this technology came in 1983 when genetic linkage between a RFLP marker on chromosome 4 and Huntington's disease was described (39,50).

Thus, RFLP analysis can be useful for families where the precise mutation is unknown but general location of the locus of the mutation is known to be linked to a RFLP marker. Indirect analysis of this type is most often used in prenatal diagnosis, but is likely to be used in other diseases, such as adult-onset polycystic kidney disease (see box 5-A) and Wilson's disease. Linkage analysis is limited for three primary reasons: 1) at least one living affected family member is usually required; 2) genetic heterogeneity will confound the analysis if an affected member is not available because different mutations at different loci may produce indistinguishable disease manifestations, or phenotypes; and 3) paternity must be known. Successful linkage studies have also been completed for cystic fibrosis (for which the gene has now been found), myotonic dystrophy, familial amyloidotic polyneuropathy, familial Alzheimer's disease, and Duchenne muscular dystrophy. Table 5-1 lists selected diseases for which DNA diagnosis is possible or within reach.

Figure 5-l—Detection of Restriction Fragment Length Polymorphisms Using Radioactively Labeled DNA Probes



Variations in DNA sequences at particular marker sites are observed as differences in numbers and sizes of DNA fragments among samples taken from different individuals (shown here as samples A, B, and C).
SOURCE: Office of Technology Assessment, 1990.

[1]In sickle cell, the mutation that causes the disease results in an alteration in a restriction site so the restriction analysis constitutes a direct test for the disease.

Box 5-A—Adult Polycystic Kidney Disease

Adult polycystic kidney disease (APKD) is a dominant **disorder with age of onset between 20** and 35 in most families. Renal dialysis or transplantation are the primary treatment modalities. The disorder can be diagnosed by ultrasonography, but false negatives are common, For example, a 20-year-old at risk may have a negative ultrasound but develop the disease 10 years later.

A **number** of flanking DNA linkage markers have been identified very close to the disease locus on chromosome 16. If multiple affected and unaffected individuals in an APKD family can be tested for the presence of the marker, the coupling phase between the marker and the disease gene can be set, and predictive diagnoses can be made. his constitutes a presymptomatic diagnosis. The physician can then be alerted to monitor the blood pressure, renal function, and weight status of the patient knowing that he or she is markedly at risk for ultimately manifesting the disease.

SOURCE: Office of Technology Assessment, 1990.

Table 5-l-Common Monogenic Disorders for Which DNA Diagnosis Is Possible or Within Reach

Autosomal dominant	**hypercholesterolemia**
	polycystic kidney disease
	Huntington's disease
	neurofibromatosis
	myotonic dystrophy
	polyposis coli
	tuberous sclerosis
Autosomal recessive	**hemochromatosis**
	alpha-1 -antitrypsin deficiency
	cystic fibrosis
	phenylketonuria
	adrenogenital syndrome
	retinitis pigmentosa
	retinoblastoma
	sickle cell anemia
	thalassemias
X-linked	**fragile X mental retardation**
	Duchenne muscular dystrophy
	hemophilia A and B
	ichthyosis vulgaris
	adrenoleukodystrophy

SOURCE: Adapted from H.H. Ropers and B. Wieringa, 'The Recombinant DNA Revolution: Implications for Diagnosis and Prevention of Inherited Disease," *European Journal of Obstetrics and Gynecology* **and** Reproductive Biology 32:15-27, 1989.

Use of RFLPs in Population Studies

Population differences are important to recognize in both genetic screening and monitoring. In screening, it is important to remember that certain rare alleles are often concentrated within certain ethnic groups, e.g., Tay-Sachs and Gaucher's diseases affect Jewish people of Ashkenazi descent. An individual of this background, therefore, would more appropriately be screened for these traits than would individuals of different ethnic or racial backgrounds. In the case of monitoring, the ethnic composition of the population being tested might be an important consideration in deterrnining allelic frequencies.

In addition to using RFLPs in clinical diagnosis, they provide the potential for elucidating a range of information in the study of human populations. Population-specific alleles or allele frequencies have been found. For example, the number of polymorphisms due to the presence or absence of a dihydrofolate reductase gene has been found to differ between Blacks and Caucasians. And one of the six known RFLPs in the human growth hormone cluster was found only in Blacks although the other five were present in Caucasians. RFLPs linked to the alpha-1 -antitrypsin Z allele (which is associated with increased risk of emphysema and liver disease and is an occupationally important marker) have only been described in Europeans. RFLPs linked to clinical hypertriglyceridemia differ between Caucasians and Japanese (100). Population differences in RFLPs are attributed to racial divergences and explain, in part, ethnic and racial differences in disease morbidity.

HLA Typing and Genetic Disease

More recently, linkage analysis relying on the genetic organization of the major histocompatibility complex (the genes that regulate and control the immune system) has provided useful information for organ and tissue transplantation, paternity determinations, and disease susceptibility (26). The utility of typing of the human leukocyte antigens (HLA) for genetic studies is due to the high degree of genetic polymorphism in the HLA region (i.e., HLA antigens are among the most variable proteins of the human genome).

Genetic susceptibility to a variety of diseases has been linked in family studies with specific HLA types. Polymorphisms of the HLA loci have been associated with specific diseases such as insulin-dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis, and myasthenia gravis. As more polymorphisms in the HLA complex are identified,

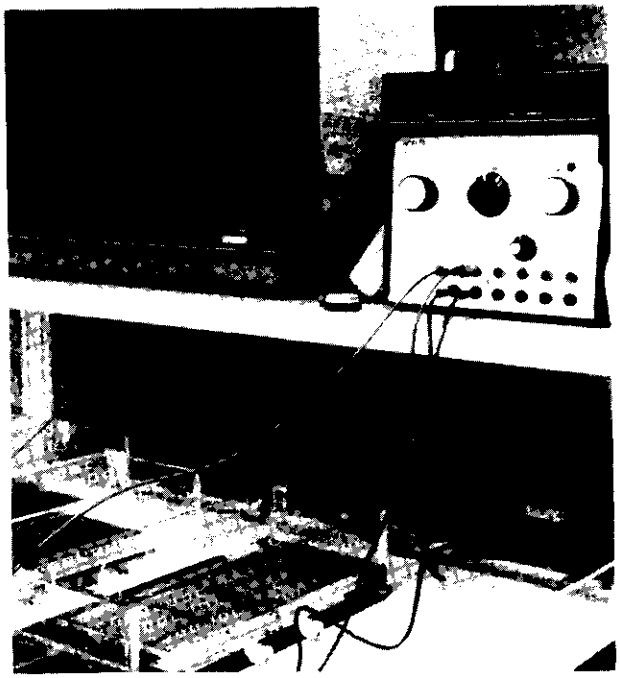


Photo credit: Robyn Nishimi

Gel electrophoresis of DNA samples.

HLA-based probes will provide an additional tool for linkage studies, and possibly direct analysis of mutant genes. The high degree of variability at the DNA level in the HLA loci suggests that DNA markers in the region are of great importance in characterizing population groups.

Direct Analysis of Mutant Genes

In a small percentage of cases (5 to 10 percent), point mutations responsible for genetic disease can be directly detected by restriction analysis and the use of synthetic oligonucleotides as probes (4). Sickle cell disease is one such example. Direct analysis of mutant genes involves cloning the mutant allele and sequencing through the mutation. This is a laborious process because most genes are large (the globin genes have been sequenced because they are small). If the gene can be sequenced, oligonucleotide probes can be synthesized that specifically recognize the mutant or normal alleles.

DNA probes have been in use for nearly 10 years to detect point mutations. A probe is a short sequence of single-stranded DNA that is complementary to the DNA sequence being sought. If short, they may be chemically synthesized DNA segments. ASO probes refine diagnostic accuracy by perfectly matching the nucleotide sequence of a portion of the gene in question (17). These probes are long enough to represent unique sequences but short enough to be specific to a target molecule. Before being used, the probe is labeled with a fluorescent or radioactive marker so it can be detected. A method of amplification, described below, can then be used to permit extremely accurate identification of the target gene.

This approach has been applied successfully in alpha-1-antitrypsin deficiency, sickle cell disease, several of the thalassemias, cystic fibrosis, and hemophilia A, to name a few. Because of the difficulty of sequencing and producing probes for large genes, indirect, or linkage analysis, is more commonly used for diagnosis. The use of probes for direct analysis has been limited because, for most single-gene disorders, there are many different mutations that cause the same disease. As in linkage studies, accurate diagnosis often depends on the availability of several affected family members.

It is likely that the complete physical map of the human genome will serve as the ultimate source of DNA probes for any human gene (62).

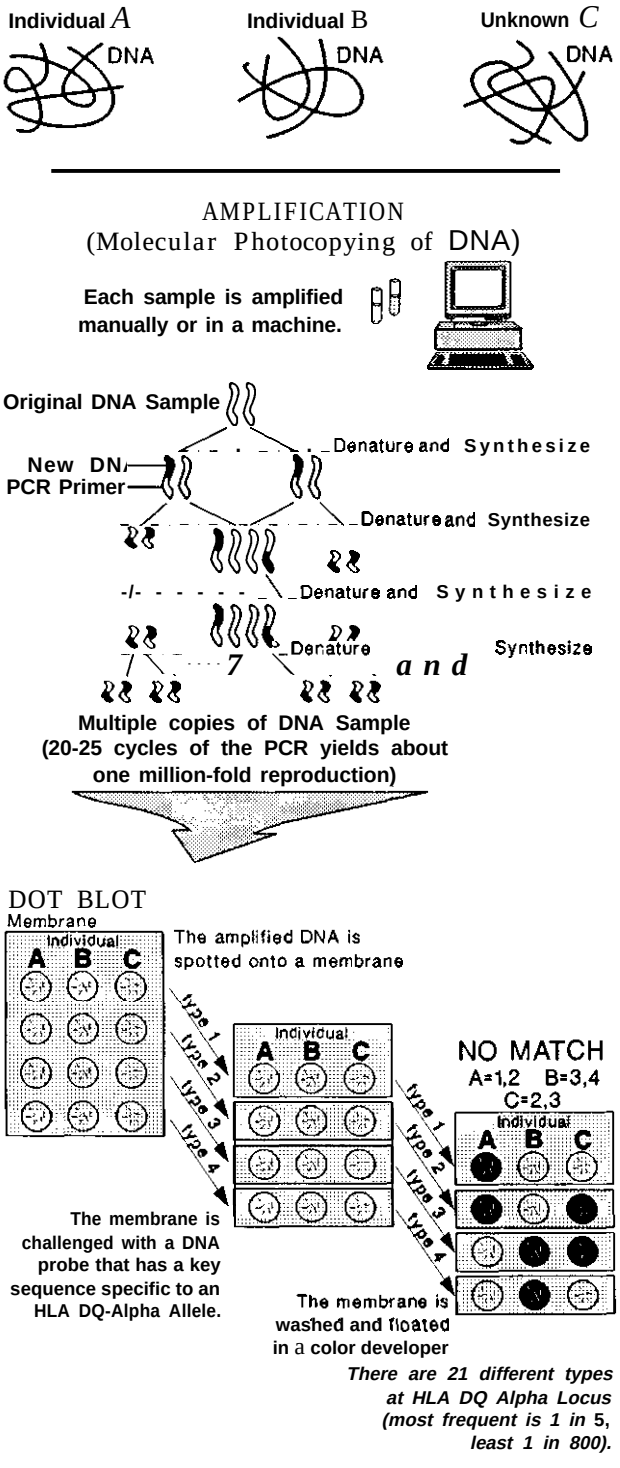
Polymerase Chain Reaction

PCR, first reported by Cetus Corp. in 1985, facilitates the use of probes by greatly increasing, or amplifying, the number of copies of target DNA. For example, selected areas of a gene can be amplified through repeated cycles, a probe can be hybridized directly to the amplified DNA and a rapid diagnosis made. PCR produces enough of the target sequence so that simple, rapid, and accurate methods for identification can be employed (74). In some respects, it can be thought of as molecular photocopying (see figure 5-2).

PCR will probably be the method of choice for identifying monogenic disorders in which point mutations account for the majority of gene defects and will make DNA diagnosis possible at any major medical center (4). It has great potential value for carrier screening programs. The possibilities for use of PCR in diagnosing monogenic diseases through linkage studies are also great (52).

Briefly, PCR involves using two specific sequences, called primers, that flank the area the scientist wants to copy. The scientist then sets conditions in the reaction that allow new copies of

Figure 5-2—The Polymerase Chain Reaction



SOURCE: Office of Technology Assessment, 1990.

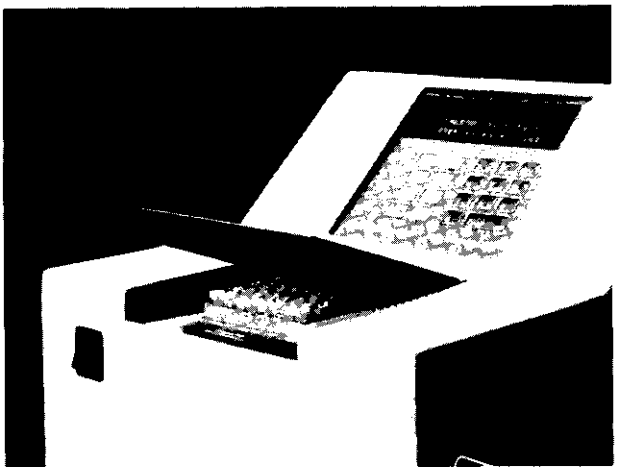


Photo credit: Perkin-Elmer Cetus

DNA thermal cycler for automated PCR analysis.

the DNA of interest to be produced from the primers. Because the products generated in one sample can serve as templates in the next cycle, the number of amplified copies doubles with each cycle. Thus, 20 cycles of PCR yields about a millionfold reproduction. This extraordinary ability is also PCR's greatest weakness. PCR assays can lead investigators astray when trace quantities of contaminating DNA molecules find their way into the reaction sample. Handling of samples when using PCR requires much greater care than with routine RFLP analysis.

Automation of DNA Diagnostic Procedures

A number of instruments have been developed that can increase the speed and volume of routine DNA diagnostic procedures. Some examples include:

- The DNA extractor prepares DNA suitable for Southern blots from eight tissue samples in 3 hours. Future extractors will be able to handle hundreds of samples daily (62).
- The DNA synthesizer, or 'gene machine,' can assemble oligonucleotides up to 200 nucleotides in length with a synthesis rate of 12 to 15 minutes per cycle. The synthesizer is crucial for probe development (43,62).
- Laboratory robotic workstations are being developed that can rapidly and accurately perform routine manipulations including RFLP analyses and DNA sequencing.

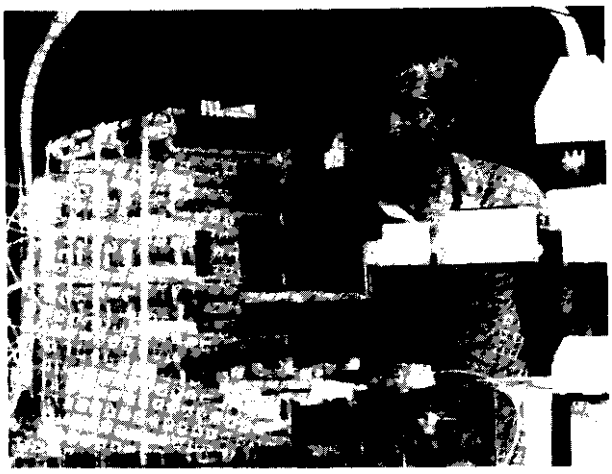


Photo credit: Human Genome Center, Lawrence Berkeley Laboratory

Computerized robotics used to speed repetitive tasks of mapping and sequencing DNA.

- An instrument has been developed that can size-separate very large DNA segments through pulsed field gradient gel electrophoresis. This will be useful in identifying deletions, translocations, and amplifications of DNA sequences and in determining RFLPs over large DNA segments (62).

Novel computing systems are being designed specifically to handle the computational tasks of sequencing. Automation of DNA diagnostic procedures will make large-scale screening faster and more affordable.

The Limits of Molecularly Based Tests

No matter what the mode of screening, two questions must be asked before administration of the test: 1) does the test reliably identify either the genetic trait or specific damage? and 2) does this particular trait or damage cause the individual to be at increased risk for disease? The frost question is more easily answered than the second. To answer the first question, the test must be subjected to scientifically recognized analytical criteria; validity, reliability, predictive value, and relative risk (111). These issues are discussed in chapter 4 and will not be repeated here.

As discussed previously, linkage studies are limited by the requirement for samples from informative relatives and by variable expressivity. This makes linkage testing uncertain for some individuals. Currently, widespread application of linkage studies is limited by the number of probes available, but this obstacle will gradually be overcome. And, as more disease genes are cloned, linkage studies will be replaced by direct tests.

Even with direct tests, however, variable expressivity, incomplete penetrance, and heterogeneity will interfere with the ability to predict correctly that certain individuals will develop disease (42). Heterogeneity lowers sensitivity and variable expressivity lowers specificity. (See ch. 4 for discussion of specificity and sensitivity.)

In any case, before widespread screening of populations is begun, the validity of the tests should be determined in a large number of unrelated people with clinical expression of the disease and in others who have no signs of the disease. Such efforts will require a large test population.

Reliability is measured by the ability of a test to accurately detect that which it was designed to detect and to do so in a consistent fashion. Other than the routine laboratory problems that lead to unreliable test results (human error, contamination), DNA-based tests can fail to yield reliable results for a number of reasons, most often because of incomplete digestion of DNA, faulty hybridization in the Southern blot, or contamination of the PCR amplification. Quality control is likely to become a major issue as the volume of tests at laboratories grows (42). These are already issues in forensics applications (109).

SCREENING FOR SUSCEPTIBILITY TO WORKPLACE EXPOSURES

At the end of the 1960s, some scientists sought to provide perspectives for research on the interaction of genetics, drugs, and environmental agents by showing its application to the field of industrial hygiene (98). Today, the term “ecogenetics” often refers to the field dealing with genetic predispositions to drugs or any type of environmental agent (10). At present, approximately 50 human genetic diseases have been identified as having the potential to enhance an individual’s susceptibility to toxic or carcinogenic effects of environmental agents (14) (see table 5-2 for examples).

This section briefly reviews selected genetic conditions from the 1983 OTA report that some believe enhance susceptibility to environmental

Table 5-2—Identification and Quantification of Genetic Factors Affecting Susceptibility to Environmental Agents

High-risk groups	Estimated occurrence	Environmental agents to which group is (may be) at increased risk
RBC conditions		
G-6-PD deficiency	American Black males 16%; Mediterranean Jewish males 11%; Greeks 1%-2%; Sardinians 1%-8%	Environmental oxidants such as ozone, nitrogen dioxide, and chlorite
Sickle cell trait	7%-13% of American Blacks are heterozygotes	Aromatic amino and nitro compounds; carbon monoxide, cyanide
The thalassemias	Alpha: 4%-5% in Americans of Italian and Greek descent; Beta: 2%-7% American Blacks and 2%-3% American Greeks	Lead; benzene
NADH dehydrogenase deficiency (MetHb reductase deficiency)	Estimated 1% of population are heterozygotes	MetHb-forming substances
Catalase Hypocatalasemia	About 2% of U.S. population based on Swiss gene frequency	Ozone; radiation
Acatalasemia	1/10,000-20,000 of U.S. population based on Swiss gene frequency	
Low SOD activity	Frequency of genetic variants in population 1 to 2/10,000; normal population exhibits unimodal distribution; persons at low end of distribution may beat increased risk	Wide variety of environmental oxidants; paraquat; radiation; ozone
ALA dehydratase deficiency	Unknown, but thought to be rare	Lead
Hb M	Unknown, but rare	Carbon monoxide
Erythrocyte porphyria	1.5/100,000 in Sweden, Denmark, Ireland, West Australia; 3/1 ,000 in South African Whites; rare in Blacks	Chloroquine; hexacholorobenzene; lead; various drugs, including barbiturates, sulfonamides, others
GHS-Px deficiency	Rare	Environmental oxidants
GSH deficiency	Rare	Environmental oxidants
Liver metabolism		
Defect in gluocuronidation		
Gilbert's syndrome	6% of normal, healthy adult population	Wide variety of xenobiotics including polychlorinated biphenyls
Crigler-Najjar syndrome	Few persons live to adulthood	
Defect in sulfation	Unknown	Wide variety of xenobiotics; best association is with tyramine-captaining foods
Acetylation phenotype, slow v. fast	Slow: 50% Whites; 50% Blacks; 10% Japanese Fast: 50% Whites; 50% Blacks; 90% Japanese	Aromatic amine-induced cancer; numerous drugs, e.g., isoniazid and hepatitis
Gout	0.27%-0.3% prevalence in U.S. and Europe	Lead
Oxidation center defects	9% of British Whites; 8% of Nigerians; 6% Ghanians; 1% Saudi and Egyptians are poor oxidizers	Numerous xenobiotics requiring oxidative metabolism for detoxification
OCT deficiency	Unknown, but thought to be rare	insect repellant (DET)
Paraxonase variant	25%-30% of population	Parathion
Rhodanese variant	Unknown	Cyanide
Sulfite oxidase deficiency heterozygotes	Unknown	Sulfite, bisulfite, sulfur dioxide
inadequate carbon disulfide metabolism	Upward of 30%-40%	Carbon disulfide
Alcohol dehydrogenase variant	5% English; 20% Swiss; 70% Japanese	Metabolize (e.g., ethanol) more quickly than normal
Wilson's disease	Homozygous 1/100,000 while the heterozygote may approach 1/500	Copper, vanadium
Serum variants		
Albumin variants	Less than 1/1,000 in Europeans, much higher frequency in North American and Mexican Indians	Unknown
Pseudocholinesterase variants	Highly sensitive homozygous and heterozygous persons of European ancestry have combined frequency of about 1/1,250; moderatelv sensitive genotypic variants of European ancestry have frequency of 1/15,000	Organophosphate and carbamate insecticides; muscle relaxant drugs

* Abbreviations used are: G-6-PD, glucose-6-phosphate dehydrogenase; NADH, nicotinamide adenine dinucleotide (reduced form); SOD, superoxide dismutase; ALA, aminolevulinic acid: GSH, reduced glutathione; Px, peroxidase; OCT, ornithine carbamoyl transferase; IgA, immunoglobulin A; PKU, phenylketonuria; PTL, phenylthiourea; XP, xeroderma pigmentosum; AT, ataxia telangiectasia; FA, Fanconi's syndrome.

SOURCES: E.J. Calabrese, *Ecogenetics: Genetic Variation in Susceptibility to Environmental Agents* (New York, NY: Wiley Interscience, 1984); and E.J. Calabrese, "Ecogenetics: Historical Foundation and Current Status," *Journal of Occupational Medicine* 28(10):1096-1102, 1986.

agents, and evaluates any progress made since that report (111). Following that, several new associations between genetic traits and environmental agents are analyzed.

Glucose-6-Phosphate Dehydrogenase Deficiency

Individuals whose blood cells are deficient in the enzyme glucose-6-phosphate dehydrogenase (G-6-PD) are at enhanced risk for hemolysis (destruction of red blood cells) if exposed to a number of oxidant drugs and industrial chemicals, especially certain aromatic amino and nitro compounds such as naphthalene and TriNitroToluene. G-6-PD deficiency is inherited as an X-linked trait. Although G-6-PD deficient persons could be at increased risk of anemia if exposed to specific hazards in the workplace, epidemiologic studies designed to actually assess G-6-PD deficient workers are lacking (14). A direct DNA test for some mutants causing G-6-PD deficiency is available (4).

Sickle Cell Anemia and Sickle Cell Trait

Sickle cell anemia and sickle cell trait result from the presence in red blood cells of an abnormal hemoglobin molecule (HbS v. normal HbA). Persons with sickle cell anemia are homozygous for HbS, that is they have two copies of the abnormal beta-globin gene, and 100 percent of red blood cells contain HbS. Individuals who have sickle cell trait have only one copy of the abnormal gene (i.e., are heterozygous) and only 20 to 40 percent of their red blood cells have HbS. Under certain conditions, when the oxygen level or environmental temperature drops, HbS-containing red blood cells can sickle. This leads to varying degrees of adverse health consequences, depending on the individual's level of HbS. Although the sickle cell gene has been cloned, a simple, and relatively inexpensive, biochemical assay can detect HbS. The principal use of both a DNA probe for sickle cell and PCR lies in prenatal diagnosis (4).

Individuals with sickle cell anemia have reduced lifespans and many health problems directly attributable to being homozygous for the sickle cell gene. But as in the 1983 OTA report, whether sickle cell trait carriers are at increased risk from the challenges of rigorous training at high altitudes (where oxygen is low) remains unresolved. Limited evidence suggests that possession of sickle cell trait is a contributing factor in reported cases of injury or death during or after vigorous exercise (51), but other confounding factors are most likely present (14). Neither the experimental or epidemiological evidence has confirmed the hypothesis that persons with sickle cell trait are at increased risk when exposed to several chemicals (14).

The Thalassemias

Thalassemia is a deficiency in the production of hemoglobin that results in smaller red blood cells. The disease is inherited in an autosomal recessive pattern and it varies in severity and type (there are alpha and beta forms of the disease). It has been suggested that beta thalassemic individuals are at increased risk after exposure to several chemicals, including benzene and lead. Again, while limited clinical observations have suggested that persons with thalassemia could be at increased toxic risk from benzene and lead, data since 1983 remain insufficient and unconvincing. Continued assessment, epidemiological investigations, and a predictive animal model to test lead- or benzene-induced blood toxicity will be required before an association can be made between this genetic trait and enhanced occupational illness (14,15).

Acetylation Phenotype

Acetylation is a common liver pathway for detoxification of a variety of compounds. The enzyme involved in acetylation, N-acetyltransferase, is coded for by one gene, and humans are either slow or fast acetylators. At the time of the 1983 OTA report, slow acetylation was implicated in increased risk of bladder cancer, and susceptibility to bladder cancer was not equal among those generally grouped as slow acetylators (16). Since then, a growing body of epidemiologic studies further suggests that slow acetylation is a predisposing factor for the recurrence of arylamine-induced bladder cancer (115), and the hypothesis of increased susceptibility is well-characterized with animal models (45,70,1 15). Epidemiologic studies of industrial cancer populations are necessary (78). Because 50 percent of North American Caucasian and Black populations are slow acetylators, the incentive to develop these studies is great.

On the other hand, in addition to the association of slow acetylation with bladder cancer reported in the 1983 OTA report, several recent studies reveal a statistical link between fast acetylation and colorectal cancer (47,64).

Serum Alpha-1-Antitrypsin Deficiency

Homozygous serum alpha-l-antitrypsin (SAT) deficiency is an important genetic factor in emphysema, and some research from animal and human studies supports the hypothesis that an intermediate deficiency of SAT deficiency is a contributing factor in the development of emphysema in heterozygotes. Nevertheless, it is now recognized that emphysema has a multifactorial etiology and that the heterozygote state, by itself, is not a major predisposing factor. Rather, in combination with other predisposing factors, intermediate SAT deficiency can enhance risk of emphysema. Since the 1983 OTA report, data from several clinical and epidemiologic studies indicate that heterozygotic carriers of SAT deficiency display enhanced risk of developing chronic obstructive pulmonary disease (COPD), even in the absence of occupational or lifestyle factors, such as smoking (44). The risk is, however, exacerbated by smoking (25), occupational risk factors, such as grain dust (44), and other nonidentified factors (55). Thus, while it would appear that a genetic factor is important in risk of COPD for carriers of SAT deficiency, a better understanding of all aspects of emphysema is probably necessary before implementing widespread SAT screening. A DNA-based test for SAT has been used for direct analysis of mutation (58), as well as in prenatal diagnosis (57).

Homozygous alpha- l-antitrypsin deficiency, because it is so thoroughly understood at the molecular level, is a good candidate for gene therapy. It has been proposed that genetically engineered alpha-1 in aerosol form could serve the function of shielding against natural destruction of the respiratory tract. Such therapy is in early experimental stages (19).

Aryl Hydrocarbon Hydroxylase and Cytochrome P-450

Cytochrome P-450 enzymes play a central role in metabolizing an enormous range of molecules, including steroids, other drugs, carcinogens, and an array of environmental agents. Both because of their wide spectrum of action and their genetic variability among humans, P-450 enzymes have a marked potential to affect individual susceptibility. Research in cytochrome P-450 has exploded (75) and information continues to mount about genetic differences in human P-450 enzymes, as well as the relationship between P-450 enzymes and cancer (35,75,76,117). This section examines two cytochrome P-450 enzymes: aryl hydrocarbon hydroxylase (AHH) and debrisoquine 4-hydroxylase (D4-H),

The 1983 OTA report examined the role of individual differences of AHH and lung cancer. A key feature of this discussion relied on scientists' ability to reliably measure AHH changes in white blood cells and correlate those changes with changes in lung cells. Experimental limitations to elucidate the role of changes in enzyme levels of AHH in lung cancer led investigators to identify the role of other P-450 genetic markers in environmentally induced cancers, including D4-H (5,13). Nevertheless, concrete evidence that enzyme levels of AHH or D-4H could serve as markers for differential cancer susceptibility to lung cancer (5) remained elusive until recombinant DNA methods were used to define the inheritance of a number of P-450 enzymes, including AHH and D4-H.

With advances in molecular biology, scientists anticipate clinical studies to correlate inheritance of RFLPs associated with (or genetically linked to) various P-450 enzymes with individual cancer risk (75). In the case of D4-H deficiency, where 5 to 10 percent of people are affected, molecular characterization of the phenotype (36) shows promise of revealing the relationship among individual differences in D4-H, environmental exposure to certain agents, and cancer susceptibility (46). Characterization of other P-450 genes is likely to yield insight into predicting individual toxicity to some types of antibiotics, including erythromycin, a commonly prescribed antibiotic, and other agents (14).

Ataxia Telangiectasia Heterozygosity

Ataxia telangiectasia (AT) is an autosomal recessive disorder displaying simultaneous neurological, oculocutaneous, and immunological complications (61,101). Diagnosis is usually made in childhood based on the appearance of poor motor control and telangiectasia, or spider-like lesions, on the skin and eyes. Such individuals are predisposed to both immune deficiencies and certain cancers (1,31,81). The cancer risk is over 100 times greater than for control groups. Patients usually die in early adulthood from respiratory ailments or lymphoproliferative disorders.

Several studies have noted that the AT gene may have some clinical effects in persons who are

heterozygous. Among those effects found in some AT heterozygotes are defective immunity, oculocutaneous telangiectasias, and enhanced cancer susceptibility (31,102). AT heterozygotes are particularly sensitive to ionizing radiation.

AT homozygotes are relatively uncommon at approximately 25 per million (or 1 in 40,000). However, population-based studies have estimated the incidence of the heterozygote in the United States to be about 2.8 percent, or 6 to 7 million Americans (14). For AT heterozygotes younger than age 45, the risk of dying from a malignant neoplasm is greater than five times the risk for the general population. AT heterozygotes comprise more than 5 percent of all persons dying from cancer before age 45. The types of cancer increased in AT families are ovarian, gastric, and biliary system carcinomas, and leukemia and lymphoma. In addition, there is evidence to support some predisposition of AT heterozygotes to basal cell, breast, pancreatic, cervical, and colon cancers. AT heterozygotes appear to be at markedly enhanced risk of breast cancer (14,72,82).

The emphasis on environmental-occupational exposures and their effects on the AT heterozygote is currently focused on radiation, x-rays in particular. For example, occupational exposures of breast tissue to x-rays, or even diagnostic exposures such as mammography, have been raised as cause for concern (102).

A test has been developed to detect AT heterozygotes. Progress in this area could lead to identification of individuals at risk for cancers as a result of radiation exposure.

Paraoxonase Variants

Paraoxonase is one esterase found in human serum that metabolizes paraoxon, a metabolize that is the active ingredient of the organophosphate insecticide parathion. Paraoxonase activity shows considerable variability in human populations, with significant interethnic differences (20,34,83). Individuals with variations in esterase activity are expected to be at increased risk to organophosphate toxicity from any given exposure and would require longer recovery before resuming pesticide spray work (32,79). Insufficient research has been done to determine at what levels of exposure individuals with decreased paraoxonase activity are at risk.

HLA Associations

Each individual has a specific set of proteins on the surface of his or her cell membranes that make him or her different from everyone else. This array of cellular surface proteins is called the HLA system. HLA typing has been used for several years in matching tissue and organ donors with recipients and for paternity determinations. Increasingly, various HLAs are being associated with specific human diseases (106).

The classic and most striking example of an HLA associated with disease is that between ankylosing spondylitis (AS), an arthritis of the spine. Among Europeans, approximately 90 percent of patients with AS display the antigen HLA-B27, while it is present in only 8 to 9 percent of the general population. A number of other joint diseases also display strong positive associations with the B27 antigen.

Allergies, cardiovascular disease, immune system diseases, dermatological disorders, renal disease, ophthalmologic disorders, gastrointestinal diseases, and certain malignancies have been associated with the presence of one or more HLA types (73,88). Despite some striking statistical associations of certain diseases with specific HLAs, any mechanistic relationship is yet to be determined, precluding the possibility of knowing whether the relationship is causal or merely statistical. Nevertheless, the recognition of the statistical relationship of HLAs with a wide range of human diseases—some of which are known to also be occupationally related, such as bladder cancer, asbestosis, and farmer's lung-suggests that inherent genetic factors are affecting the occurrence of the disease within the population (14).

SCREENING FOR NONOCCUPATIONALLY RELATED DISEASE

Recent progress in developing tests to detect conditions not associated with worksite exposures—e.g., Huntington's disease or heart disease--raises new issues for containing health care expenses, for both the employer and employee, and for employee "wellness programs." The implications of the various motivations for screening for nonoccupationally related traits and disease are discussed more extensively in chapter 2.

This section covers genetic traits that have been identified and for which genes have been cloned (table 5-l), or where the abnormal gene can be detected indirectly through DNA-based tests. It is not a comprehensive treatise on all genetic conditions that have been cloned, but rather a discussion of selected conditions intended to illustrate the vast progress in this field.

The determination of 'predisposition to disease' used to be based on gross physical examination, family history, and lifestyle habits such as eating and drinking. Molecular biology has enhanced this determination by seeking out and finding genes or markers associated with disease. Individuals found to have the gene or the marker can then be identified, sometimes with near certainty, to be candidates for disease. The influence of environment remains the wild card in most cases, because possession of the genetic predisposition alone may not be sufficient to cause disease. It is likely that for some time modern science will be more successful in identifying the genes and the markers than in identifying the environmental agent(s) necessary for activation of the predisposing genes.

Predispositions to certain cancers have been the focus of much research in the past few years, as have those to atherosclerosis, diabetes, mental illness, and chemical addiction. Advances in those areas are discussed below.

Research is also providing insight into possible genetic predispositions to such common ailments as lower back injuries, obesity, allergies, and arthritis. While predictive tests are not immediately foreseeable in any of those areas, as more populations are studied and more linkage maps prepared, it is not improbable that screening tests will be developed.

Predisposition to Cancers

Cancers resemble other common diseases in-so-far as some forms are associated with chromosomal anomalies, others with single mutant genes, or environmental agents (as discussed in ch. 4). The vast majority, however, are best explained by a genetic-environmental interaction. Clearly, some individuals are predisposed to certain types of cancer given the right environmental exposure. Thus, viruses and carcinogenic agents act as environmental triggers in individuals with a hereditary predisposition to cancer. This "two-hit" theory, first posed in the early 1970s (59), states that sporadic v. inherited forms of cancer could both result from mutations in the same gene. These mutations act recessively at the cellular level, and both copies of the normal gene must be altered or lost for the cancer to develop. In sporadic cases, both events occur somatically whereas in cancer families, susceptibility is inherited through a germline mutation and the cancer develops after a somatic change in the normal allele. Recent developments in the study of oncogenes corroborate this theory (7,69).

Occupational exposures have been implicated in lung, bladder, testicular, and laryngeal cancers, as well as leukemias. As the connections between cancer and genetics become clearer, so may the relevance of occupational exposure to genetic disease.

Increasingly, predisposition to certain cancers will be detected through the identification of oncogenes, as well as DNA repair, metabolizing enzymes, and immune function. The following section describes recent developments in identifying individuals predisposed to cancer. Evidence from studies of high-risk cohorts of workers exposed to carcinogenic agents shows that some workers do not develop tumors. Possible explanations for this differential effect could be variation in exposure, diet, or other lifestyle factors, or genetic factors. Little is known about the role of genetic predisposition to cancer following exposure to carcinogenic agents, but as the genetic defects of various neoplasms are identified, the prospects for better understanding improve.

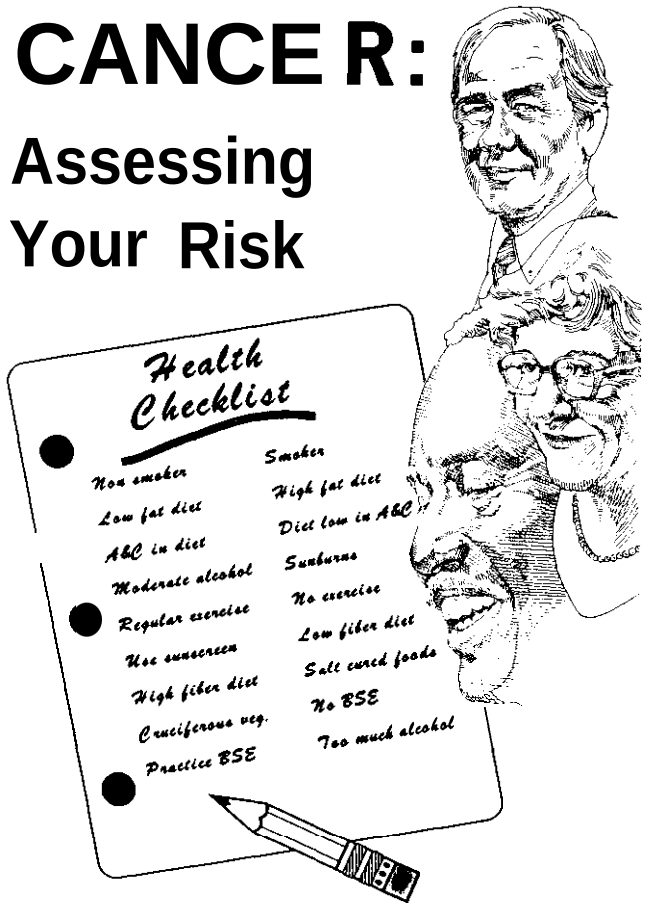
Recent developments in the identification of cancer genes, or oncogenes, and tumor-suppressor genes are discussed below.

Oncogenes

One of the most spectacular results of the new DNA techniques has been the discovery that certain genes, called oncogenes, play a role in the development of cancer (40). Activation of individual oncogenes appear to be necessary, but not sufficient, to trigger cancer. As many as 10 distinct mutations may have to accumulate in a cell before it becomes cancerous (68). In some cases, chromosomal breaks, deletions, translocations, or insertions of foreign DNA place a potential oncogene (also called a proto-oncogene) near a regulatory element that activates it (94). The clastogenic (chromosome-breaking) effects of radiation and certain chemi-

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LUNG CANCER

1 SEX: a Male (2) b Female (1)

2 AGE: a. 39 or less (1) b 40-49 (2) c 50-59 (5) d 60+ (7)

3. **EXPOSURE TO ANY OF THESE:**
a. Mining (3) b. Asbestos (7) c. Uranium & radioactive products (5) d. None (0)

4. **HABITS:** a. Smoker (10)* b. Nonsmoker (0)*

5. **TYPE OF SMOKING:**
a. Cigarettes or little cigars (10) b. Pipe and/or cigar, but not cigarettes (3) c. Nonsmoke

6. **NUMBER OF CIGARETTES SMOKED PER DAY:**
a. 0 (1) b. Less than ½ pack per day (5) c. ½-1 pack (9) d. 1-2 packs (15) e. 2+ packs

7. **TYPE OF CIGARETTE:**
a. High tar/nicotine (10)** b. Medium tar/nicotine (9)** c. Low tar/nicotine (7)** d. Nonsmoke

8. **LENGTH OF TIME SMOKING:**
a. Nonsmoker (1) b. Up to 15 years (5) c. 15-25 years (10) d. 25+ years

SUBTOTAL ____

REDUCING YOUR RISK — * If you stopped smoking more than 10 years ago, count yourself as a nonsmoker. If you have stopped smok the past 10 years, you are an **ex-smoker**. Ex-smokers should answer questions 5 through 8 according to how they previously smoked. Then ex-smoker **reduce** their point total on questions 5 through 8 by 10% for each year they have not smoked. Current smokers also answer questions 5 through 8

I am stopping smoking today. (Subtract 2 points.) TOTAL ____

** High Tar/Nicotine 20 mg or more tar / 1.3 mg or more nicotine Medium Tar/Nicotine (6 19 mg tar / 0.7 1.2 mg nicotine Low Tar/Nicotine 15 mg or less tar / 1.0 mg or less

COLON RECTUM CANCER

1. **AGE:** a. 49 or less (10) b. 50-59 (30) c. 60 and over

2. **HAS ANYONE IN YOUR IMMEDIATE FAMILY EVER HAD:**
a. Colon cancer (20) b. One or more polyps of the colon (10) c. Neithe

3. **HAVE YOU EVER HAD:**
a. Colon cancer (100) b. One or more polyps of the colon (40) c. Ulcerative colitis
d. Cancer of the breast, ovaries, stomach, or uterus (10) e. None of the above (1)

4. **DO YOU HAVE BLEEDING FROM THE RECTUM** (other than obvious hemorrhoids or piles diagnosed by your physic
a. Yes (75) b. No (1)

SUBTOTAL

REDUCING YOUR RISK

5. I have altered my diet to include less fat and more fruits, fiber and cruciferous vegetables (broccoli, cabbage, cauliflower, Brussels sprouts) (Subtr points.)

6. I have had a negative test for blood in my stool within the past year. (Subtract 10 points.)

7. I have had a negative proctoscopic (sigmoidoscopic) exam within the past year. (Subtract 20 p

TOTAL

SKIN CANCER

1. Live in the southern part of the U.S.: Yes
2. Frequent work or play in the sun: Yes
3. Fair complexion or freckles; (natural hair color of blonde, red, or light brown, or eye color of grey, green, blue, or hazel): Yes
4. Work in mines, around coal tars or radioactivity: Yes
5. Experienced a severe, blistering sunburn before the age of 18: Yes
6. Have any family members with skin cancer or history of melanoma: Yes
7. Had skin cancer or melanoma in the past: Yes
8. Use or have used tanning beds or sun lamps Yes No
9 Have large, many, or changing moles Yes No

REDUCING YOUR RISK

10. I cover up with a wide brimmed hat and wear long sleeved shirts and pants Yes
11. I use sun screens with an SPF rating of 15 or higher when going out in the sun. Yes
12. I examine my skin once a month for changes in warts or moles Yes

Photo credit: American Cancer Society: Texas Divis

A written self-test that assesses an individual's cancer risks.

cals, therefore, have the potential for activating an oncogene (see ch. 4).

Approximately 40 dominant-acting oncogenes have been found that can induce transformation when introduced into a cell in a structurally altered form or when improperly expressed. The most commonly studied oncogene, called "ras, " is found in 50 percent of colon carcinomas, 30 percent of adenocarcinomas of the lung, and more than 90 percent of cancers of the pancreas (3,28,54,90,113). Most pancreatic carcinomas and about one-third of colorectal cancers reveal the presence of a dominant-acting oncogene activated by a single nucleotide substitution.

Chronic myelogenous leukemia (CML) exhibits the Philadelphia chromosome (named after the city in which it was identified) which results from chromosomal translocation. The translocation indirectly activates an oncogene. Biotechnology companies have developed probes for the CML and breast cancer oncogenes.

In recessive oncogenesis, the cells appear to have lost both copies of a tumor suppressor gene (62). Suppressor genes, or "anti-oncogenes," are necessary for the inactivation of the oncogene, and therefore, the malignant cell growth. Suppressor gene loss is at least as important in carcinogenesis as oncogene activation. It usually takes two separate mutagenic events to eliminate a suppressor gene, because alleles are paired and both probably have to be inactivated (68). Two candidate turner suppressor genes have been cloned, for retinoblastoma and Wilm's tumor, but the existence of others has been inferred from experiments in which specific chromosomal regions were deleted in turners (86,114).

Retinoblastoma (Rb) is an intraocular tumor of early childhood that can be inherited in an autosomal dominant fashion but is thought to result from a recessive-acting oncogene. The Rb gene provides a model system for recessive oncogenesis. This gene also has been shown to be inactivated in some breast cancer cell lines. Inheriting a mutant allele for the Rb gene predisposes a recipient to Rb. The sporadic loss of the Rb gene through mutation is correlated with increased cell proliferation and oncogenesis (23). Inactivation through mutation of the Rb susceptibility gene has been implicated in the genesis of Rb and certain other human neoplasms, suggesting a broad role for this gene in oncogenesis (65).

Recessive-acting oncogenes also have been associated with common solid tissue tumors such as carcinomas of the bladder, colon, breast, and lung.

There is a significant distinction between dominant-acting oncogenes and recessive-acting suppressor genes. The oncogenes that have been identified to date are activated through somatic mutations—genetic changes occurring in one or another target organs and not in the germ cells. Mutant, activated oncogenes are therefore not transmitted from parent to offspring and can be detected only in tumor cells. In contrast, mutant forms of suppressor genes might be found in sperm or eggs, and can be passed onto future generations (116). This difference distinguishes those who are predisposed to cancer at birth from those who are not.

The rapid development of synthetic probes and gene amplification techniques will increase the capability to detect the presence or recurrence of malignant cells with genetic characteristics associated with oncogenes and tumor suppressor genes. An experimental approach, termed "gene targeting," proposes to stop or counter the action of oncogenes by introducing a synthetic strand of DNA to block the message arising from the activated oncogene.

Colon Cancer

Colon cancer is the second most common cancer in North America, estimated to account for about 62,000 deaths in 1988 (54). A recent study concluded that a gene inherited by a third of all Caucasian Americans may be responsible for most cancer of the colon and rectum. Inheriting the gene does not mean that one is destined to have cancer. Other factors, both genetic and environmental, play a role in inducing cancer in those who inherit the gene. One study found evidence that a series of four to five genetic mutations and deletions are necessary for colon or rectal cancer to occur. If it takes four or five steps to get the cancer, those who have inherited one of the mutations in those steps have, in a sense, a "head start' and are more likely to get the cancer (54).

Two types of mutations have been detected in colorectal tumors. The first involves point mutations in ras proto-oncogenes. The second type involves deletions of specific chromosomal regions. Deletions can be detected through RFLP analysis. The deleted sequences have been hypothesized to in-

elude tumor-suppressor genes necessary for inhibition of neoplastic growth (54,114).

Advances in this area will lead to earlier detection and intervention and to greater understanding of environmental influences on the activation of the oncogene.

Lung Cancer

Lung cancer is the overall leading cause of cancer death among Americans. There is evidence that a genetic defect contributes to the development of an important form of lung cancer that makes up at least 20 percent of all lung cancers. In some studies of lung cancer patients, a portion of chromosome 3 is deleted, possibly taking with it suppressor genes (60). Some lung cancers also demonstrate loss of heterozygosity on the short arm of chromosome 17. The p53 gene located in chromosome 17 has the features of a tumor suppressor gene (103).

Some occupational exposures are among the known causes of lung cancer, as is cigarette smoking. It has been suggested that, in males, 15 percent of lung cancers in the United States are due to occupational exposure (21). Employees in asbestos-related occupations, including asbestos production workers, pipefitters, boilermakers, roofers, and shipyard workers, have long demonstrated above average incidence of lung cancer (112). Workers exposed to polycyclic hydrocarbons, such as mechanics and railroad workers, also have a higher incidence of lung cancer. It is unclear how these exposures might induce the mutation necessary for initiation of carcinogenesis, but breakage and rearrangement of chromosomal material is the likely predictor of the deletions containing the suppressor genes.

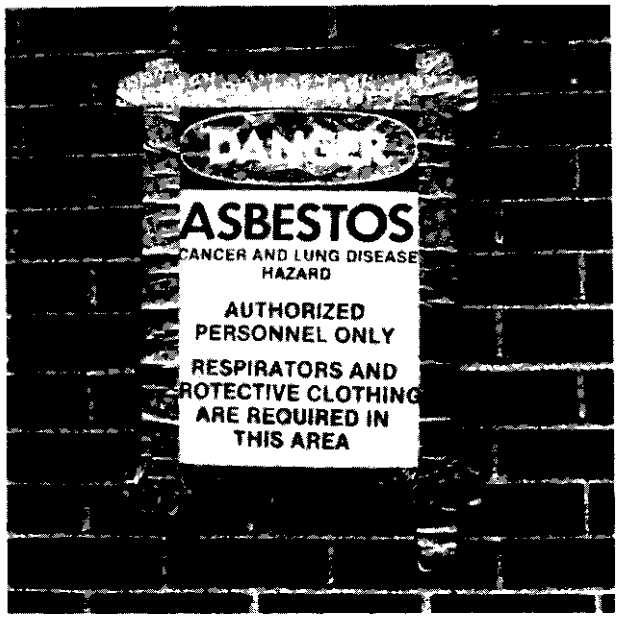


Photo credit: Gianna Bosko

A sign displayed at an asbestos removal site warning that asbestos is a cancer and lung disease hazard.

Future research exploring the relationship between genetic predisposition to lung cancer and environmental exposure will focus on these groups of workers. It is conceivable that once a predisposing gene or set of genes is located, use of probes and PCR will facilitate rapid identification of a subpopulation of workers at higher risk if exposed to certain genotoxic agents. Recent use of RFLPs and probes has detected marker antigens on cells at least 2 years before the clinical appearance of lung cancer (77). Widespread application of this early test could dramatically improve prognosis for cancer patients, whether or not the cancer was attributed to environmental exposure.

Bladder Cancer

More than 49,000 Americans develop bladder cancer each year and about 10,000 die annually. Historically, the major known risk factors were environmental, particularly occupational exposures to aromatic amines. As described earlier in this chapter, phenotypic variants of the autosomal recessive trait for the enzyme N-acetyltransferase have been associated with bladder cancer in workers exposed to aromatic amines. Various genetic polymorphisms have been associated with bladder cancer, including an excess of the A gene of the ABO blood group and an excess of two HLA genes, B5 and CW4 (92). But much of this latter work has not been corroborated.

Activated oncogenes and chromosomal changes have recently been identified with bladder cancer. It has been demonstrated that cells from urogenital tissue derived from patients with bladder cancer are missing genes on the short arm of chromosome 11. As in colorectal and lung cancers, it is theorized that among those missing genes are genes responsible for suppression of growth (27). A transforming oncogene (H-ras-1) has been isolated from a cell line of human bladder cancer cells (89).

If a genetic component in bladder cancer can be confirmed, screening programs could be targeted to worker populations at high risk. The National Cancer Institute (NCI) estimates that one out of four cases of bladder cancer in Caucasian male Americans is related to occupational exposure. The risk is highest among painters, truckdrivers, employees of the oil, aluminum, and railroad industries, and drill press operators (18). Future research on these populations might lead to a better understanding of the subtleties of predisposition and environmental insult. Some analysts, however, feel that the NCI figures are based on soft, or insufficient data (2,95).

Hereditary Cancer Syndromes

Human cancers that are associated with autosomal dominant mutations have been collectively referred to as hereditary cancer syndromes (HCS) (29). Approximately 60 to 90 percent of individuals with HCS develop a specific type of cancer at an early age. Family members with HCS tend to develop the same type of neoplasm at multiple stages in the same organ or bilaterally in paired organs (3). Examples of dominantly inherited HCS include retinoblastoma, Wilm's tumor, neuroblastoma, nevoid basal cell carcinoma, familial poly - posis coli, von Hippel-Lindau tumors, neurofibromatosis, and familial cancer syndrome. Syndromes inherited in an autosomal recessive fashion include Fanconi's anemia and xeroderma pigmentosum.

Predisposition to Mental and Addictive Disorders

New research has shown some mental and behavioral disorders to be, in part, genetically deter-mined. The exact nature of genetic influence, however, remains in dispute for most disorders. Nonetheless, it is widely believed that there is likely a genetic component to manic depression, schizophrenia, autism, hyperactivity, some compulsive disorders, and alcoholism (6,63,67). There is even evidence that addiction to narcotics is influenced by physiological differences determined, in part, by our genes. Scientists have identified a gene in rats involved in the activation of dop amine, an important neurotransmitter (12). Abnormal dopamine function has been linked to schizophrenia, manic depression, Parkinson's disease, and chemical addiction (105).

Currently, disputes center not so much on whether these disorders are genetic, but rather on where their predisposing genes are found. Most recently, two different research teams linked two different markers to schizophrenia (53,93). While it has long been known that schizophrenia shows a tendency to cluster in families, the exact nature of genetic influence has been unclear. Although it might appear that the identification of two distinct markers for the disorder is contradictory, most geneticists view the discrepancy as confirmatory that schizophrenia is a heterogeneous disorder subject to unknown environmental influences (30,63).

Similarly, a research group claimed to have located the gene predisposing individuals to manic depression. Subsequent studies revealed that conclusions drawn from the earlier study were premature and the linkage association was greatly diminished (24,56).

Recent studies of Alzheimer's disease show that at least 10 percent of the cases have a family history with an autosomal dominant pattern and the gene for the inherited form of the disease has been reported to be on chromosome 21 (84). Other studies failed to confirm that finding (104). The majority of cases may be sporadic, with the clinical features identical to the inherited form. The primary cause of Alzheimer's disease remains unknown. Both environmental and genetic factors have been implicated. It is clearly a heterogeneous disorder with an unknown environmental component in at least 85 percent of the cases (91,97).

More conclusive is the evidence for a genetic predisposition to alcoholism. Researchers studying the children of alcoholics have detected specific biochemical and behavioral differences in their responses to alcohol. Specifically, alcoholics have a greater ability to synthesize a unique derivative of alcohol known as phosphatidylethanol. While the contribution of that trait to a predisposition is not clear, it is feasible that testing for levels of phosphatidylethanol could serve as a biological marker for alcoholism (8).

The one neuropsychiatric disorder for which a definitive test has been developed is Huntington's disease, a progressive disease of the central nervous system with no treatment and certain death an average 15 to 17 years after onset some time in mid-adulthood. Huntington's disease is inherited as an autosomal dominant trait with complete lifetime penetrance. In 1983, Gusella and co-workers discov-

ered a RFLP on the short arm of chromosome 4 that is linked to the Huntington's disease locus (39). Linkage analysis is 95 percent accurate. That is, 5 percent of those with the gene for the disease will be missed because of the genetic distance of the marker to the Huntington's disease gene. As more markers have been found, linkage studies have gained an accuracy of approximately 99 percent (9,38). As with other linkage tests, individuals whose test results are uninformative will have to wait until a second family member develops symptoms, or until other polymorphisms are identified, before they can receive definitive results. When the Huntington's disease gene and the mutations producing the disease are discovered, the uncertainty may disappear. Linkage analysis will be unnecessary, only the at-risk person will have to be tested.

The Huntington's disease case is the exception in understanding the genetics of neuropsychiatric illness. Researchers are beginning to appreciate the difficulties in examining the genetics of complex mental illnesses. Scientists are often unable to replicate linkage work performed by others because of the multiple causes of what appears to be the same disorder, the lack of large family pedigrees and large numbers of pedigrees, misdiagnoses of affected relatives, and the sheer complexity of mental illness (6). This has led some to propose that the statistical scores conventionally used to establish linkage be made more stringent for mental disorders. Currently, a logarithmic ratio of 3 is taken as minimum evidence for linkage, meaning that the likelihood is 1,000 to 1 that the marker and gene are linked rather than randomly distributed (6). Raising that ratio to 6 would raise the requirement for linkage and would take into consideration genetic heterogeneity and variable expressivity of the disorder (84). This, and improving clinical diagnostic criteria, can protect against misleading results until the genes for these disorders are actually found.



Photo credit: Nich Kelsh/Kelsh-Marr Studios

Huntington's patient being rowed across Lake Maracaibo, Venezuela.

Predisposition to Atherosclerosis

The associations between coronary artery disease, or atherosclerosis, and cholesterol have been well-established. High-density lipoprotein (HDL) cholesterol promotes efflux of cholesterol from arterial walls, thus earning the reputation of 'good cholesterol." Low-density lipoprotein (LDL) cholesterol causes cholesterol deposition in arterial walls, thereby earning the reputation of 'bad cholesterol." Apolipoprotein A-I is the principal protein constituent of HDL. Decreased plasma concentrations of both HDL and A-I have been associated with premature coronary artery disease (80).

Early coronary artery disease and atherosclerosis exhibit definite familial aggregation. Several different HDL-deficiency states have been reported. The recent cloning of the apolipoprotein A-I gene provides the necessary molecular probe for RFLP analysis of normal and HDL-deficient states. Mutations of the A-I gene are found in 32 percent of people who had severe coronary artery disease before age 60, but only in 3 percent of people with healthy heart arteries (80).

In addition, a single-gene defect at the LDL receptor locus binds apolipoprotein B (apoB) and accounts for the clinical entity known as familial hypercholesterolemia (11). The heterozygote form occurs in 1 out of every 500 individuals. The more lethal homozygous form occurs 1 in 1 million births. Genetic variation affecting LDL levels influences atherosclerosis susceptibility (33).

Significant genetic variation in both the A-I and apoB gene might explain variations in the onset and severity of coronary artery disease among individuals. Biochemical screening for HDL and LDL will continue to be the most reliable predictors of predisposition to disease. The most obvious advantage of genetic screening over current methods is that RFLP marker tests need only be conducted once. Understanding the significance of the muta-

tions at the A-I and apoB loci will lead to more effective and earlier therapy (41).

Predisposition to Diabetes

Diabetes is a disorder in which the body does not produce or properly use insulin, a hormone needed to convert sugars and starches into energy sources for the body. One million of the Nation's 11 million diabetics are insulin-dependent (called type 1 or insulin-dependent diabetes mellitus (IDDM)). Individuals with IDDM exhibit an immunological dysfunction, resulting in the destruction of the islets of Langerhans, groups of cells in the pancreas where beta cells reside to produce insulin is produced. Recent studies reveal an inherited susceptibility in 95 percent of individuals with IDDM (108). Millions of Americans, possibly 50 percent of the entire population, possess the DR3 and DR4 markers (107,108). Despite the prevalence of these susceptibility markers, relatively few people develop the disease, leading to the conclusion that other genes, or some viral or toxic insult, might be necessary to trigger the disease. In addition, geographic variation in rates supports the concept of an environmental role.

COMMERCIAL DEVELOPMENT OF GENETIC TESTS

With accelerating interest in tests to detect abroad range of genetic disorders and increasing investment in biotechnology industries, the market demand for tests, especially DNA-probe tests, is expected to expand. In addition to academic research centers, several biotechnology companies are developing a range of genetic tests (table 5-3), with projections of market value in the millions. While the population affected by genetic conditions for which there is a test available is still somewhat small, the potential future test population for multifactorial diseases is enormous (see table 5-4).

In a 1987 OTA survey of biotechnology companies, it was found that biotechnology companies developing DNA-based tests expected their products to be used by 1990 in: genetic and health department clinics, health department screening programs, prepaid health groups, private primary care practices, reference and DNA labs, insurance companies, the military, places of employment, private nongenetic specialty practices, correctional institutions, public schools, and homes (110).

Table 5-3-Some Companies Offering DNA-Based Diagnostic Tests

Company	Test
California Biotechnology, Inc.	
Mountain View, CA	susceptibility to atherosclerosis and hypertension
Cetus Corp.	
Emeryville, CA	sickle cell anemia
Collaborative Research	
Bedford, MA..	adult polycystic kidney disease cystic fibrosis lymphomas
Genescreen	
Dallas, TX	insulin-dependent diabetes sickle cell anemia hemophilia familial hypercholesterolemia
Genetrix	
Alameda, CA	leukemias
Integrated Genetics	
Framingham, MA.	adult polycystic kidney disease Duchenne muscular dystrophy Huntington's disease cystic fibrosis sickle cell anemia hemophilia B alpha and beta thalassemia
Lifecodes Corp.	
Valhalla, NY	non-Hodgkin's lymphoma lymphocytic leukemia breast cancer oncogenes sickle cell anemia cystic fibrosis
Nichols Institute	
San Juan Capistrano, CA.	cystic fibrosis Duchenne muscular dystrophy sickle cell anemia hematologic malignancies
Oncogene Science	
Mineola, NY.	chronic myeloid leukemia

SOURCE: Office of Technology Assessment, 1990.

Although biotechnology firms developing genetic tests did not overall rank places of employment as important sites for testing in 1990, 5 of 12 thought it likely that employers would be using genetic tests to screen job applicants by the year 2000. Seven of twelve agreed that health risks identified by genetic screening could be used appropriately to exclude susceptible workers from hazardous jobs; 9 of 12 thought this use likely by the year 2000. Other sources predict that by then, most people will have genetic profiles, possibly obtained through their place of employment. Some companies are interested in employee "wellness" programs that include family histories and susceptibility to disease (22,71,1 10). Five of the twelve companies thought it likely by the turn of the century that insurance

Table 5-4-Genetic Tests Available and Total Americans Affected

Genetic condition	Total cases
Currently available:	
Adult polycystic kidney disease	500,000
Fragile X syndrome	100,000
Sickle cell anemia	65,000
Duchenne muscular dystrophy	32,000
Cystic fibrosis	30,000
Huntington's disease	25,000
Hemophilia	20,000
Phenylketonuria	16,000
Retinoblastoma	10.000
Total	798,000
Potential future tests:	
Hypertension	58,000,000
Dyslexia	15,000,000
Atherosclerosis.	6,700,000
Cancer	5,000,000
Manic-depressive illness	2,000,000
Schizophrenia	1,500,000
Type 1 diabetes	1,000,000
Familial Alzheimer's	250,000
Multiple sclerosis	250,000
Myotonic muscular dystrophy	100,000
Total	89,800,000

SOURCE: *Medical World News*, p. 58., Apr. 11, 1988.

companies would be using genetic tests on applicants (110).

Table 5-4 lists some of the tests currently available from commercial interests. Biotechnology companies developing tests for genetic disease or predispositions are generally employing one of three strategies: l) linkage-based tests for family-centered testing programs; 2) tests for single-gene disorders or predictive tests for common polygenic disorders; and 3)development of test processes or instrumentation(110). Tests generally range in price from $200 to $980 per individual. The test for Huntington's disease offered by Integrated Genetics (Framingham, MA) costs $450 per sample (48). Several tests, specifically oncogene-based tests, are awaiting U.S. Food and Drug Administration approval.

SUMMARY AND CONCLUSIONS

There are two categories of genetic characteristics that are relevant to the occupational setting: those that predispose the individual to adverse health effects because of environmental exposure and those that predispose the individual to adverse health effects regardless of job, thereby having an impact on employee "wellness' and possible job performance. In both cases, identification of predisposed individuals remains problematic because not all people carrying predisposing genes develop disease. Variable expressivity, heterogeneity, and reduced penetrance confound the certainty of diagnoses, lowering both the sensitivity and specificity of many current tests.

Most DNA-based tests are indirect, relying on linkage studies to identify those at risk. But even direct tests for mutant genes can be ambiguous without affected family members.

The obstacles to certainty, however, are slowly being removed as the use of synthetic probes, PCR, and automated DNA-sequencing machines increase the efficiency and lower the cost of mass screening. These advances are providing insights into the genetic predisposition to adverse health effects from drugs and environmental agents, cancers, diabetes, atherosclerosis, and mental illness. Fifty human genetic traits have been identified as having the potential to enhance an individual's susceptibility to toxic or carcinogenic agents.

Yet, the environmental agents that trigger the predisposition often remain the wild card. Even though science has shown that cancer is often the result of the activation of oncogenes or inactivation of tumor suppressor genes, the agents that cause these changes are hardly known, and speculated on at best. It may be that as the associations between mutation, carcinogenesis, and genetics become more clear, the boundaries between occupational and genetic disease will become more blurred.

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Chapter 6

Legal Considerations

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Chapter 6
Legal Considerations

Only a limited body of law exists dealing directly with genetic monitoring and screening in the workplace, because the technologies are so new. However, a substantial body of law has developed in dealing with the broad subject of medical testing. Most likely, the body of law governing genetic monitoring and screening in the workplace will grow out of the rules dealing with this related practice. As disputes arise, courts can look to analogies with medical technologies that share common features. An analysis of the law of genetic monitoring and screening in the workplace, therefore, is largely an examination of ways that legal disputes governing other kinds of medical testing of workers have been handled. This chapter will examine this broader area of medical testing law, noting where genetic monitoring and screening arguably differ from medical testing in general, and where special rules regarding genetic monitoring and screening have developed.

Whether workplace or clinical applications are in question, techniques for analyzing an individual's genetic makeup present unique concerns. A person generally has little control over his or her genetic traits. When lifestyle issues such as drug use or alcoholism are in question, it can be argued that there is at least some element of individual choice. An individual's genetic composition, however, is acquired with no choice, but, it can be influenced to some degree with prenatal diagnosis and eventually with gene therapy (41). Analyzing these personal characteristics raises legal questions of the most sensitive sort. Among the fundamental legal issues raised by genetic monitoring and screening are privacy from unwanted testing, confidentiality of the intimate information obtained, discrimination in employment opportunities, and ultimately, the health of the testing subject (see chs. 4,5, and 7).

Genetic monitoring and screening in the workplace are governed by both statutory and common (judge-made) law. Statutes governing genetic monitoring and screening include the Occupational Safety and Health Act (OSH Act) (29 U.S.C. 651 *et seq.),* which establishes a framework for regulating workplace injury and disease hazards by the Occupational Safety and Health Administration (OSHA). The work of other Federal agencies, including the National Institute for Occupational Safety and Health (NIOSH), is also important in this regard. Common law applicable to genetic monitoring and screening includes employee relations, medical malpractice, negligence, and the right to privacy. There are also discrimination issues addressed by workers' compensation statutes, Title VII of the Civil Rights Act of 1964 (42 U.S.C. 2000e), and the Rehabilitation Act of 1973 (29 U.S.C. 791 *et seq.).* Issues governed by collective bargaining are covered by the National Labor Relations Act (NLRA) (29 U.S.C. 151 *et seq.).*

FEDERAL RESPONSIBILITY

A relationship between health hazards in the workplace and disease has been recognized since the early 1700s, when Bernardino Ramazzini penned *A Treatise of the Diseases of Tradesmen (see* box 6-A) (69). He wrote:

> When you come to a sick Person says Hippocrates, it behoves [sic] you to ask what Uneasiness he is under, what was the Cause of it, how many Days he has been ill, how his Belly stands, and what Food he eats: To which I'd presume to add one Interrogation more: namely, what Trade he is of (69).

In modern times, the U.S. Government has assumed some responsibility for safeguarding worker health by establishing various agencies to oversee workplace safety. Several of these agencies are discussed below.

Occupational Safety and Health Administration

OSHA has regulated some employer practices that could have a bearing on genetic monitoring and screening, including employee access to medical records and communications about hazards by employers to employees. The limited experience with genetic technologies will be addressed first, followed by a more thorough discussion of experience involving related techniques.

Direct Experience With Genetic Monitoring and Screening

In 1980, OSHA found itself embroiled in a controversy concerning several of its carcinogen

Box 6-A--Occupational Disease Throughout the Ages

Occupational disease is not a recent phenomena. As long as men and women have work@ they have suffered disease, illness, and injury as a result of their workplace environments. The following examples illustrate occupational diseases prevalent in 17th and 18th century Europe:

. Miners--Individuals who work in the mines suffer from ''difficulty of breathing, swellings of the feet, falling of the teeth, ulcers in the gums, pains and tremblings in the joints. They especially fall prey to the ''mineral spirits which the lungs suck in along with the air, and corrupt and taint the natural temperament of the brain and the nervous juice, from whence spring the tremblings and stupidity. "

• ***Brewers— "The*** servants employed in the brewing of ale and beer, undergo all the symptoms and inconveniences of drunkenness merely from their being constantly employed in pouring out wine and taking the grapes out of the press. In a word, those who do this sort of work for several months together and spend most of the winter in such laboratories, grow lethargic and dejected with little or no appetite. "

• ***Tobacco workers— "Those*** who make snuff find that their lungs do gradually become dry and withered. The powder they work with pricks and dries the tender coat of the lungs and windpipe, and with their foul steams not only cloud the Animal Spirits in the brain, but at the same time corrupt the ferment of the stomach by enervating the acid of that part. "

. Gilders-Gilders become asthmatic and their complexion assumes a dangerous ghostly aspect. Their neck and hands tremble, their teeth fall out, their legs are weak and mauled with the Scurvy' due to their exposure to mercury in the air.

• ***Bakers--"*** Bakers, in sifting flower, in kneading it into dough, and in baking that in the oven, are exposed to infinite fatigue and toil. The inspiration of the flying particles of the meal stuff up not only the throat, but the stomach and the lungs with a tough paste; by which means they become liable to coughs, shortness of breath, hoarseness and at last to asthma. Sometimes the hands of bakers are swelled and pained. Kneading dough squeezes the nutritious juices out of the arteries of the hands. Last, both millers and bakers are generally troubled with lice. "

• ***Fishermen— ''Fishermen*** and mariners have a skin as hard as an elephants and suffer from ulcers that are dry and sordid, as if they were pickled with salt. And indeed sailors are forced to feed upon gross food, salt meat, half rotten water, and bread half worm-eaten, we cannot but conclude that their bodies are crowded with bad juices and disposed to malignant fevers. '

• Field Workers—" Sifters of corn work with a grain powder that I am tempted to suspect has worms in it imperceivable to the senses; and that these worms being put into motion, and dispersed through the air, in the sifting and measuring of corn; some of them stick to the skin and mouth and cause the burning heat and itching that is observed both in the throat and all over the body.

. ***Academics--" All*** Men of Letters in the Learned World do not escape ***from*** disease. 'Tis a known saying that a man grows wise by sitting, and is not aware of the inconveniences accruing to his body, All the Men of Learning complain of a weakness of the stomach. For while the brain is employed in digesting, what the itch of knowledge and the love of learning throws in, the stomach can't but make an imperfect digestion of the ailment, by reason that theAnimal Spirits are diverted and taken up in the intellectual service. "

SOURCE: B. Ramazzini, *A* Treasure *oj the Diseases of Tradesmen* **(London, England: Publisher** Unknown, **1705).**

standards (56). Thirteen of the standards required a preassignment examination by a physician before an employee could be assigned to a regulated area. The standards specified that the examination include the personal history of the employee, family and occupational background, including genetic and environmental factors **(29 CFR** 1910.1003(g)(l)(i)). Subsequent to publicity surrounding this language, OSHA later clarified that these words do not require genetic screening or the exclusion of qualified employees based on genetic findings (64).

While it may have chosen in 1980 not to recognize a genetic screening requirement, OSHA still may include such a rule in its standards in the future. The OSH Act is silent on genetic monitoring and screening. In the absence of a clear prohibition, nothing in the Act appears to prevent OSHA from requiring genetic monitoring and screening as it does other kinds of medical tests.

OSHA actively considered using this authority on one occasion. During 1983, as part of the standard-

setting process for ethylene oxide, OSHA explored the use of genetic monitoring for possible inclusion in the standard's medical surveillance requirements (48 FR 17,284, 17,285). The monitoring merely would have been recommended, though, since OSHA felt that it lacked sufficient information on which to base mandatory requirements (48 FR 17,305). In the final rule a set of mandatory tests not including genetic measures was required to ensure uniformity, and a proposed nonmandatory test for chromosomal damage was dropped (49 FR 25,784).

Thus, OSHA considers genetic monitoring a permissible medical surveillance procedure but has not yet required it. This leaves open the possibility that such tests could be mandated as part of a future standard. They could also be recommended for use subject to employer discretion. Whether an employer could require them is unresolved.

Requirements for Conventional Medical Testing

While leaving genetic monitoring and screening to future proceedings, OSHA has addressed the use of more conventional medical tests on several occasions. Medical surveillance, encompassing both the use of specific biological exposure measures and routine clinical examinations, is required in over 20 OSHA standards governing workplace exposure to hazardous substances. Under the OSH Act, OSHA must ensure for each chemical controlled by a standard that no employee suffers material impairment of health even if exposed throughout his or her working life (6(b)(5) OSH Act).

Further authority is contained in a number of other provisions of the OSH Act. Most notable among these is the section which says that a standard shall prescribe the type and frequency of medical examinations or other tests to be made available by the employer (or at his or her cost) in order to most effectively determine exposure risks (6(b)(7) OSH Act).

Medical surveillance in one form or another is also mandated in OSHA standards dealing with noise and the occupation of diving. While these standards prescribe certain tests that must be offered to employees, they do not prevent employers from supplementing them with other tests of their own choosing. Therefore, even though OSHA does not require the use of genetic monitoring and screening measures, the exposure standards would not prevent employers from choosing to use them.

The OSHA lead standard (29 CFR 1910.1025) has generated considerable legal controversy. This is the only OSHA standard calling for actual biological monitoring rather than more general medical surveillance (see box 6-B).

Role of the General Duty Clause

Another section of the OSH Act provides OSHA a more general authority that could be used to require genetic monitoring and screening. Known as the general duty clause, this section requires employers covered by the Act to maintain a workplace free from recognized hazards that are causing or likely to cause death or serious physical harm to employees (5(a)(1) OSH Act). A vigorous OSHA could interpret a workplace "free from recognized hazards' to be one in which workers have been genetically tested for susceptibility to environmental exposures capable of inducing toxic harm.

It can be argued that the clause requires employers to use genetic monitoring tests if these measures can provide a safer workplace or to use screening to identify individuals with specific susceptibilities. Failure to use them could demonstrate that an employer had not taken all necessary precautions before placing an employee in a high-risk job (99). Further, absent the availability of other technologies, an employer wishing to use the tests could argue that monitoring and screening tests provide the only means to ensure a safe and healthy workplace (99). Arguments against the use of genetic monitoring and screening, however, are the availability of other means to achieve safety, the lack of established efficacy for most newly proposed tests, and the adverse risks to employees when tests are used inappropriately or the results are misinterpreted (18). On balance, it seems unlikely that an employer could successfully contend that the general duty clause requires genetic monitoring and screening, absent a directive on their use from OSHA.

Protections Against Genetic Monitoring and Screening and Their Consequences

Considerations discussed so far involve sources of authority in the OSH Act for mandating the use of genetic monitoring and screening tests. On the other side of the issue are the protections the Act provides for employees who refuse testing, or who wish to limit the negative consequences of unfavorable test

Box 6-B—The Lead Standard

The history of the lead standard provides insight into the factors that could influence OSHA to adopt genetic monitoring or screening requirements in the future. Before genetic monitoring or screening could be required, there should be a readily available measure of exposure that is reasonably inexpensive and diagnostically reliable, similar to that used in blood lead testing. The measure must also be a valid predictor of a disease process. Analysis of sister chromatid exchanges, for example, provides a general indicator of cellular harm but not a predictor of a specific illness (see ch. 4). In addition, there must be a medical benefit to be gained from early diagnostic information. A chance must exist that absorption of a toxin can be reversed or that a disease process can be halted. Further, if the experience of the lead standard is a guide, OSHA will probably only require genetic monitoring if ambient exposure controls are not available as a reasonable alternative. Another solution is removal of the worker from the workplace site.

The lead standard, which calls for periodic blood tests of workers exposed to lead, requires medical removal protection (MRP) for workers found to have high blood lead levels. Under this procedure, the employee must be removed from the job and placed in another involving no lead exposure with existing pay and benefits for up to 18 months. If no alternative job can be found, the employee still must be removed from the job while retaining full pay and benefits, These requirements were upheld by the Circuit Court of Appeals for the District of Columbia citing the provisions of the OSH Act.

Another aspect of the debate over the lead standard has interesting implications for the use of genetic monitoring. The lead industry had argued that compliance with exposure standards be measured through biological monitoring of individual workers to determine whether workplace lead levels were having measurable health effects. Organized labor, however, contended that ambient air measurements were appropriate indicators of workplace health effects. It feared that use of biological monitoring for this purpose would create an incentive for employers to discharge workers who were sensitive to lead rather than to reduce exposure levels. The final OSHA standard called for ambient lead levels to be used to measure workplace exposure and for biological monitoring to be used to assess the health of individual workers. This resolution could be a model for the use of genetic monitoring in exposure standards.

In addition to such health benefits of monitoring, reduction of ambient lead levels involves tremendous engineering costs that may be beyond the means of many smaller companies. Biological monitoring and MRP may be less expensive when weighed against the costs of these alternative measures. Of course, requirements that full pay be given for 18 months means MRP creates an incentive to reduce ambient levels and maintain worker productivity, While biological monitoring involves both indirect (e.g., anemia) and direct (e.g., elevated blood and urine lead concentrations) indicators of excessive lead intake, medical surveillance follows symptoms (e.g., weakness, impaired mental function, disorders of peripheral nerves). Biological monitoring makes it possible to identify effects or symptoms before toxins produce disease.

SOURCES: office of Technology Assessmcnt, 1990, based on R.I. Field, "The Federal Role in Biological Monitoring," unpublished manuscript, Boston University Center for Law and Health Sciences; *United Steelworkers v. Marshall, 647* F.2d 1189 (D.C. Cir. 1981).

results. Such protections are limited, however, and apply to only certain situations.

The OSH Act contains a protection for workers having religious objections to OSHA practices (20(a)(5) OSH Act). OSHA has granted a limited number of exceptions to its safety standards for such workers (76). It seems unlikely that many workers would take advantage of this provision. An explicit antidis crimination clause of the OSH Act prohibits employers from firing or otherwise discriminating against employees who have exercised any right under or related to the Act (29 U.S.C. 660(c)).

Applying this language to discrimination resulting from genetic monitoring and screening, however, appears to be limited to instances of OSHA-mandated monitoring and screening programs, of which there are none (39). If the employer instituted genetic monitoring or screening on its own, the worker would be protected only if some aspect of the program violated the OSH Act unless, of course, the worker refused to participate in the monitoring or screening program.

Access to Medical and Exposure Records

The OSH Act also governs employee access to medical and exposure records kept by employers (29 CFR 1910.20). Such standards seek to prevent abuses that could result from the availability of these data (56). These records can serve a number of

purposes. By using them, OSHA can monitor compliance, NIOSH can conduct research with patient-identifying information removed, unions can learn about workplace exposure levels, and employees can obtain information of possible value in treatment or counseling by a private physician (34). Such records can also be transferred to subsequent employers.

The definition of 'employee medical records' in the standard is fairly broad (29 CFR 1910.20 (c)(6)(i)) and would clearly cover results from genetic monitoring and screening. Records include, among other things, results of medical examinations, whether preemployment, preassignment, periodic, or episodic, and laboratory tests, including all biological monitoring results (29 CFR 1910.20(C)).

Workers also have access to their "employee exposure record' which includes environmental monitoring or measuring, biological monitoring results, and material safety data sheets or 'any other record which reveals the identity . . . of a toxic substance or harmful physical agent. " The regulations also grant employees access to various types of analyses that use these records.

The extent of the protection afforded workers by these rules, however, is limited, since mere access neither aids an employee unable to interpret the data nor allows for the correction of erroneous information (74). The antidiscrimination provision of the OSH Act protects employees from retaliation for exercising their rights to see their medical records (11(c)(1) OSH Act). This would also apply to genetic monitoring and screening records. When test results are wrong, unreliable, or invalid measures of the traits they are purported to reflect, employees would most likely have to rely on other legal protections, such as a common law right of action for defamation or for medical malpractice.

Finally, the regulations require employers to provide medical information to employees only on request. Once a request is made, all medical and exposure records, including analyses based on them, must be provided. These regulations apply only where the employee has been exposed to certain hazardous substances. Employees could fail to gain access, however, if they are unaware the information exists.

Recordkeeping Requirements

Another OSHA regulation of potential relevance is the requirement for recordkeeping involving occupational injuries or illnesses (29 CFR 1904.2). According to the regulation's definition, occupational illness of an employee is any abnormal condition or disorder, other than one resulting from an occupational injury, caused by exposure to environmental factors associated with employment. It includes acute and chronic illnesses or diseases that may be caused by inhalation, absorption, ingestion, or direct contact.

Thus, genetic damage could be viewed as an occupational illness provided the link between the genetic defect and the subsequent disease were clearly demonstrated. If OSHA were to adopt this interpretation, then employers would have to include in their logs any positive results of genetic monitoring tests.

The scope of this rule has been the subject of conflicting interpretations by the Occupational Safety and Health Review Commission (OSHRC), which reviews OSHA enforcement actions. In one case, OSHRC found congressional intent favoring a broad interpretation of the reporting regulations to provide information "for future scientific use" (36). The employer argued that it did not have to record the illnesses of three workers because the illnesses had not resulted from occupational exposures. OSHRC held that the requirement to record illnesses is not limited to those directly caused by occupational exposures and includes conditions for which these exposures were either a contributing factor or aggravated a preexisting condition.

In another case, OSHRC deferred to the employer's judgment as to what is reportable and ruled that the standard does not require the employer "to do more than make a reasonable judgment based on the information and expertise available to it" (7). The employer failed to record the illnesses of eight employees with asbestosis. The occupational health physician initially had not given this as the diagnosis, but did diagnose asbestosis in light of additional information after the company received a citation. OSHRC found that the medical evidence initially had been unclear, so that no duty to provide the correct occupationally related diagnosis existed. Some argue that this decision signals a view by OSHRC that all doubts about recordability

should no longer be resolved in favor of recording (78).

Hazard Communication Standard

OSHA has issued a regulation mandating that certain information on hazardous workplace substances be communicated to employees (29 CFR 1910.1200). Essentially, this rule amounts to a workplace right-to-know law. Employers must keep records of hazardous substances and provide labels, data sheets, and written communications to employees.

The Hazard Communication Standard deals with information on substances and not on individual workers, so its effect on worker test data is likely to be indirect. Genetic monitoring and screening tests could, however, influence the scope of the rule. The regulation very broadly describes the kind of data needed to indicate a health hazard (sec. (d)(2)). For health hazards, evidence which is statistically significant and which is based on at least one positive study conducted in accordance with established scientific principles is considered to be sufficient to establish a hazardous effect if the study results meet the health hazard definitions. Health hazards are defined as hazards that may cause measurable changes in body function such as decreased pulmonary function. Employees exposed to such hazards must be apprised of both the change in body function and the signs and symptoms that signal change.

Employers have considerable leeway in construing this language. Chemical manufacturers, importers, and employers evaluating chemicals are not required to follow any specific methods for determining hazards, but they must be able to demonstrate that they have adequately ascertained the hazards of the chemicals produced or imported in accordance with established criteria.

This language is also significant because it appears to relieve employers of any obligation to use genetic monitoring procedures to evaluate toxicity. Such a freedom to ignore genetic tests, however, applies only in the context of communicating hazards and would not preclude the inclusion of genetic monitoring and screening requirements in exposure standards.

The hazard communication regulation could have one other effect on genetic monitoring. Genetic monitoring tests, when developed, could be extremely sensitive measures of toxic effects that could detect early preclinical biological effects not revealed by conventional techniques. To the extent that genetic monitoring indicates health effects before other measures, it could trigger a finding of a health hazard and an obligation to provide employee information. Such an obligation could serve to discourage the use of genetic monitoring in cases dealing with toxic substances covered by the hazard communication standard. However, some believe the evidence to date does not establish clearly the potential of genetic monitoring tests to predict future disease (18).

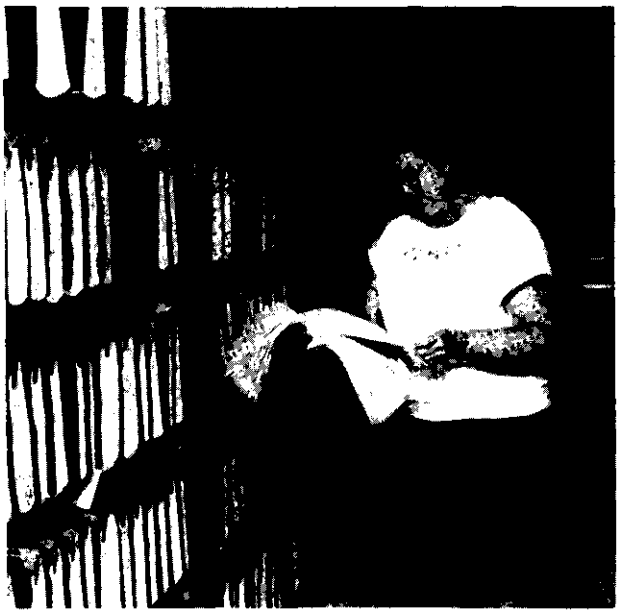


Photo credit: Kathy Goldberg

Epidemiological research at the National Institute for occupational Safety and Health, Cincinnati, OH.

High Risk Occupational Disease Notification Act

Because of its possible relevance to future genetic monitoring and screening, the High Risk Occupational Disease Notification and Prevention Act deserves attention. If passed by Congress, the legislation will establish a scheme to identify and notify all current and former workers exposed to hazardous chemicals during the last 30 years who are determined to be at an increased risk of occupational disease. The purpose is to enable them to seek early medical screening and treatment for any toxic effects.

Given the intent of early notification, identification of the most vulnerable workers could be an issue. This legislative scheme could thereby become

an impetus for application and evaluation of genetic screening to locate susceptible workers. There is the opposing view that this would have been resolved at the risk assessment stage (73).

National Institute for Occupational Safety and Health

NIOSH is charged with conducting research to support OSHA's regulatory activities, even though it has no regulatory authority of its own (29 U.S.C. 671). As one of the foremost research organizations in the field of occupational safety and health, NIOSH, however, can have considerable influence with OSHA and the occupational health community.

Based on its expertise and express statutory authority, NIOSH is probably the most appropriate Federal agency to conduct extensive research on workplace medical screening (76). Seven areas where NIOSH has authority to develop recommendations with relevance to genetic monitoring and screening have been identified:

- research on substances likely to affect sensitive employees,
- research to identify individuals most likely to be sensitive,
- certification of monitoring and screening procedures,
- development of guidelines for evaluating test results,
- development of medical criteria for using tests,
- investigation of protective policies needed for high-risk workers, and
- development of guidelines for personnel actions based on test results (74).

At the time OSHA's medical surveillance and biological monitoring requirements for hazardous substances were being developed, NIOSH played an active role. In particular, it aided in creating the lead standard and provided support in developing testing standards, certifying laboratories performing tests, and establishing medical removal and wage retention protections.

NIOSH is an appropriate agency to conduct research into the medical consequences of workplace genetic monitoring and screening, but has yet to undertake substantial work in this area due to budget limitations. An additional role of NIOSH in such genetic monitoring and screening should be mentioned. Because medical monitoring programs provide considerable sources of data for occupational health research, if genetic monitoring and screening results were to become available and accessible to NIOSH under OSHA access to medical records rules (29 CFR 1904), tremendous opportunities for research would ensue. Nevertheless, the sensitive nature of this information could require special confidentiality and anonymity protections for workers. More importantly, research is needed to determine the validity and predictive value of genetic monitoring and screening tests in the working population (18).

Environmental Protection Agency

While its mission is not directly related to worker health, the Environmental Protection Agency (EPA) administers a number of programs that could have relevance for genetic monitoring and screening. EPA's mission of protecting the general population from toxic pollution often intersects with the responsibilities of OSHA. Several programs of interest have possible implications for workplace monitoring and screening.

The Toxic Substances Control Act (TSCA) (15 U.S.C. 2610 et seq.), the primary statute regulating the chemical industry, requires testing and labeling of hazardous chemicals. These procedures could provide important information to genetically susceptible workers. Although the right to information on specific chemicals under this Act is limited, TSCA requires that toxic substance manufacturers develop adequate data with respect to the substances' effects on public health and the environment.

Two programs administered by EPA as part of the Superfund program could also have implications for genetic monitoring and screening. The original Superfund law, the Comprehensive Environmental Response, Compensation, and Liability Act (42 U.S.C. 9601 *et seq.),* established the Agency for Toxic Substances and Disease Registry (ATSDR), whose responsibilities include assessing health effects of toxic substances found at hazardous waste dump sites and creating registries of individuals living near these sites who might have been exposed to these substances. The Superfund Amendments and Reauthorization Act of 1986 (SARA) (Public Law 99-499) substantially increased the responsibilities of ATSDR and established timetables for its work. ATSDR has met those timetables by issuing

toxicological profiles for high priority chemicals, health assessments for all the National Priorities List Superfund sites, and procedures for developing exposure and disease registries.

Genetic monitoring could provide a useful measure of the exposures experienced by people on the registries. Genetic screening could help to identify those most at risk. While ATSDR's mission is to protect members of the general population living near hazardous waste dump sites, its procedures would be applicable to the protection of workers at these sites, as well, either directly through EPA guidelines or indirectly through adoption by OSHA. In fact, ATSDR has worked with NIOSH, the Centers for Disease Control, and unions with hazardous waste site workers.

SARA also included an extensive right-to-know provision, Title III, requiring manufacturers and others that regularly emit hazardous waste into the environment to report the substances used and regularly emitted to State and local authorities. Genetic monitoring of populations exposed to chemicals as the result of leaks, whether workers or members of the local community, may be one way of dealing with such emergencies. Genetic screening results could help to identify those in most need of assistance in these circumstances.

Title VII of the Civil Rights Act of 1964

Title VII of the Civil Rights Act of 1964, as amended (42 U.S.C. 2000e), prohibits discrimination in hiring, discharge, compensation, or other terms, conditions or privileges of employment because of an individual's race, color, religion, sex, or national origin. All forms of employment and preemployment bias are forbidden, including discrimination in hiring, discharge, promotion, layoff and recall, compensation and fringe benefits, classification, training, apprenticeship, referrals for employment, union membership, and all other "terms, conditions, or privileges of employment. "

The Act applies to employers, labor unions, and employment agencies. Private firms with 15 or more employees and engaged in an "industry affecting commerce" are covered. While State and local governments are subject to Title VII, the Federal Government is specifically exempted along with Indian tribes, departments and agencies of the District of Columbia, and bona fide private membership clubs.

The Supreme Court has found as a central purpose to Title VII "to make persons whole for injuries suffered on account of unlawful employment discrimination' (l). Although the term "discrimination" is not defined in Title VII, it has been defined by one court as "a failure to treat all persons equally where no reasonable distinction can be found between those favored and those not favored" (10). The Supreme Court has recognized two main forms of employment discrimination, "disparate treatment' and "disparate impact. " Disparate treatment occurs when an employer simply treats some people less favorably than others because of their race, color, religion, sex, or national origin. Proof of discriminatory motive is required. Disparate impact involves employment practices that appear to be neutral in their treatment of different groups but in fact affect one group more severely and cannot be justified by the requirements of the job or business. Proof of discriminatory motive is not required.

The disparate impact concept was established by the Supreme Court in *Griggs v. Duke Power Co. (37)* when it unanimously held that an employer's use of certain standardized tests violated Title VII because they disqualified Black applicants at a substantially higher rate and were not shown to predict job performance.

In another case (l), the Court clarified *Griggs* and held that a plaintiff may establish a prima facie case of disparate impact by showing that the tests at issue select applicants for employment or promotion in a racial pattern significantly different from that of the pool of applicants. The burden was then on the employer to show that any given requirement has a distinct relationship to the employment in question. The plaintiff could still rebut this evidence, however, by demonstrating that other tests or selection procedures, without a similarly undesirable racial effect, would also serve the employer's legitimate interest in efficient and trustworthy workmanship (l).

The recent Supreme Court decision in *Wards Cove Packing v. Atonio* imposes more stringent standards on workers attempting to use statistics to prove discriminatory employment practices (96). Some critics of the decision claim that it overrules the Court's ruling in *Griggs.* According to *Griggs,* once an employee presented sufficient statistical evidence that certain employment practices had a discriminatory effect on women or Blacks, the

employer had the burden of proving that the challenged practices were a justified business necessity.

It has been argued that the *Wards Cove* decision is a victory for employers and forces employees to bear the burden of disproving employers' business justifications for discriminatory practices. Employers, using genetic monitoring and screening to identify workers or applicants susceptible to certain illnesses, could discharge, fail to promote or hire, or in other ways discriminate against such individuals and claim business justification. Employees would then be placed in the more difficult position of disproving the need for that claim. This could mean that certain minorities that are susceptible to certain diseases (e.g., sickle cell disease, Tay-Sachs, hypertension) could face disproportionate discrimination in job situations where genetic screening is used. Many genetic screening procedures have a disparate impact (e.g., sickle cell disease, glucose-6-phosphate dehyrogenase (G-6-PD) deficiency that could implicate Title VII.

Workers' Compensation Programs

Workers' compensation programs were devised in the early part of the 20th century to provide no-fault compensation to workers suffering harm as a result of their employment. There are also two Federal workers' compensation programs: the Federal Employees Compensation Act for Federal Government workers and the Longshore and Harbor Workers' Compensation Act for shipyard and maritime workers. In addition, the Federal Employers' Liability Act provides compensation for railroad employees, and the Jones Act provides the same for sailors. All of these programs seek to provide speedy recoveries without the need to adjudicate fault, but they require that the harm have a work-related cause.

Initially, workers' compensation programs dealt with traumatic injuries and not with work-related diseases. As the workplace origin of many forms of illness became apparent, workers' compensation systems responded either through statutory change or judicial construction. A particular challenge is posed, though, by diseases with long latency periods between exposure to a causative agent and onset of illness. It is the compensation of such long latency conditions that presents the most likely opportunity for the application of genetic monitoring and screening.



Photo credit: Earl Dotter

The **use of protective clothing can help prevent occupational illness and injury.**

With a lapse of up to 40 years between exposure to a toxic substance and manifestation of illness, the task of determiningg which exposure caused the disease and whether it is work related can become problematic. When the disease is one that is generally caused by workplace substances, such as asbestosis or silicosis, it is easier to establish the work-relatedness of the worker's claim. When it is one that can be caused or aggravated by outside factors, such as many forms of cancer, the long interval can make evidence of work-relatedness harder to establish.

According to one legal expert (48) genetic monitoring and screening obviously have many advantages for employers, not the least of which is the reduction of the cost of workers' compensation claims. Workers' compensation claims have escalated substantially in recent years, and employers are finding the cost to obtain and maintain this insurance extremely high. Compensation claims are becoming more expensive because most cases require that the compensation board determine whether the injury is a work-related injury. In some cases, this is a particularly difficult factual question. For responsible employers, determiningg this question early is cost-saving because it reduces the need to legally challenge an employee's claim for compensation (48).

Role of Genetic Test Data as Evidence

Genetic monitoring and screening data may help claimants with the evidentiary task of proving the workplace etiology of occupational diseases. Generally, proof of a workers' compensation claim for occupational disease involves three primary elements (30). First, there is the hazardous nature of the substance that is the suspected causative agent. This can be based on OSHA or NIOSH reports and standards, as well as on general scientific findings. Second, there is the nature of the claimant's illness and resulting disability. This is usually based on the testimony of an examining physician. Third, the worker must establish the link between the hazardous exposure and the disease. This can be a difficult step, especially when the disease is one that is common outside of the workplace. An often-cited example is lung cancer, which can result from workplace asbestos exposure but also from smoking outside of the workplace.

To prove this third element in the chain, monitoring and screening data obtained in the workplace can be extremely helpful. Most studies linking occupational diseases to toxic agents are based on studies of large populations or on animal responses. Extrapolating from these data to individual instances of a disease gives questionable results. Genetic monitoring and screening data can support causality claims in two ways. First, they can serve the same function as conventional medical tests. Screening produces a baseline to demonstrate a worker's level of genetic composition before employment has begun. Monitoring shows the worker's response to the agent as exposure progresses. The link between workplace exposure and illness is thereby revealed. Genetic screening can serve a second role of showing whether the worker had a special susceptibility to the substance involved. If the claimant did, it will be easier for the claimant to assert that the disease is work-related.

Monitoring and screening data are particularly relevant to the issue of multiple causation. States vary in their treatment of diseases that have both work-related and outside causes. In some States, such as California, workers are fully compensated even when outside factors are involved (54).

In other States, such as Arkansas, workers can only be compensated for the portion of their disease caused by workplace factors (Arkansas Labor Code sec. 14(a)(3)). In these States, genetic screening may help workers show to which agents they are particularly sensitive and are most likely to contribute to their illness. Monitoring may help them demonstrate a pattern of progressive biological harm corresponding to a workplace exposure. At the same time, employers may be able to show that nonworkplace factors were the ones most likely to have harmed the claimant and that workplace exposure did not contribute to harm. In either case, genetic test data may be able to improve the accuracy of compensation decisions.

Workers' Compensation of the Susceptible Employee

In most States, a claimant's right to workers' compensation is not affected by a preexisting condition. The general rule is that an employer takes the worker as the employer finds the worker, with no allowance for a disability that developed before employment that predisposes the worker to occupational illness. Presumably, this rule would extend to a preexisting genetic vulnerability to workplace toxins.

Once an employer has hired a genetically susceptible individual, an employer faces an increased likelihood of paying compensation which may discourage hiring susceptible applicants. Many States have tried to mitigate this possible effect in one of a number of ways.

The frost approach is the use of second injury funds. These are State-run funds that contribute to the compensation of a worker whose work-related injury or disease also has a preemployment cause (49). The existence of such a fired, if applicable, would reduce the risk to an employer who hires a genetically susceptible worker. The availability of screening, moreover, would make it easier to use this mechanism, since the role of preemployment factors would be more clearly revealed.

The second approach allows workers to waive their right to file an occupational disease claim, once a vulnerability is found. There are 5 States that permit such waivers and another 15 that allow waivers for claims involving aggravation of a preexisting condition (76). Massachusetts, however, expressly forbids such waivers (Mass. Ann. Laws, ch. 152, sec. 46).

The availability of waivers could present a serious dilemma for workers' compensation. If genetic screening were available, employers could screen all

workers and ask the susceptible ones to waive their right to bring claims. This could eliminate virtually all liability for occupational disease while leaving workers who develop work-related illnesses with no available compensation. The issue of waivers is an area that may require further examination if workplace genetic screening becomes available.

The final approach apportions liability between the employer and other responsible parties, including the worker, when a preexisting, nonemployment cause is involved. The issue still arises, however, of the amount of responsibility to attribute to each cause. In the case of a genetic predisposition, the question of liability maybe more one of ethics or of public policy than of law. Another complicating factor is the general rule that a prior nondisabling condition is not a disability for purposes of apportionment (49). A latent genetic trait would appear to fall under this category. Thus apportionment as presently structured might not apply to susceptibilities found in genetic screening.

Admissibility of Genetic Monitoring and Screening Data

In the spirit of granting compensation to workers as quickly and efficiently as possible, compensation proceedings are held informally, generally without formal rules of evidence (49). In addition, most States presume that the worker's condition is compensable in the absence of evidence to the contrary (49). Genetic monitoring and screening are likely to remain controversial for some time after their initial use, and there will likely be questions of reliability and appropriateness of such tests. It is possible that hearing officers, unaccustomed to novel forms of medical evidence, will look on genetic data with suspicion or give it more credence than it deserves. They may tend to ignore any doubt that the data cast on the compensability of claims. Employers may face a heavy burden in seeking to rely on genetic monitoring and screening to reduce occupational disease liability.

Rehabilitation Act of 1973

The Rehabilitation Act of 1973 (29 U.S.C. 701-796) enacted a comprehensive ban on discrimination against handicapped individuals in a broad range of areas. The principal provisions of the Act regarding employment rights are found in section 501, which requires affirmative action in Federal Government employment (29 U.S.C. 791); section 503, which regulates the practices of employers who have service, supply, or construction contracts with the Federal Government (29 U.S.C. 633a(c)); and section 504, which applies to practices of entities that operate programs receiving Federal financial assistance (29 U.S.C. 794). The Act was amended in 1978 to add enforcement procedures for Federal applicants and employees claiming a violation of section 501 (29 U.S.C. 794a(a)(l)) and to adopt the rights and remedies prescribed by Title VI of the 1964 Civil Rights Act for enforcement of section 504 (29 U.S.C. 794a(a)(2)).

The Act targets discrimination and deeds which adversely "limit, segregate, or classify" handicapped applicants or employees. Among the practices specifically forbidden by interpretive regulations are discriminatory recruitment, transfers, job assignments, leaves of absence, hinge benefits, and "any other term, condition, or privilege of employment" (28 CFR 41.52; 34 CFR 104.11).

Sections 503 and 504 prohibit discrimination against otherwise qualified individuals with handicaps in employment and other areas. The term "individuals with handicaps" is defined for this purpose as "any person who (i) has a physical or mental impairment which substantially limits one or more of such person's major life activities, (ii) has a record of such impairment, or (iii) is regarded as having such impairment" (29 U.S.C. 706(6)(B)).

Under section 503, all Federal contracts and subcontracts in excess of $2,500 must include clauses obliging the contractor to refrain from discrimination and take affirmative action to promote employment opportunities for the handicapped. By regulation, an employer with a contract exceeding $50,000 and having more than 50 employees must prepare a written affirmative action plan outlining the contractor's practices and procedures for increasing opportunities for the handicapped (41 CFR 60-741-4 to 60-741-6). Absent a waiver (41 CFR 60-741.3), contractors are subject to the affirmative action obligation in all of their activities so long as they are performing the government contract. Contracts with State and local governments, however, require affirmative action only in the agencies performing work on the contract (91).

Section 504 prohibits discrimination against otherwise qualified individuals with handicaps regardless of ethnicity or other similar characteristics, by entities that receive or administer Federal financial

assistance. This section tracks Title VI of the 1964 Civil Rights Act except that section 504, unlike the latter, includes employment coverage and covers programs conducted by the Federal Government. The Civil Rights Restoration Act of 1987 was passed in response to a 1983 Supreme Court decision that had the effect of narrowing the applicability of section 504 (and other civil rights statutes) to apply only to the particular "program or activity' receiving Federal financial assistance, and not to the institution as a whole (38). In response to the Court decision, the Restoration Act specified that section 504 (and other civil rights statutes) apply to all operations of the entity receiving Federal financial assistance, and not only to the particular activity receiving such assistance.

In order to fall under the protection of the Rehabilitation Act, an employee must prove that his or her genetic trait is an impairment, or is regarded as an impairment. Although the statute does not define the term impairment, Department of Health and Human Services regulation implementing section 504 defines physical impairment as:

> . . . any physiological disorder or condition, cosmetic disfigurement, or anatomical loss affecting one or more of the following body systems: neurological; musculoskeletal; special sense organs; respiratory, including speech organs; cardiovascular; reproductive; digestive; genito-urinary; heroic and lymphatic; skin; and endocrine (45 CFR 84.3(j)(2)(i)(A) (1983)).

Under the guidelines and model regulations promulgated to implement section 504, an employer receiving Federal financial assistance may not make preemployment inquiry about whether the applicant is handicapped or about the nature and severity of an existing handicap unless a preemployment medical examination is required of all applicants and the information obtained from the examination is relevant to the applicant's ability to perform job-related functions. The basic purpose of section 504 is to ensure that handicapped individuals are not denied jobs or other benefits because of the prejudiced attitudes or the ignorance of others (79). The Supreme Court, applying a balancing test to section 504, has observed a balance between the statutory rights of the handicapped to be integrated into society and the legitimate interests of Federal grantees in preserving the integrity of their programs (2). While a grantee need not be required to make fundamental or substantial modifications to accommodate the handicapped, it maybe required to make reasonable ones.

In addition, to be covered under section 504, a handicapped individual must be otherwise qualified. This term has been defined judicially as meaning a person who is able to meet all of a program's requirements in spite of his or her handicap (81). Accordingly, an individual with a genetic predisposition for a disease or illness may not be eliminated from consideration for employment or promotion simply because of the predisposition so long as the individual is otherwise qualified for the position. In such a case, the employer would have to make reasonable accommodation for the person.

The Americans with Disabilities Act of 1990

The Americans with Disabilities Act of 1990 (ADA) (Public Law 101-336) is a recently enacted civil rights bill that extends a clear and comprehensive prohibition of discrimination on the basis of disability to the private sector. Title I bans discrimination against individuals with disabilities in hiring, discharge, compensation, or any term, condition, or privilege of employment by an employer engaged in an industry affecting commerce. In July 1992, Title I will apply to employers with 25 or more employees and, in July 1994, to employers with 15 or more employees.

According to ADA some 43 million Americans have one or more physical or mental disabilities, and this number will increase as the population ages. The Act defines disability as:

> (A) **a** physical or mental impairment that substantially limits one or more of the major life activities of such individual;
> (B) a record of such an impairment; or
> (c) being regarded as having such an impairment.

However, questions have been raised concerning the use of the word "impairment" in the ADA definition of disability (29). For example, is it an impairment when:

- an employee is at risk of developing cancer 20 years in the future from present-day workplace exposure to a hazardous substance;
- an employer is at risk because the employee may become disoriented from exposure to a workplace toxin and damage some equipment; or

. the public is at risk because a pilot with a genetic marker for heart disease suffers a heart attack and crashes the plane?

Isa "fictional impairment" such as limb deformity, epilepsy, or deafness the same as an increased risk of possibly becoming ill in the future? An increased risk of developing cancer at some future point is an injury that courts have recognized. However, increased risk of future disease or illness does not relate to present job performance in the same way that present fictional impairment does. The possibility of developing cancer or asbestosis 20 years in the future would not presently impair a worker so that it substantially limits one or more of the major life activities nor would it prevent the worker from currently performing the job (29).

When applied to genetic monitoring and screening the definition of disability does not expressly address the question of increased risk of disease based on genetic factors. The emphasis in the definition of "impairment" suggests that some increased risk of disease without actually having the disease (if the disease is considered an impairment) would not be a disability. Moreover, the definition addresses individuals presently having an impairment or being so regarded or having a record of such an impairment in the past. It does not address "future" impairments. On the other hand, if an employer 'regards' any individual with a marker or trait for a genetic condition as impaired, then perhaps the individual would come under the protection of the Act. This has not yet been tested in court.

The exclusion from the scope of some protection under ADA of individuals who have contagious diseases or infections (so long as the disease about which there is a genetically based increased risk is only potentially a hazard, not currently contagious or infectious, or is not a contagious or infectious disease at all, i.e., genetically transmitted conditions), argues strongly that such increased risk diseases could be considered a disability if the other requirements are met (11). Thus, would such an increased risk limit one or more of an individual's major life activities? If yes, that person is disabled and probably protected by ADA.

An employer may have a defense to a charge of discrimination under the Act if the employer can demonstrate that qualification standards, tests, or selection criteria that screen out or tend to screen out or otherwise deny a job or benefit to an individual with a disability are job-related and consistent with business necessity, and no reasonable accommodation is possible. Under the Act reasonable accommodation is defined as:

(A) making existing facilities used by employees readily accessible to and usable by individuals with disabilities; and

(B) job restructuring, part-time or modified work schedules, reassignment to a vacant position, acquisition or modification of equipment or devices, appropriate adjustment or modifications of examinations, training materials or policies, the provision of qualified readers or interpreters, and other similar accommodations for individuals with disabilities.

Accordingly, an employer could possibly deny a transportation or public safety job (e.g., airline pilot, bus driver) to a worker with a genetic marker for heart disease. The genetic screening that would identify the marker for heart disease could take place only after a job offer has been made and before employment duties begin. The job offer may be conditioned on the results of such an examination provided that all new employees are subjected to the same examination and the confidentiality requirements of the Act are observed. If a genetic problem is discovered, the employer may have to offer reasonable accommodation in the form of a desk job or other assignment where the possible heart problem would not affect public safety.

As to whether ADA permits or prohibits genetic monitoring and screening, Title I section 102 subsection (c)(2) prohibits preemployment medical examinations or inquiries designed to uncover information about disabilities unless the inquiry is designed to reveal the applicant's ability to perform the job-related tasks. Strict interpretation of this language means that a covered entity may not require a medical examination unless that examination is job-related and consistent with business necessity. An employer's attempt to lower costs by reducing its contribution to group health insurance premiums by detecting increased risk of experiencing diseases or conditions based on genetic factors would appear not to be 'job-related' or a' 'business necessity, ' no matter how advantageous such actions might be for the employer. The job-relatedness of the medical examination or inquiry and consistency with business necessity requirements would

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seem to preclude remote cost-cutting measures aimed at weeding out genetically costly employees (11).

Employment safety and health issues are perhaps in a different class to the extent to which a disabled individual under ADA poses a threat to the workplace and co-workers or to the general public. Threats caused by that individual's disability may not be afforded protection under ADA. Increased risk of disease--even if contagious—would have to present a clear and present danger rather than a simply statistically greater likelihood of ultimate disease contraction (11). ADA appears to prohibit genetic screening as a part of prohibited medical examinations and genetic information obtained by means of a prohibited inquiry.

CONFIDENTIALITY AND PRIVACY ISSUES

Beyond the role of occupational health and safety regulation, common law rules regarding confidentiality and privacy are relevant to genetic monitoring and screening in the workplace. These include the right to:

- confidentiality of test results;
- have information forwarded to other health care personnel;
- have information regarding implications for immediate family;
- know test results, the right to have a copy of test results;
- accuracy of test results; and
- refuse testing.

Right To Confidentiality

There are four elements of the common law cause of action for public disclosure of private facts:

- the facts must be disclosed to the public;
- the facts disclosed must be private;
- the facts made public must be highly offensive and objectionable to a reasonable person of ordinary sensibilities; and
- the public must not have a legitimate interest in the information.

It can be argued that employers who learn of their employees' genetic defects and susceptibilities through genetic screening in the workplace could have a duty to keep this information confidential and not disclose it to anyone absent express consent of the employee. Failure to do so could result in a charge of invasion of privacy brought by an employee against an employer. There is also the argument that genetic information may not be considered highly offensive and objectionable as would, for example, some diseases. Under this line of reasoning, genetic information may not be subject to the same constraints with respect to privacy and confidentiality as some other conditions.

The existence of a right to confidentiality depends on the relationship between the test subject and test administrator. When a patient and physician are involved, an obligation of confidentiality can generally be found to flow from physician to patient. Since physicians must necessarily be entrusted with communications of the most personal and private nature in order to effectuate proper diagnoses and cures (70), the confidentiality obligation has been part of ethical codes for physicians since Hippocrates. In 1984, the American Medical Association's (AMA) Judicial Council reaffirmed the Hippocratic Oath in publishing its most recent statement on confidentiality which says that the information disclosed to a physician during the course of the relationship between physician and patient is confidential to the greatest possible degree. The patient should feel free to make a full disclosure of information to the physician in order that the physician may most effectively provide needed services. The patient should be able to make this disclosure with the knowledge that the physician will respect the confidential nature of the communication. The physician should not reveal confidential communications or information without the express consent of the patient, unless required to do so by law *(5).*

Ethical standards of the medical profession did not have legal counterparts in common law. Early English law indicated that neither a voluntary vow of secrecy nor the privacy of the relationship alone were sufficient to establish a privileged communication (98). Under common law, a physician could disclose in court and elsewhere a patient communication. In jurisdictions, such as Georgia, that still follow the common law approach, the result is a harsh one for patients.

Evolving case law in most States, however, has come to recognize a right of patients to sue when a physician has made a disclosure of medical informa-

BERRY'S WORLD JIM BERRY



"Pity! *You, yourself, tested out well. Your GENES didn't make it."*

Photo credit: United Media

tion about the patient without the patient's consent. The route taken toward recognizing the physician's duty to maintain confidentiality has varied. In some States, courts have pointed to the Hippocratic Oath and AMA's statement to support the common law requirement of confidentiality between doctor and patient. Other States point to such a policy by referring to statutory enactments such as the testimonial privilege statutes or the confidentiality provisions of the physician licensure and discipline statutes.

Under the testimonial privilege statutes in virtually every State, physicians may not testify in court about a patient's condition unless the patient has either consented to the testimony or waived the right to consent. Only eight States lack testimonial privilege statutes regarding physicians and patients (Alabama, Connecticut, Florida, Kentucky, Maryland, Massachusetts, New Mexico, and South Carolina). Numerous cases have based a duty not to disclose on the State testimonial privilege statute.

Twenty States protect the relationship between a patient and his or her physician by providing that the disclosure of confidential information by the physician is a ground for revocation of the medical license or other disciplinary action. In an Ohio case, for example, the plaintiff sued an insurance company for fraudulently inducing his physician to divulge confidential information obtained from the plaintiff in the course of the doctor-patient relationship (40). The court used three indications of public policy—the medical profession's code of ethics, the statutory discipline provisions subjecting physicians to discipline for breach of confidentiality, and the testimonial privilege statute-to hold that a patient can recover damages from a physician for unauthorized disclosure concerning the patient.

Several grounds on which testimonial privilege can be based have been described (74). Many States recognize a testimonial privilege that permits a patient to prevent a physician from divulging medical information in court. State medical licensing statutes may also create a cause of action. In California, there is statutory protection in the form of the Confidentiality of Medical Information Act (Cal. Civ. Code sec. 56) which provides for recovery of compensatory damages, punitive damages up to $3,000, attorney fees up to $1,000, litigation costs, and criminal penalties for unauthorized disclosure of medical information.

There may also be a cause of action for unauthorized disclosure of medical data based on the breach of a contractual relationship. The obligation of the physician to maintain confidentiality of medical information can be seen as part of a contractual obligation to the patient. Physicians also have a responsibility to maintain confidentiality as part of the generally accepted standards of professional conduct in medicine.

A problem may arise, however, for subjects of genetic monitoring or screening in employment situations. In these cases it could be argued that the physician is acting as an agent of the employer and not as the patient's representative. Moreover, in many instances, the testing may be done by a nurse or medical technician, with no physician involved at all. The legal obligations of a medical professional in these circumstances are not clear, but many courts have held that there is no physician-patient relationship (74). In a Michigan case (7 1), the court held that a physician who examines a patient for a purpose

other than diagnosis or treatment for the benefit of someone other than the patient does not owe a duty of care that would subject him to liability for malpractice.

Even more problematic is the status of a genetic screening subject who is a job applicant. In this case, the subject lacks even the responsibilities created by the employer-employee relationship to rely on for legal support. Other sources of law must be looked to for protection and will be discussed later.

One formidable obstacle that employees will face is the right of their employer to see their test results. When the employer has provided the physician and paid for the procedure, there is little legal basis for asserting that it should be denied access to the results. The physician's primary duty in this situation is to the employer who hired him. There are few legal restrictions on employer access to workplace records and, in many instances, workers are unaware of the disclosures (74). The OSHA standard for access to medical records does not limit an employer's access but merely guarantees employee access.

One source of limited protection for employees is contained in the Code of Ethics for Physicians Providing Occupational Medical Services (6,74). The confidentiality obligations of physicians are described in strong terms, limiting disclosure of information to requirements of law or overriding public policy. The code also prohibits disclosure to other physicians unless requested by the subject "according to traditional medical ethical practice. ' The information that can be provided to the employer is limited to "counsel about the medical fitness of individuals in relation to work.' Employers may not be given "diagnosis or details of a specific nature. '

While the code lacks legal authority, it does establish the accepted standard for medical practice in this field, lending possible support to a claim for malpractice for unauthorized disclosure of confidential medical information. The effectiveness of this provision, though, would depend on the circumstances. Genetic screening results indicating susceptibility to the effects of a workplace toxin would, presumably, be reported to the employer as a lack of fitness for a particular job because of medical sensitivity.

An employee or a job applicant who is subjected to genetic monitoring or screening must assume that there will be at least some employer access to the results. The question then becomes protection against disclosure beyond the immediate employment setting. In that context, the worker can rely on two sources of law. For release of accurate information, a worker can look to professional and contractual obligations of the physician and employer. For disclosure of false or unreliable information, a worker may look to a claim for defamation.

Protection against release of information to the general public is, for the most part, provided. Some States, however, require reporting of individuals with certain serious communicable diseases, such as AIDS, but a genetic defect is not a communicable disease and is unlikely to fall in this category.

There is an exception in California to the confidentiality rule for psychotherapists, who have a duty to warn persons in immediate danger of harm from a psychotherapy patient (87), but genetic monitoring and screening results are not likely to reveal an immediate risk to others. It is, of course, likely that a genetic defect is shared by other family members and that it can be passed onto offspring. Disclosure in these circumstances, however, is generally a matter of patient discretion and not a matter of legal obligation of the physician. Unlike the case of a communicable disease, there is no immediate threat of harm to others.

The obligations of an employer who releases employee medical records without authorization are less clear. In California, such disclosure triggers statutory civil and criminal penalties, as discussed. Furthermore, the California Constitution explicitly guarantees a right to privacy (Cal. Const. art. I, sec. 1). In other States, a worker could rely on a common law claim for invasion of privacy.

Disclosure of inaccurate genetic monitoring or screening information can be seen as a form of libel. The key element of a libel claim is that the information divulged is untrue, so such a claim would be invalid when accurate test results are released. If test data are incorrect, though, libel can be found.

A question arises as to the libelous nature of test results that are accurate but subject to possible misinterpretation. This is an important issue for genetic monitoring and screening information,

which is new and could be misunderstood by those receiving it. A direct analysis of a subject's chromosomes is likely to be reliable in terms of the presence or absence of a particular gene. Whether the gene always expresses itself through a particular trait, however, may be subject to considerable individual variation. A test result, for example, may reveal that a worker has an undesirable gene that may predispose the worker to susceptibility to toxic harm. Environmental or countervailing genetic factors, though, may negate this susceptibility. A medical report that includes the test result will be accurate in terms of whether the subject has the gene, but might bean unreliable predictor of whether the worker will develop the disease in question.

It is unclear whether disclosure of such technically accurate information could constitute libel. There may be an analogy to other kinds of tests whose validity is subject to question (e.g., intelligence tests). In general, it is unlikely that an employer or physician would commit libel for simply reporting the test result. Any conclusions based on it that are communicated to others, though, might be suspect if careful qualifications are missing.

Another means of legal relief for patients whose medical information has been disclosed is a suit for tortious public disclosure of private facts. Such a cause of action is part of the 20th century common law protection of privacy. Common law privacy action protects medical records because such records involve intensely personal facts, which when disclosed are generally disclosed to an individual (a health care professional) and not to the public. In an Alabama case, the court recognized such an action, stating that unauthorized disclosure of intimate details of a patient's health may amount to unwarranted publicization of one's private affairs *(42)*. Neither the public nor the employer has a legitimate interest in knowing each and every detail of an employee's health. Certainly, there are many ailments about which a patient might consult a private physician, but which have no bearing or effect on one's employment.

The Supreme Court in *Whalen v. Roe (97)* recognized that the physician-patient relationship falls within a constitutionally protected zone of privacy. Plaintiffs in *Whalen* challenged a New York law that required physicians prescribing certain drugs to report the drug name, dosage, pharmacy, and patient's name, address, and age to the State Department of Health. The law was enacted to address a concern that prescription narcotic drugs were being diverted into unlawful channels either by stolen or multiple prescriptions, unauthorized refilling of prescriptions, or over-prescribed medications. While the Court recognized the need to protect the privacy of the physician-patient relationship, it held that the particular disclosure requirement did not violate a patient's constitutionally protected privacy right because the information was securely stored, the information was not publicly disclosed, and an individual was not deprived of the right to acquire and use the medication. The Court recognized "the individual's interests in avoiding disclosure of personal matters." However, the Court distinguished between an individual's interest in autonomy and an individual's interest in nondisclosure: the former clearly being protected by the Constitution (97).

Finally, at least five States--California, Montana, Rhode Island, Utah, and Wisconsin-maintain a more direct means of protecting the patient from unauthorized disclosures of medical information by adoption of statutes that specifically protect such information (Cal. Civ. Code 56.10- 56.16; Mont. Code Ann. 50.16-525- 50.16-553; R.I. Gen. Laws 5-37.3-1 to 5-37.3-11; Utah Code Ann. 63-2-88; Wise. Stat. Ann. 146.82).

At least three States have specific legislation addressing genetic health care information. In Maryland, genetic information is targeted as warranting protection. Under a Maryland statute, information collected in hereditary disorder programs must be kept confidential (Md. Health-Gen. Code Ann. 13-109(c)). Rhode Island and Utah laws protecting privacy of genetic or general health care information have special provisions providing for compensation of patients when confidentiality is breached. Rhode Island law provides that a patient can collect actual and exemplary damages and, at the discretion of the court, attorney fees maybe awarded when a health care professional breaches the confidentiality act. Under the Utah Information Practices Act, if State officials improperly and intentionally disclose health care information, the patient can receive exemplary damages of $100 to $1,000 (Utah Code Ann. 63-2-88). Even if State law does not specifically mention compensation for the patient, the existence of statutes could serve as basis for a private lawsuit claiming breach of confidentiality.

There is concern about whether doctor-patient confidentiality extends to other types of health professionals. Some States have enacted confidentiality statutes that apply to communications between patients and any health care provider or officer, employee or agent of a health care provider or facility (R.I. Gen. Laws 5-37.3-.3(a)). Such would be the case if paramedical health care providers did genetic monitoring and screening in the workplace. In other jurisdictions, courts have noted that the rationale for creating physician-patient privilege to protect the patient's right of privacy justifies extending the privilege to cover people assisting physicians, even in the absence of a specific statute so providing (101). The trend seems to be to extend the duty of confidentiality to include other health care professionals, which would mean that providers of genetic services who were not physicians would nevertheless be required to maintain confidentiality.

One could argue that no physician-patient relationship exists in the occupational health setting when the company-hired physician has not been chosen by the employee. When health examinations are a condition of employment, submitting to an examination by this physician maybe something an employee cannot refuse. Further, if no treatment is given, only health monitoring or screening, this, too, supports the lack of a physician-patient relationship. When, for example, a physician employed by an insurance company examines an individual for the purpose of insurance qualification, the physician owes no duty to the individual to treat or to disclose problems discovered during the examination (27). Physicians in these circumstances would still be expected to adhere to the standard of care for any health care rendered but may not be held to the traditional fiduciary duty that a traditional physician has to a traditional patient. The difficult question arises when the condition or disease discovered in the examination is one caused or exacerbated by conditions in the workplace environment. In that instance, it can be argued that a company physician does have an ethical and moral duty, if not a legal duty, to inform the employee-patient of any findings.

Duties of the Occupational Health Physician

Occupational health physicians evaluate the medical fitness of applicants and employees in the workplace. Occupational health physicians are different from private physicians in training, loyalties, and legal and ethical duties (75). When an occupational health physician undertakes genetic monitoring or screening of an employee or job applicant, there can be some question whether legal precedents protecting confidentiality in the physician-patient relationship apply. If the occupational health physician is hired by the employer, either on a contract basis or as a salaried employee, to do genetic monitoring or screening of other employees, it could be argued that the occupational health physician's first duty is to the employer and not to the test subject. If the employer is paying for the tests this, too, could support the argument that the employer is entitled to receive any test results. However, other legal precedents based not on fiduciary or contractual aspects of the physician/employer-patient/employee relationship, but on specific ethics codes or statutes applying to occupational health physicians, as well as more general precedents regarding tortious public disclosure of private facts or violation of a constitutional right to privacy provide a basis for holding occupational health physicians liable for unauthorized disclosure of medical information about a job applicant or employee. Occupational health physicians are left then to balance patient privacy and confidentiality on the one hand with employer need-to-know on the other.

Occupational health physicians do not practice medicine in an ethics vacuum. The American College of Occupational Medicine Code of Ethical Conduct (formerly American Occupational Medical Association (AOMA)) specifies that occupational health physicians should maintain confidentiality. Even with respect to disclosures to employers, it cautions that occupational health physicians should provide bottom-line information, not specific details. The relevant provision states that: "Physicians should treat as confidential whatever is learned about individuals served, releasing information only when required by law or by overriding public health considerations, or to other physicians at the request of the individual according to traditional medical ethical practice, and should recognize that employers are entitled to counsel about the medical fitness of individuals in relation to work, but are not entitled to diagnoses or details of a specific nature" (6). This code may provide the policy basis for recognition of a legal duty of occupational health physicians to maintain confidentiality, just as the Hippocratic Oath and the AMA statement have



General:

- Care of work-related illnesses and injuries
- Follow-up treatment coordinated with your personal physician
- Occupational Rehabilitation Therapy
- Respirator fit testing
- X-rays
- Medical laboratory testing (eg. cholesterol risk factor analysis, throat cultures)
- immunizations
  - Allergy shots
  - influenza vaccine injections
  - Immunizations required for company travel
- Blood pressure screening (walk-in)
- Non-prescription cold medications (walk-m)
- Percent body fat measurements



Tests/Exams

- Chemical Specific Periodic Medical Exams (offered to certain groups of employees with potential exposures to regulated chemicals or physical agents)
- Health Exam (offered every two years as a supplement to your personal physician's physical exam)

  Included:
  - Health history
  - Blood pressure
  - Height and weight
  - Blood and urine analysis (drug testing is NOT included in these exams)
  - Hearing test
  - Eye pressure testing for glaucoma (employees over 40 years)
  - Tests for lung capacity
  - Stool exam for blood (ernployees over 40 years)
  - Vision testing
  - Chest X-ray
  - Electrocardiogram
- All non-emergency tests and examinations should be by appointment

Health Education

- Health promotion program which includes presentations on a variety of topics including:
  - CPR Training
  - Nutrition
  - Stress
  - First Aid
  - Hypertension
  - Shift Work
  - * Eyes
  - Poisons
  - Coronary Risk Factors
  - * AIDS
  - * Basic First Aid
  - Computer Terminals
  - Cancer Prevention (Breast Self Examination
  - Ergonomic Evaluation
  - Hearing Conservation
  - Sports Injuries
  - * Back Injury Prevention
  - Substance Abuse Intervention
  - Hypothermia
  - Hyperthermia
- * Exercise Classes
- Brochures on a Variety of Topics



Counseling

- Assistance for lifestyle changes such as drinking, weight loss and smoking cessation
- Employee Assistance Program
- . Medical consultations
- Pre-placement counseling
- Pregnancy in the workplace counseling

Photo credit: The Dow Chemical Co., Michigan Division

A pamphlet describing a medical department's programs.

provided a basis in some States for judicial recognition of a duty on behalf of private physicians not to disclose. On the other hand one commentator has pointed out that the AOMA use of the word "individual' in the code rather than 'patient' is an attempt to make the occupational health physician-patient relationship not a traditional doctor-patient relationship (73).

The need for protection of health care records in the hands of employers has been recognized by legislatures. Statutes in Connecticut and California specifically protect confidentiality of medical records obtained in the course of employment (Corn. Gen. Stat. Ann. 31-128f; Cal. Civ. Code 56.20 (a)(c)). Public employers in Wisconsin have an obligation to maintain confidential records of work-related injuries and illnesses (Wise. Stat. Ann. 101.055(7)(a)). A Montana health care confidentiality statute could also be read to include occupational health physicians. It covers even those health care professionals who merely diagnose (Mont. Code Ann. 50-16-101 *et seq.). The* preamble to the statute states that persons other than health care providers obtain, use, and disclose health record information in many different contexts and for many different purposes. It is the public policy of this State that a patient's interest in the proper use and disclosure of his or her health care information survives even when the information is held by persons other than health care providers (Mont. Code Ann. 50-16-101-502(4)).

Rhode Island law protects confidentiality of health care information about a "patient," even when that information is in the hands of third-parties such as employers. However, information obtained outside of a doctor-patient relationship through genetic monitoring or screening "arguably" would not be considered information about a "patient" (R.I. Gen. Laws 5-37.3-4(a)). Accordingly, Rhode Island protections would only cover more traditional health care information (e.g., information from an employee's personal physician about the employee's genetic status) that makes its way to an employer's files.

In Florida, employees of the school systems are guaranteed confidentiality of their medical records except that a hearing officer or panel can have access to the records at a hearing on the competency of the employee (Fla. Stat. Ann. 231.291(3)(a)(5)).

In Connecticut, the law protecting the confidentiality of employee medical records has an exception allowing dissemination of information pursuant to terms of a collective bargaining agreement. Thus, employees or unions may be able to obtain information about health care risks to the employee population as a whole in order to bargain for better health and safety standards (Corn. Gen. Stat. Ann. 31-128f').

Various statutes protecting confidentiality of health care records in the workplace might be used as the basis for a private suit against an occupational health physician or employer for breach of confidentiality. There have been no such cases brought so far. The occupational health physician's or employer's duty to an employee who is a union member may also be created by terms of the collective bargaining agreement. Thus, an employee might bring a claim for violation of privacy under the bargained labor agreement. Also, as is the case with physicians generally, occupational physicians or employers could be held liable for tortious or unconstitutional invasion of privacy in disclosing confidential information.

COLLECTIVE BARGAINING CONCERNS

NLRA sets forth a relatively complex scheme governing relationships of employees, labor organizations (unions), and employers engaged in businesses affecting interstate commerce (29 U.S.C. 151 *et seq.).* Implementation of workplace genetic monitoring and screening programs implicate NLRA provisions from several perspectives.

The Act allows employees to organize unions and negotiate with employers over so-called "mandatory subjects of bargaining' '-i.e., wages, hours, and other terms and conditions of employment (sec. 8(d) of the NLRA). NLRA also governs the relationship between individual employees and their unions by stating that unions must "make an honest effort to serve the interests of all. . . members [of an appropriate collective bargaining unit], without hostility to any." Such efforts do not preclude unions from entering into agreements with employers that have unfavorable impacts on some employees in the appropriate collective bargaining unit (3 1).

The Duty To Bargain Over Genetic Monitoring and Screening Programs

As employment conditions, safety and health matters have long been recognized as mandatory subjects of bargaining (61). The National Labor Relations Board (Board or NLRB) has ruled that mandatory subjects of bargaining include fitness-for-duty physical examinations including medical testing (51) and thus, has set the precedent for the inclusion of genetic monitoring and screening of current employees as mandatory subjects of collective bargaining.

Matters germane to the working environment are considered mandatory subjects unless they affect an employer's ability to exercise entrepreneurial control. To the extent genetic monitoring and screening programs are designed to assess either an employee's continued fitness to safely perform the work or an employee's ability to safely perform different work without affecting health, they are material changes in the employment relationship. As such, they are subject to bargaining insofar as they implicate both job security and disciplinary consequences in the event the employee refuses to submit to them (50,51,72). Such tests cannot be fairly construed as cutting to the core of an employer's ability to exercise entrepreneurial control of its business.

It now seems clear, however, that preemployment genetic screening of job applicants will not be considered a mandatory subject of bargaining. The seminal case on this issue is *Allied Chemical & Alkali Workers of American Local No. 1 v. Pittsburgh Plate Glass Co. (4). In* this case, the Supreme Court held that conditions applicable to retirees, as nonemployees, are subject to union bargaining if they "vitally affect" current employees. The Court, however, ruled that in this case the retirement benefits at issue lacked a sufficiently vital effect on existing employees. Thus, the contours of effects sufficiently "vital" to current employees are unclear. Undoubtedly, resolution of the preemployment drug testing questions by NLRB and the courts will have a heavy bearing on the issue of genetic screening of applicants.

Relying on *Allied Chemical, NLRB* has ruled that drug testing of applicants for employment is not a mandatory subject of bargaining (83). Although the courts have not reviewed this ruling, it can be expected to stand. The analysis used by the Board would suggest that it would not regard genetic testing differently than drug testing as applied to applicants (89).

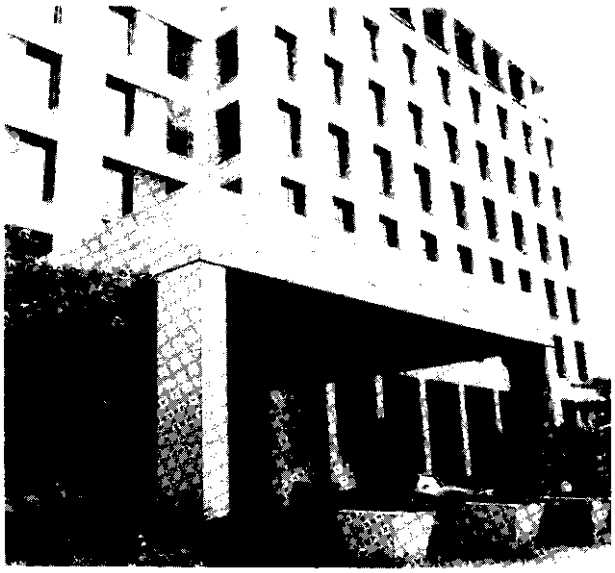


Photo credit: Gianna Bosko

Headquarters of the American Federation of Labor and Congress of Industrial Organizations, Washington, DC.

If NLRB and the courts ultimately decide that unions have a right to negotiate preemployment conditions, it might logically follow that this right carries with it the corresponding duty to fairly represent the interests of applicants. This question, however, has yet to be addressed.

The duty to bargain in good faith recognized in sections 8(b)(3) and 8(a)(5) of NLRA also includes corresponding duties of unions and employers, respectively, to provide on request information relevant to the subject of negotiations (23,63). For example, if an employer seeks to negotiate a change, the union must be given access to information in the employer's possession supporting its proposals. In terms of proposed implementation of genetic monitoring and screening requirements, the union would have the right to receive information such as the scientific literature the employer used in developing a testing proposal and data on known workplace exposures to chemicals that may be implicated by that testing proposal (63). It is important to note that this duty to supply information on request extends beyond the conclusion of negotiations. On request, employers must provide unions with information

that is necessary to police the employer's compliance with a specific term of employment such as genetic monitoring or screening as well as the collective bargaining agreement as a whole (60).

Scope of the Duty To Bargain Over Genetic Monitoring and Screening Programs

A threshold determination that genetic monitoring and screening are mandatory subjects of bargaining under section 8(d) of NLRA leads to a duty to bargain initial implementation and subsequent changes only if the union has not otherwise waived its right to bargain. Employers may implement a change affecting an area subject to bargaining if they have negotiated the provision in good faith and those negotiations resulted in an impasse (62,86). At that point, the union is free to use its economic weapons—including the strike. On the other hand, employers may not implement a proposal if such a change represents a modification of an existing collective bargaining agreement. Section 8(d) of NLRA squarely prohibits such unilateral midterm modifications. Hence, a collective bargaining agreement that defines the contents of permissible physical examinations and does not include genetic monitoring or screening, or permits such testing with limitations, would probably serve as a bar to an employer's ability unilaterally to implement such testing or modify it during the term of the collective bargaining agreement.

Collective bargaining agreements may, however, contain waivers by the union of its statutory rights to bargain over mandatory subjects during the term of the agreements so long as such waivers are "clear and unequivocal.' Such waivers are not to be inferred lightly. The contract language relied on must be specific or the bargaining history of that language must be such that it can be concluded that the union "consciously yielded." Broad, so-called management rights clauses have been regarded by NLRB's General Counsel as not permitting unilateral imposition of drug testing (55). A similar position could be anticipated with respect to genetic monitoring and screening.

While such waivers turn on the totality of circumstances, including bargaining history and wording of the clause at issue, it is fair to assume that imposition of genetic monitoring or screening of current employees may well be regarded by NLRB as a significant change requiring a particularly clear and unequivocal waiver even in the face of a history of more "routine" forms of workplace medical surveillance. The very controversial nature of genetic monitoring and screening, like that of drug testing, may well dictate a heightened standard of waiver by contract or by past practices regarding medical surveillance.

Union inaction is considered another form of waiver. An employer meets its duties under section 8(a)(5) of NLRA by giving the union notice of its intended changes and thereby giving the union an opportunity to negotiate. If it is otherwise permissible to implement the change, the employer may institute it if the union fails to request negotiations in a timely fashion (20,44). Hence, an employer would not violate NLRA if it announced its intention to use either genetic monitoring or genetic screening of either current employees or applicants, and the union, by its silence, acquiesced in the change. This, of course, assumes that the intended change was not presented to the union as a *fait accompli* over which bargaining would be fruitless (19,66,82).

Once it is assumed that a duty to bargain genetic monitoring and screening exists, absent waiver, that duty encompasses an obligation to meet and discuss all aspects of the monitoring and screening process itself as well as its effects, including the uses to which it can be put and protections for affected employees.

While either party could insist to the point of impasse on the use or abandonment of a specific test, it is fair to assume that impasse would be far more likely in situations where screening is used to predict tendencies towards disease that bear little or no relationship to occupational exposures. The lack of immediate relationship to present ability to perform or to possible deleterious effects of workplace exposure could be regarded by the union as strong reason to adamantly oppose the screening. On the other hand, resistance by the union might be less in the case of tests that predict susceptibility to occupational agents such as dusts or fumes. This would include screening for homozygous serum alpha antitrypsin deficiency to assess increased risk of emphysema in workers exposed to dusts. In all probability, discussions of such screening would focus on the accuracy of the tests and the employer's responses thereto.

Virtually all aspects of a mandatory genetic monitoring and screening proposal would be subject to negotiation. Regardless of whether proposed tests

were to be used for applicant screening, employee screening, or employee monitoring, the parties would be required to discuss test selection. In this context, the union would be free, and indeed duty bound to explore with the employer the validity of the test as applied to the workplace. The employer would then be required to demonstrate why, in its opinion, the proposed test furthers its interests in maintaining employee health and safety.

Another area of negotiations that could apply to genetic screening of job applicants, and genetic monitoring or screening of current employees would be the weight accorded test results. In this context, the predictive and diagnostic value of tests would be significant. If the test detected genetic changes or abnormalities that bore on an employee's or applicant's present ability to work, such workplace relevance would support hard bargaining by employers and acquiescence by unions without fear of violating a duty of fair representation. On the other hand, if such a test bore little relevance to present job fitness and was, at best, an unspecific predictor of potential, future ill effects, both the employer and the union would be effectively constrained from agreeing to monitoring and screening that violated State or Federal handicap antidiscrimination laws. Within these two extremes, unions and employers could use their economic powers (strike and lockout, respectively) to "convince' each other of the workplace relevance, or lack thereof, of a particular test as well as to determine the weight it would be given in other job-related matters.

Even if a particular genetic screening program could be said to have sufficient workplace relevance, unions could be placed in a difficult position with respect to their duty of fair representation if organ-specific genetic conditions disclosed by the screening occurred significantly more frequently in identifiable ethnic groups. Such is the case with screening for sickle cell disease, G-6-PD deficiency, and thalassemia (76). If responses to such testing would have a disparate impact on a particular ethnic group, a union's duty to fairly represent all bargaining unit members would be heightened (31,88). Absent a cogent showing of business necessity, it could not safely agree to such genetic screening.

Another bargainable element of a proposal regarding genetic monitoring and screening would be access to test results. A variety of existing laws and regulations already provide strict rules governing the release of medical records. However, in order to carry out their obligations to protect the safety and health of bargaining unit members, unions could (under section 8(a)(5) of NLRA) insist on receiving summary data regarding genetic monitoring and screening that did not disclose individual employee results (29 CFR 1910.1001; 20 CFR 1910.1017).

Perhaps the most sensitive aspects of negotiations regarding genetic monitoring and screening would be those focusing on effects of a test result that would disqualify employees from their existing jobs or preclude them from moving to a different, and perhaps, higher paying job. Both forms of disqualification would implicate existing wage and seniority provisions in collective bargaining agreements. Unions would, therefore, be obligated to explore in depth effects of genetic monitoring and screening with employers.

Presumably, genetic monitoring or screening of employees in connection with their current jobs could result in discovery of changes or traits, respectively, that would require removal from the presumed deleterious workplace exposure. If this could be accomplished, unions could insist in bargaining that those changes be implemented before the job status of an employee is adversely affected. Employers may insist, or the circumstances may dictate, that the only "safe" alternative is removal of an employee to a job free from the deleterious exposure. If such a job existed, questions would have to be resolved as to whether an employee so disqualified could use seniority to displace (bump) a junior employee or whether an employee could only use seniority to claim available open jobs. In either case, one result could be no available job which an employee could safely perform. Hence, the parties would have to address the issue of benefits available for medical discontinuance (termination). Another result could be movement to a lower paying job. In such circumstances, the parties would have to explore the possibility of maintaining an employee's former rate of pay for some fixed period of time or perhaps permanently (so-called red circling).

Genetic Monitoring and Screening Refusals

Employee refusals to submit to employer-required genetic monitoring and screening fall into two categories, namely "concerted" refusals of one or more employees and individual refusals. Explora-

tion of any "rights" to refuse genetic monitoring and screening under NLRA requires separate analyses of these two types of refusals with the assumption that the employer has otherwise complied with its bargaining obligations.

Section 7 of NLRA gives employees the right to engage in "concerted activities for the purpose of collective bargaining or other mutual aid and protection" (e.g., the strike). This right to strike is not, however, unfettered. Otherwise lawful strikes may lose the protection of NLRA under certain circumstances.

An individual's refusal to be tested at a unionized or nonunionized workplace, however, may not be protected by NLRA unless the action is an integral part of group activity-past or present. Even then, such refusals may be regarded as concerted, yet unprotected, if they violate an express or implied no-strike obligation.

Arbitral Review

Genetic monitoring and screening requirements would, at some point, typically be subject to review by arbitrators under arbitration provisions in collective bargaining agreements. This is the preferred method for dispute resolution in organized workplaces to avoid strikes and lockouts. In the wake of presumptions favoring the arbitrability of labor disputes flowing from the so-called "Steelworker Trilogy,' it is fair to assume that many disputes surrounding workplace genetic monitoring and screening would be resolved by arbitrators (93,94,95).

Genetic monitoring and screening requirements implemented under broad provisions permitting employers to take "reasonable measures' to protect health and safety can be challenged as to their reasonableness (9,100). Indeed, even absent such express management rights, arbitrators would typically infer a reserved management right to promulgate rules and regulations to ensure employee safety and health and would review such rules and regulations under a standard of reasonableness (26).

NLRA Preemption of Common Law Torts

Drawing from recent experience involving workplace drug testing programs, it is fair to assume that employees covered by collective bargaining agreements may seek to bypass contractual grievance and arbitration procedures by filing suits against their employers in State or Federal courts alleging violations of tort laws. Torts such as intrusion on seclusion, invasion of privacy, defamation, and intentional (or negligent) infliction of emotional distress could be alleged (34,77). Such suits may, however, be preempted under the strong Federal policy favoring arbitral resolution of workplace disputes implicit in section 301 of the Labor Management Relations Act. OSHA's development of medical records access requirements inspired controversy on several points, including trade secret protections, the use of unreasonable searches and seizures, and the right to access for representatives of employees (56).

USE OF GENETIC MONITORING AND SCREENING RESULTS IN EMPLOYMENT DECISIONS

Right of Employer To Use Monitoring and Screening Data in Terminating Employment

As in the case of the employer's right to medical examinations of employees, the right to use the results of medical tests in employment decisions is limited primarily by Title VII of the Civil Rights Act of 1964 and by the Rehabilitation Act of 1973. Common law rights in this area grow out of the doctrine of employment-at-will. This rule formed the basis for most employment relationships, absent an explicit contract between the parties, and gave the employer virtually unlimited authority to terminate the employment relationship at any time (76).

The doctrine of employment-at-will includes the right to refuse to hire an individual because of a perceived physical inability to perform the job (24) and the right to terminate employment because of a belief that the employee is no longer able to perform adequately (67). With respect to genetic monitoring and screening, this would mean that an employer could use either in any way, including personnel decisions. Even if test results were inaccurate or unreliable, the employer would be protected in basing employment actions on them.

In recent years courts have begun to erode the scope of the at-will doctrine by creating exceptions. While some courts have found contractual obligations that override the doctrine, the more commonly used exception is based on a tort of wrongful discharge founded on public policy considerations (59).

One such case that relied on a public policy exception to the employment-at-will doctrine has some relevance for genetic screening (68). The court held that an employee had a cause of action for wrongful discharge after he had been terminated for refusing to take a polygraph test, even though the State he was employed in, Pennsylvania, has a statute prohibiting such a requirement. In the absence of a remedy for the employee in the statute, the court ruled that he could sue under the common law public policy exception to employment-at-will. It was found that "Pennsylvania's anti-polygraph statute embodies a recognized facet of public policy" that would give rise to a cause of action for tortious discharge under Pennsylvania law, if refusal to take a polygraph test was the basis for the discharge (68). Under this holding, in a State with a statute prohibiting the use of genetic monitoring and screening, an employer would be constrained from terminating an employee based on refusal to take such a test. Had a statute on the subject not existed, however, it is not clear whether the court would have reached the same decision.

A New Jersey law based on atypical genetic traits, may create an even broader exception to the at-will doctrine for personnel actions based on genetic test results (NJ Stat. Ann. sec. 10:5-5(y)). This law appears to limit employers in taking any action including dismissal, based on genetic screening results that might have a discriminatory impact. A question might arise, though, concerning the use of monitoring. Chromosomal damage reflects harm to genetic material, but is this harm a genetic trait? An argument can be made that it is not, since the damage is likely to affect specific cells and not a change in the individual's genetic makeup. An inherited trait would not be at issue. Under this analysis, the New Jersey statute would not apply to genetic monitoring results.

Courts may react differently when genetic monitoring and screening results indicate occupational susceptibilities than when they suggest a higher risk for a nonoccupational condition. For example, employees genetically at risk for manic-depressive illness may never develop the condition. Whether they do or not may depend on nonoccupational exposures. In this case, the employer would be taking a personnel action based on a purely non-work-related factor. On the other hand, some employers are now excluding smokers on similar grounds. The ultimate effect on the employee may be speculative, since the expression of many genetic traits depends on environmental influences, and their ultimate expression may also be beyond the employee's control. This may appear to some judges to present a more compelling violation of public policy principles than a personnel action based on work-related health effects.

Even when a nonoccupational medical condition is present, however, a court may still decline to find a public policy exception to the at-will doctrine. In one case (17), a Federal appeals court upheld an employer's decision to discharge an employee with diabetes based on an adverse medical report. It is possible that many courts will find that employers have broad discretion to make medical judgments of the fitness of employees and that reliance on genetic monitoring and screening for this purpose does not violate public policy.

The weight of public policy arguments in favor of exceptions to the at-will doctrine for genetic monitoring and screening findings may also depend on whether a trait is more common in a specific racial or ethnic group. Exclusion based on such a trait raises issues under Title VII, since it could amount, in practice, to racial or ethnic discrimination. If a public employer were involved, this kind of exclusion could directly raise issues of equal protection under the Constitution. Because of the constitutional issues and profound public policy concerns raised by racial or ethnic discrimination, courts may be more likely to find a public policy exception to the at-will doctrine when genetic monitoring and screening touches on questions of discrimination.

Uses of Genetic Monitoring and Screening Data in Other Employment Actions

While exceptions to employment-at-will have grown to cover different grounds for dismissal, they have not been applied to other kinds of employment actions. Employers have few common law constraints in taking other actions, such as hiring, promotion, and placement. It has been observed that in the absence of a statutory protection, 'monumental changes in the at-will doctrine will be required before anything even approaching a good-cause standard can be applied to an employer hiring decision or promotion, transfer, work assignment, or other related matters' (76). In these other areas, OSHA regulations--e.g., the medical removal and



Photo credit: Earl Dotter

An auto painter in a spray booth.

rate retention rules for various hazardous substances, and statutes, including Title VII and the Rehabilitation Act—provide the only existing constraints on employer use of genetic monitoring and screening for personnel decisions.

It should be noted that Title VII may provide substantial limits on employer actions. In one case (103), the court considered the defendant's practice of excluding fertile women from certain jobs involving exposure to hazardous chemicals. The plaintiff claimed that this violated Title VII as discriminatory, and the defendant asserted that it was necessary to protect future offspring. The court placed a heavy burden on the defendant to justify the practice and ruled that it must demonstrate a business necessity for the practice by showing that within the scientific community there is sufficient opinion that female workers face a significant risk. Moreover, plaintiffs can rebut this defense by demonstrating that there are alternative employment practices available that would accomplish the same protection with a lesser differential impact. While a further discussion of the role of this case in extending Title VII protection to nontermination employment actions is beyond the scope of this chapter, it can be observed that Title VII can place significant constraints on health and safety employment practices that have a discriminatory impact (8). In a recent case (90), the Ninth Circuit upheld the employer's fetal protection policy. The case is pending before the Supreme Court.

Common Law Right to a Safe Workplace

As discussed earlier, employees have a right to a safe workplace under common law, as well as under the OSH Act. The obligation to provide such a workplace may be affected by the availability of genetic monitoring and screening data. It might be argued that the obligation to provide a safe workplace has been met if the workplace contains only employees who have met reasonable genetic standards. An employer might contend that a safe workplace has been provided, if, absent other safeguards, all of the workers have been screened and found not to be susceptible to workplace chemicals. It may be impossible, however, to show that no risk remains for the workers who are not susceptible to workplace chemicals. As one commentator points out, even if the most susceptible workers are removed from the workplace, the remaining workers may also face a serious risk (85).

According to one employer, perhaps the best approach is to improve the OSHA requirements for disclosure of workplace hazards to give current employees the opportunity to receive regular voluntary monitoring, to provide the information only to employees, and to allow the employees to make an informed decision about whether to accept new employment or continue working in an area where principles of assumption of the risk would reduce employer liability (assuming knowing and intelligent waivers are made by employees who have access to the information needed to make a responsible decision). Since employers are currently obligated to provide a workplace free from recognized hazards, employer liability should not be diminished by genetic monitoring, nor should employer responsibility be reduced merely because the employer's workforce has been monitored, and those individu-

als with genetic susceptibility eliminated from the workforce population (48).

The effects of genetic test data on the duty to provide a safe workplace are subject to considerable speculation, but a few observations can be made. As discussed, there appear to be few common law limits on an employer's right to use preemployment screening and to make hiring decisions at will. Even under the Rehabilitation Act or ADA, an employer can refuse to hire a handicapped individual when a legitimate business qualification is involved. If genetically susceptible job applicants can be screened out, employers may have an easier task of creating a safe workplace.

With regard to monitoring, though, the duty may be increased. If sophisticated new tests become available to detect preclinical harm, then unsafe workplaces could become easier to identify. Furthermore, employers may have a duty to use any reasonable test to ensure workplace safety. However, one commentator has pointed out that even if a common law duty existed, employees may not have any remedy (73). As with other legal issues discussed, workers, unlike job applicants, have legal protections and may see benefits from genetic monitoring and screening.

Right of Employee To Know Monitoring and Screening Results

Whether or not genetic monitoring and screening results are communicated to employers or to others, employees have an interest in knowing what they are. An employee, for example, may wish to take personal health precautions based on the results or may choose to decline employment that is revealed to be hazardous. An employee may use the results as the basis for a legal action, or may have a general interest in knowing information that may have personal significance. There are several sources of law available to compel such access.

First, there is the OSHA access to medical records rule, discussed above. This regulation is broad in scope, going beyond records maintained under specific OSHA toxic exposure standards, but only when exposure to certain substances occurs. Employees are also protected by common law obligations of physicians and employers concerning known hazards. Physicians have a duty to inform patients (but not necessarily applicants or employees) of diseases that are discovered (74). Massachusetts has a statute that requires an employee to be provided a copy of the medical report for employer-required exams (Mass. Ann. Laws ch. 149, sec. 19A (1976)). Several cases have found company physicians liable for failing to detect or to inform employees of illnesses such as lung cancer (12), Hodgkins disease (13), and tuberculosis (102).

Beyond medical information on an individual basis, employers have obligations to inform workers about workplace hazards. The obligation created by the OSHA hazard communication standard has already been discussed. Employers also have a common law obligation to provide safe working conditions (32). This includes a duty to warn about hidden dangers. In a California case, the court held that while an employer does not have a duty to discover whether an employee is fit for work, if the employer assumes this task, the employer is liable if it is performed negligently (21). This case could have clear implications for genetic screening. Should an employer decide to use a screening program, whether through the use of genetic or conventional tests, the employer must meet a reasonable standard of care. It may be the case that if the employer assigns an employee to a job for which the employee is genetically unfit, liability could ensue especially if the employee is never informed of the screening results.

The duty of physicians to inform patients of medical findings applies to job applicants as well as employees. The physician's professional responsibility in this regard is to protect the patient's health, regardless of employment considerations. The duty of employers to warn of workplace hazards, however, would not protect job applicants. If not hired, the screening subject cannot claim a need to know about hazards in the workplace. Subjects might want to know their test results, but absent a clear contractual understanding, they would have no rights in this regard.

Right of Employee To Refuse Genetic Monitoring and Screening

If monitoring and screening are performed in response to an OSHA standard, the employee is free to decline the test. The OSH Act does not give OSHA the authority to require employees to submit to medical examinations (OSH Act 6(b)(7); 29 U.S.C. 656(b)(7) (1976)). OSHA's regulations do not require employees to be tested against their will

or provide sanctions against employees who refuse testing. The rights of workers in relation to their employers regarding employer-instigated genetic monitoring or screening programs, however, are less clear. Several arbitrators have held that employers can require employees to take medical examinations as a condition of employment to enable the employers to meet safe and healthful workplace maintenance obligations (15).

If they wish to be hired, job applicants probably have few, if any, rights to decline. Their primary legal rights would be based either on Title VII of the Civil Rights Act of 1964 (42 U.S.C. 200e) (53) by asserting that the tests were discriminatory or on the Rehabilitation Act of 1973 or ADA by asserting that the tests were not job-related. Beyond that, there is no common law right to be considered for employment after refusing to submit to a preemployment qualification.

Applicants for public employment, as well as public employees, may have a remedy in the protection of the Fourth Amendment to the Constitution against unreasonable searches and seizures (58). While not every medical test is necessarily a search and seizure, the Supreme Court has held that taking a blood sample can constitute an unreasonable search (80). A number of cases limiting employer testing rights have relied on the obligation of government bodies to provide this protection (84).

The reasoning in this case could be extended to tests for markers of genetic diseases since the analysis of blood for genetic conditions could easily be analogous to the analysis of urine for traces of specific substances. This analysis could be upheld, if a government employer had a compelling need for the information, if the testing were done only once and with warning, and if the employee knowingly submitted to the testing in order to be transferred to a new job. A key question would clearly be what constitutes a compelling need for the information. An agency might argue, for example, that it needs to know whether an applicant for a job involving access to sensitive or secret information might develop a psychological condition, e.g., schizophrenia or manic-depressive illness, that would compromise the applicant's trustworthiness. It might also claim that knowing an employee's susceptibility to toxic exposures was needed to ensure protection from a job involving such exposures. Given the apparent willingness of many courts to permit government drug testing in the face of acknowledged constitutional concerns, it may be possible that these arguments could prevail for a genetic monitoring or screening program that involved a government job found to be sensitive enough.

A medical test to which the employee does not consent, then, can be a search if it is performed by the government. As a result, medical tests by public employers can only be performed on reasonable grounds and only with the subject's consent.

There are at least two situations in which this protection may extend to private employers (52). The first is when an employer's activities are closely intertwined with the government so that a government entity reserves the right to hire, promote, terminate, or reinstate employees. The second is when testing is government-mandated. It seems unlikely that an indirect government connection of a private employer (e.g., conducting government-mandated medical tests or receiving government funds) would be sufficient to establish government involvement in a genetic monitoring or screening program that would trigger constitutional protections against unreasonable searches and seizures.

An employee's only reliable recourse in asserting a right to refuse genetic monitoring or screening would be found in statutes that specifically prohibit use of such tests or related information for employment purposes. Three States—Florida, Louisiana, and North Carolina-have laws prohibiting discrimination based on sickle cell trait. A refusal to submit to a test for this trait would likely be upheld on public policy grounds.

Of particular interest is the New Jersey law discussed earlier banning discrimination based on any "atypical heredity, cellular or blood trait" (NJ Stat. Ann. sec. 10:5-5(y)). Such traits include sickle cell and Tay-Sachs. An employee could argue that this legislation forbids use of the results of genetic screening for employment decisions, so an employer may not require that genetic tests be administered as a condition of employment. In States without such laws, employees refusing to take genetic screening tests must look to other legal authorities for protection against dismissal.

Liability of Employer for Inaccurate Monitoring and Screening Results

As discussed, physicians may face malpractice liability for producing inaccurate genetic monitoring and screening results. Physicians may also face actions for libel if they disclose incorrect information about testing subjects. Another form of liability may exist if employers use inaccurate test results in making employment decisions.

It is unclear whether such a claim would succeed, unless the use of genetic information was already established to be against a State's public policy. With respect to other employment decisions, the common law offers little recourse. Job applicants would have even less in the way of legal protection. The employee's primary recourse would appear to be against the physician or other health professional administering the test for malpractice or libel.

The accuracy of test results is an area that may need further legal attention. Most discussions of genetic monitoring and screening have focused on the individual who is found to be genetically vulnerable. Different problems may arise for the individual who is incorrectly thought to be vulnerable but who is, in fact, not. Box 6-C illustrates some specific claims that might be available to employees.

Of equal concern are the false negatives, the individuals for whom genetic tests show an ability to withstand exposure to a toxic substance but who are actually susceptible to it. Based on genetic test results, these workers may be placed in contact with hazardous chemicals with which they would not otherwise wish to work. Their legal remedy would most likely be against the test administrator for malpractice and against the employer for negligent supervision of the test administration. These workers would, of course, be able to collect workers' compensation for their harm, but in some States this might not be a substantial recovery.

Workers with false negative test results are not directly protected by other sources of law. They would have access to their medical records under the OSHA rules, but they would likely have no reason to examine them for errors. The employer, moreover, may have fully complied with applicable OSHA testing standards. All medical tests leave some chance for mistaken results, even when properly administered. If there is a regular practice of producing incorrect test results, the employer might face liability for malpractice constituting gross negligence or for failure to provide a safe workplace. Isolated instances of inaccuracy, though, might be well within accepted testing standards. Additional legal remedies in this area may be needed (92).

JUDICIAL USES OF GENETIC MONITORING AND SCREENING DATA

Use *of Genetic Monitoring and Screening Data in Civil Liability Proceedings: Nature of Civil Suits for Workplace Injury*

One kind of civil suit related to genetic monitoring and screening has already been discussed. These are suits against physicians and others administering tests for inaccurate test results. These actions may be based on claims of malpractice or libel. The most profound effect of genetic monitoring and screening on civil liability, however, is likely to be on suits for harm from occupational diseases.

Direct tort actions against employers for workplace injuries are barred in every State by provisions in workers' compensation laws making them the exclusive remedy for workplace harm (49). In return for the right to this simpler form of compensation, workers' compensation laws prohibit employees from bringing actions for civil claims directly against their employers. Two routes around this ban are available. The frost is to use one of the limited exceptions to the prohibition that are available inmost States, as will be discussed. The second is to sue a third-party, such as a manufacturer who supplied a product that caused or contributed to the harm.

Third-party suits for toxic workplace harm have often relied on a claim that a defendant failed to warn of its product's hazardous properties. A court permitted such a suit against an asbestos manufacturer based on the defendant's knowledge and concealment of the dangers of asbestos (16). The lack of an adequate warning was seen in this case to make the product unreasonably dangerous.

Genetic Monitoring and Screening Data as Evidence in Occupational Disease Suits

Genetic monitoring and screening data may serve much the same role in tort suits for occupational

Box 6-C-Liability Issues

Inaccurate genetic monitoring and screening can lead to a variety of claims for injury beyond those for adverse employment actions:

- Emotional Distress—If an **employee tests positive** for a genetic defect, but the test result is incorrect, the resulting mental distress may be compensable. Such distress may be considered to be foreseeable to a physician and an employer. A physician in a New York case was held liable for erroneously informing a patient that she had tuberculosis, resulting in tuberculosis phobia In a New Jersey case, a court awarded damages for emotional distress in the context of exposure t o toxic substances. A false or erroneous test result may trigger anxiety or phobic reactions with debilitating effects on a patient, rendering the employer liable. The primary issue here is whether the exclusivity provisions of workers' compensation laws will bar such suits.
- ***Failure to Counsel--If*** a monitoring or screening result is accurate and the employee-patient is positive for a genetic ailment, and the employee-patient is notified a cause **of action may still exist for the distress caused** by the news. A duty may exist to provide both pretest and posttest counseling, since otherwise the employee-patient is not prepared to handle the news of positivity. Such a failure is likely to be viewed as intentional, so that a worker may be able to sue in spite of worker's compensation.
- Failure to ***Diagnose-If the*** **monitoring or** ***screening*** is positive but the employee is not fully notified of either the results or their full implications, then a diagnosis may be missed that could have led to positive medical intervention. The courts' reactions in such a situation have been quite consistent: compensation has been awarded for any mental distress and psychic injury suffered by the patient, and also for the "loss of a chance' of treatment because of the missed diagnosis.

SOURCES: Office **of** Technology Assessment, 1990, based on Barry R. Furrow, Widener University, Wilmington, DE, personal communication March 1990; *Ayers v. Township of Jackson, 106* NJ. 557, 525 A.2d 287 (1987); ***Kraus v.*** *Spielberg, 37 Mis.* 2d *29,236* **N.Y.S.2d 143 (1%2); R.L.** Willmore, "In Fear of Cancerphobia" *Toxics Law Reporter* 3(18):559-565, 1988.

diseases as in workers' compensation claims. The data can provide a crucial link in the causal chain between exposure to a harmful substance and manifestation of illness (30). Screening data can show that the worker was susceptible to the substance before exposure began. Monitoring data can show that biological harm developed as exposure progressed.

The issue of scientific uncertainty on causation has been an important one in much toxic tort litigation (14). In the litigation over the health effects of Agent Orange on Vietnam veterans, for example, the court considered the lack of scientific certainty concerning the consequences of exposure to this substance in approving the settlement of a product liability class action case (43). Similarly, another court (3) struggled with the issue of probability of causation in awarding compensation to some plaintiffs exposed to radiation from a nuclear test. Similar issues have arisen in many other cases involving allegations of toxic harm (14,22,35). If a plaintiff in such a case were able to document a link between individual injury and a toxic exposure, rather than relying on epidemiologica1 or animal studies, the plaintiff would have a much easier time demonstrating causation.

Genetic monitoring and screening data might also help workers to use the two exceptions to the exclusivity of the workers' compensation remedy described above. If an employer compiles test data showing that injury has resulted, the employer may have an obligation to reveal it to the worker (46). Failure to do so may result in liability to direct suit for intentionally concealing a hazard.

If the employer conducts the tests, the employer may be functioning in a dual capacity (76). Any negligence in test administration could then subject the employer to direct suit. This could include liability for harm from administration of the test itself, for negligently obtaining and using incorrect results, or for misusing correct results. Such suits could include those for malpractice (25) and libel described earlier.

New Kinds of Claims Based on Genetic Monitoring and Screening Data

It is possible that the act of conducting genetic monitoring and screening will create new responsi-

bilities for employers that result in new liabilities (65). Specifically, employers may be held to have a duty to take protective measures when medical harm is found. Failure to disclose positive medical results was one basis for finding intentional concealment of a workplace hazard (46). In an earlier case (45), a court found a specific duty of an employer to disclose to an employee a disease condition found in the course of a medical examination and to refrain from assigning him work that would aggravate the condition.

Employers performing genetic monitoring and screening may have an obligation to use the results for worker protection. By gaining information that creates the option of excluding susceptible workers through genetic screening, they may also take on a duty to exclude them. Similarly, by using genetic monitoring, employers may create a duty as well as an option to remove workers who show signs of toxic harm.

This could put employers who use genetic monitoring and screening in a double bind. They face constraints in using test results for hiring, firing, and other personnel decisions based on civil rights legislation, handicapped protection legislation, and exceptions to the at-will doctrine. At the same time, they also face constraints in not using the results when risks to individual workers are found. Additionally, genetic monitoring and screening results, as discussed, could make it easier for employees to file suits against employers for occupational diseases. The threat of these new liabilities could deter many employers from using the tests.

SUMMARY AND CONCLUSIONS

The real dilemma posed by emerging technologies for genetic monitoring and screening lies in their dual nature. They may prove to be invaluable tools for preventive medicine, keeping vulnerable workers from jobs that are almost certain to cause them harm, and identifying those in need of medical attention before serious illnesses develop. On the other hand, they may present a means for discrimination against workers who, through no fault of their own, are susceptible to the toxic effects of workplace chemicals. The likely role of the legal system in regulating these technologies, therefore, will not be straightforward.

The legal system will also face a challenge in making decisions in light of scientific uncertainty. No medical test is perfectly accurate, and genetic monitoring and screening are unlikely to be exceptions. Some healthy workers will undoubtedly be screened out of jobs that would cause them no harm, and some susceptible workers will likely gain inaccurate reassurance. Who should bear responsibility for such uncertainty no one can control?

The contribution that will be made by several important sources of law have been discussed. The exact role of each will depend on the nature of the tests that are developed and their application. While it is clear that many legal tools presently exist, it is probable that new ones will be needed as unexpected challenges arise.

Over the past several years, changes directly affecting the law in this area have been modest, perhaps because genetic monitoring and screening technologies have yet to see wide application. Two changes, however, stand out. The most important has been the statutes passed in a few States limiting the use of genetic information in employment decisions. In three of these States—Florida, Louisiana, and North Carolina-the laws are specific to testing for sickle cell trait. In New Jersey, though, a fairly broad measure was passed banning employment discrimination based on genetic traits. If this measure becomes a model for other jurisdictions, the adverse impact of genetic monitoring and screening results on employees and perhaps benefits, too, could be severely curtailed. The New Jersey experience will be interesting to observe as more genetic monitoring and screening tests become available.

The second important change is the proliferation of right-to-know laws at both the State and Federal levels. Primary among these in terms of its likely effect on genetic monitoring and screening is the OSHA hazard communication standard. This rule requires that employees be given access to considerable information on the toxic chemicals with which they work. It also gives employers broad discretion in deciding whether or not to use genetic data in determining the extent of a hazard. The degree to which genetic findings are used by employers to define hazards and by employees to make requests for information may provide an early indication of the role that genetic data will play in workplace safety activities.

Other workplace right-to-know provisions include the OSHA access to medical records rule, the

chemical labeling provisions of TSCA and Title III of SARA. Congress recently gave consideration to the High Risk Occupational Disease Notification and Prevention Act of 1987, which would have required access to information, including mandatory notification, for large numbers of workers exposed to toxic chemicals.

The recently enacted ADA—which extends a clear and comprehensive prohibition of discrimination on the basis of disabilities to the private sector-could potentially have considerable impact on the use of genetic monitoring and screening in the workplace. While the law protects individuals considered to have certain physical or mental impairments, it is unclear whether individuals having a marker or trait for a genetic condition would also be covered. As to whether it permits or prohibits genetic monitoring and screening, ADA prohibits preemployment medical examinations or inquiries designed to uncover information about disabilities unless they are intended to reveal the applicant's ability to perform job-related tasks. Thus, such a requirement would seem to preclude measures aimed at weeding out individuals having certain genetic characteristics.

Changes in the common law relating to workplace genetic monitoring and screening have been incremental over recent years. An increasing body of case law is developing, however, over employer screening for drug use and AIDS. It is likely that developments regarding privacy, confidentiality, and the right of employers to make employment decisions based on test results will continue to be rapid in these areas and will form the basis for court cases regarding genetic monitoring and screening. Of particular interest in terms of common law developments is the apparent continuing expansion of the public policy exception to the at-will doctrine. This trend may also play an important role in forming judicial attitudes toward employment decisions based on genetic monitoring and screening test results.

On the whole, it appears that Federal regulatory law as administered by OSHA is likely to have the most immediate impact on the use of workplace genetic monitoring and screening. OSHA has already addressed this area to a very limited and unspecific extent. It has also dealt extensively with related practices of biological monitoring and screening that will form a ready source of rules for genetic monitoring and screening. OSHA's rules on access to medical records and hazard communication are among the most directly applicable sources of existing law.

There is a need, however, to better anticipate the impact that genetic monitoring and screening technologies will have on occupational safety and health practices. As the primary authority in this area, OSHA would seem to be the most appropriate candidate for this role. In facing this issue, moreover, OSHA can draw upon the resources of NIOSH. NIOSH is charged with providing research and recommendations for OSHA regulatory development, and it is a well-respected source of these clinical and legal issues that workplace genetic monitoring and screening will present. Guidance from these agencies as technologies develop can serve a needed role in steering other sources of law, both judicial and legislative, through the challenges that genetic monitoring and screening will present.

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Chapter 7

Ethical Issues

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Chapter 7
Ethical Issues

The benefits of genetic monitoring and screening in the workplace lie in their potential to provide reliable, long-range predictions about the health risks that employees and job applicants face. These predictions could benefit employees, job applicants, and employers by allowing workers to avoid situations likely to cause illness, thereby maintaining their productivity and defraying health care costs. However, the workplace acquisition and use of this predictive knowledge raise important ethical questions. Under what circumstances, if any, could genetic monitoring and screening programs be required of employees or job applicants? Who should have access to test results? To what purposes may such knowledge be applied?

The rights and responsibilities of individual employees, job applicants, employers, and society in such programs are not clearly defined. Several values embedded in U.S. culture conflict with each other as a result of genetic monitoring and screening: autonomy of employees, job applicants, and employers; privacy and confidentiality of medical information; rights to a safe workplace; fairness and equality of opportunity; and efficiency in the workplace and industrial competition.

Ethical and legal issues surrounding genetic monitoring and screening in the workplace share common ground. Legal and ethical arguments often express common concerns and in some instances use common language. Several laws discussed in chapter 6 confer rights or responsibilities to various parties or identify and promote moral values shared by society. For example, the Occupational Safety and Health Act (OSH Act) (Public Law 91-596) protects workers from exposure to toxic substances, ensures they are provided with information about occupational health risks, and guarantees employees access to the results of any medical tests performed in the workplace. This law could therefore be interpreted as legal enforcement of a moral obligation to provide a safe work environment and a legal "right to know' that reflects the moral value of respect for autonomy. Similarly, the Americans with Disabilities Act (ADA) (Public Law 101-336) may prevent workplace discrimination based on genetic factors.

The overlap between law and ethics, however, is limited. Law does not reflect all moral values held by members of society, nor can it necessarily be used to resolve ethical dilemmas. Ethical arguments about the use of genetic monitoring and screening in the workplace often address obligations, rights or values not explicitly covered by law, and are used to express incumbency the law does not acknowledge.

Currently, employers might not be constrained by existing statutes to always use genetic monitoring and screening in ways that reinforce human values or for purposes that are directly related to worker health protection. Employers could find that performing certain genetic screening tests on workers provides information useful in limiting workers' compensation claims or decreasing insurance premiums. These same tests, however, may be a way to fulfill legal obligations if they provide the only effective protection for the sensitive worker against irremedial damage. In this case, ethical and legal concerns will come into conflict.

The relationship between law and ethics is dynamic. Awareness of the ethical issues surrounding new technology is essential for formulating and implementing policies that reflect the greatest possible regard for human values. The formulation of new public policies often reflects ethical concerns, and new ethical issues often arise from the implementation or interpretation of law.

Although the ethical issues have not changed considerably since the Office of Technology Assessment (OTA) studied them in 1983 (17), the emphasis placed on some concerns about genetic monitoring and screening has shifted. Increased pessimism is being expressed in public debate about the risks genetic screening could have for employees' autonomy and privacy. Attention has shifted from the uncertain technical efficacy of genetic monitoring and screening in predicting or identifying illness to the potential abuses of genetic monitoring and screening in the workplace. In 1983, genetic monitoring and screening were perceived to be ethically justified to the extent they would enhance worker health in a reamer consistent with established moral principles. Considerable concern that these principles cannot be upheld has developed since that time.

Because current U.S. law does not address these ethical considerations, they are discussed in this chapter.

For the most part, the ethical issues surrounding genetic monitoring and screening involve concerns about the social rules for and the implications of their use, not the intrinsic properties of the technologies themselves. Two kinds of ethical concerns are discussed in this chapter: problems that arise as testing procedures create moral dilemmas for one or another party, and possible problems that could stem from the misuse of test results (3). The former type of concern stems from the uncertain roles of the various parties involved in testing programs, and from the fact that not all current genetic monitoring or screening tests developed are indisputably valid means of determiningg either genetically determined traits for illness or chromosomal damage (see chs. 4 and 5).

This chapter presents ethical issues raised by genetic monitoring and screening based on the perspectives of employees, job applicants, employers, and society. These perspectives describe possible considerations from each point of view, and will address the overall questions: Should genetic monitoring and screening be performed in the workplace? Should the tests be used in employment decisions? May these tests be used to deny access to jobs? How might potential policies affect employees, job applicants, employers, or society?

In discussing the interests of job applicants, workers and employers, three principal issues exist:

- the implementation of genetic monitoring and screening tests in the workplace and the use of the information they generate,
- the dissemination and storage of information gained from genetic monitoring and screening, and
- the role of genetic counseling for both employers and employees in genetic monitoring and screening programs.

Some ethical issues presented by genetic monitoring and screening in the workplace go beyond the interests of individual workers and employers to affect society as a whole. Not all the social issues discussed in this chapter are strictly ethical: some have moral significance because they create conflict among widely held values. For example, both the health of the workforce and economic competitiveness can be regarded as valued goods that should be protected, although neither has moral value in itself. If employers are held responsible for conducting genetic monitoring or screening to protect the health of the workforce, some sacrifice could be involved for both employers and society. Employers could bear the expense of monitoring and screening and taking necessary action to protect employees, and society may sacrifice some economic advantage. Values such as economic competitiveness will be included in this discussion because they often affect decisionmaking and weigh against ethical concerns.

ETHICAL DIFFERENCES BETWEEN GENETIC MONITORING AND SCREENING

The ethical issues associated with genetic monitoring and screening in the workplace vary according to whether the test performed is genetic monitoring for chromosomal damage, genetic screening' for susceptibilities to occupational illness, or genetic screening for inherited conditions or traits unrelated to the workplace.

Genetic monitoring can be effective to the extent that it detects previously unrecognized hazardous environments or identifies incipient damage in exposed workers. This form of surveillance, however, differs from traditional environmental or biological monitoring, as it is intended to detect indirect evidence of an adverse health effect that could occur in the future rather than present levels or pathological effects of the hazardous substance itself. Indirect evidence often limits the utility of genetic monitoring tests, making it unclear how to use the information gained from these tests if its predictive value is uncertain.

Genetic screening can be used for two purposes in the workplace. First, as indicated previously, it can identify genetic susceptibilities to workplace exposures. The same conditions that make genetic screening effective, however, make these tests potential threats to workers' privacy. Information obtained from genetic screening is likely to be seen by employees as extremely private, sensitive information. Because genes provide much of the basis of human individuality, information about a person's genes is likely to be seen as intensely private. Since genetic screening is meant to detect "defects" in genetic makeup, genetic disease may also carry a stigma. Genetic screening for workplace susceptibil-

ities is more controversial than genetic monitoring, but it maybe ethically justified in some situations.

Genetic screening can also be used by employers to identify genetic traits or susceptibilities unrelated to the workplace, but which indicate likelihood of future disease. Because genetic disease can affect a company's productivity or profit in terms of sick leave taken, workers' compensation, disability, early retirement, health and life insurance expenses (if these are provided by the employer), and liability for illness and injury, employers might want to know as much as possible about workers' genetic makeup. Genetic screening for traits unrelated to the workplace is controversial and many find it ethically inappropriate to conduct these tests in an employment setting.

MORAL CONSIDERATIONS FOR WORKERS AND EMPLOYERS

To the extent that genetic tests are able to detect and prevent genetic disease, both workers and employers could find genetic monitoring or screening in the workplace desirable. From the points of view of both workers and employers, however, genetic monitoring and screening raise several moral considerations.



Photo credit: Earl Dotter

A worker wearing protective clothing.

A worker's motivation for participating in a genetic monitoring or screening program would most likely be self-benefit. While a mandatory genetic monitoring or screening program might benefit employees by preventing occupational disease, such a program could also deprive them of fair treatment or the ability to make free choices. Workers are likely to want to judge for themselves what actions serve their benefit and act freely toward this end. In many cases, workers want to work and do not want their employment opportunities to be curtailed (see box 7-A). Workers therefore have an interest in maximizing their autonomy and thus their freedom.

For the purposes of this chapter, "autonomy" refers to the freedom and ability to make choices concerning one's own welfare. From the employee's perspective, autonomy consists in the liberty to make free choices about the work he or she performs, but autonomy also requires information about occupational health and safety risks so that informed decisions can be made. Autonomy depends on being able to plan and act deliberately, based on one's judgment about the consequences of certain behaviors and their value or utility to oneself or others. This leads to the notion that individuals should be free to act as they wish, regardless of how their actions appear to others and without interference by others, so long as their actions do not harm or interfere with the liberty of others. In this light, an employee might see genetic monitoring or screening as a way to obtain information necessary to make informed choices about accepting or remaining in a job.

At the same time, employers want the freedom to protect the interests of the company, and genetic monitoring and screening might benefit employers by reducing costs. A balance must be struck between promoting one party's autonomy and compromising that of the other. If employers are free to implement and enforce genetic monitoring or screening policies, the autonomy of employees will be limited. Conversely, giving the employee complete freedom to protect his or her own interests would restrict the freedom of the employer and in some instances present risk to co-workers or family. Employer and

Box 7-A—The Social Value of Work

Most persons find it is in their best interest to work. In most American social, economic, and political thought, labor tends to be regarded exclusively as an economic activity. Work has many dimensions, however, since it has always been connected to moral and ethical, as well as economic values. For example, work ties into religious perspectives, such as Puritanism which is based on a concept of work and faith in continuous tension with each other. Secular and religious meanings of work are often inseparable.

While the range of feelings about the role and meaning of work in human life is broad, work is typically viewed as a matter of practical necessity. Work is expected of those who participate in society, and adults who do not work are often regarded with some suspicion. In the Marxist view, labor determines economic value. On a more personal level, employment gives an individual dignity which is often reflected in the esteem of professional peers. Whatever the reason for employment, a number of reasons exist for why a person needs employment: to survive, to fulfill social expectations, or to maintain self-esteem.

Despite workers' compelling reasons for obtaining and retaining jobs, in the United States, decisions about beginning and terminating employment are usually left to employers. Although U.S. laws and moral codes do not specifically recognize a right to work they do acknowledge strong protectable interests in fair work opportunities and freedom from occupational injury and illness which might prevent a person from working. Genetic monitoring and screening present a moral dilemma in that these tests could meet one aim, but violate the other: they could protect workers from occupational illness but also be used to deny them employment. Different opinions are held about how to resolve this conflict.

SOURCES: Office of Technology Assessment, 1990, based on F. Battaglia, ' 'Work" Dictionary *of* **the History** *of Ideas (New York NY: Charles Scribner's Sons,* **1973); and** A.J. Vidich, ''The Morel, Economic, and Political Status of Labor in American Society,' *The Environment of the Workplace and Human Values,* S.W. Samuels (cd.) (New York, NY: Alan R. Liss, Inc., 1986).

employee interests can conflict at three points in the processes of genetic monitoring and screening:

- the decision to undergo genetic monitoring or screening;
- . the access to information gained from genetic monitoring or screening; and
- . the communication and interpretation of genetic monitoring or screening results.

The Decision To Undergo Genetic Monitoring or Screening

Who decides whether an employee or job applicant undergoes genetic monitoring or screening?

Given employers' legal obligations to prevent harmful workplace exposures and workers' interests in acting autonomously, there may be disagreement about whether employers should be able to require workers to undergo genetic monitoring or screening. Some workers will want to undergo genetic monitoring or screening to make informed decisions about the benefits of any current or potential job (e.g., the income from having that job) against risks of that job (e.g., any heightened risk of developing occupational illness). Based on genetic monitoring or screening results, they could decide to continue working at a job or take a job in spite of health hazards because they feel it is the best option available to them. Alternatively, they might decide against working in a hazardous environment, and seek transfer to another job. Other workers, however, will prefer not to be tested. They might not want to know psychologically burdensome information, or might choose to work in a job regardless of health hazards. Any of these choices could be seen as maximizing autonomy because the worker has made the decision.

Employers, however, might want to be free to conduct monitoring or screening programs and establish the conditions for employee participation and consequences for those who refuse to participate. Such practice would be consistent with current preemployment medical testing practices. Employers weigh the benefits (e.g., minimizing the costs of or liability for occupational disease) against the costs (e.g., the cost of the monitoring and screening program).

The degree of conflict between worker and employer interests varies according to whether a genetic monitoring or a genetic screening program is implemented.

Access to Information Gained From Genetic Monitoring and Screening

Who should have access to the information obtained from genetic monitoring or screening? Are workers entitled to test results? Are employers? Are others?

Because information from genetic monitoring or screening could provide the first indication that an individual is at risk for genetic disease, workers need to know test results in order to take action to protect their health. Withholding test results deprives the worker of autonomy by making it impossible for him or her to make informed choices. Thus an employee will likely find no reason to undergo genetic monitoring or screening unless test results are shared with him or her.

When patients have requested the test, medical test results are usually given to patients by their doctors. This tradition should not be taken for granted, however, if genetic monitoring or screening are performed in the workplace, especially if tests are done at the employer's expense. Unless the genetic monitoring and screening programs are established by the employer as part of an employee wellness program, employers may find no reason to provide genetic monitoring and screening results to workers.

Rather than notifying workers, employers might choose to protect employee interests paternalistically by preventing them from working in unhealthy environments. While this approach fulfills a responsibility to provide a safe workplace, such action denies the worker autonomy. Although there may be no legal compulsion to provide workers with genetic monitoring or screening results, a moral reason for doing so probably exists based on a right to information about one's own medical condition, an obligation to respect the autonomy of persons, and the social benefit of open communication between persons tested and those who conduct medical tests. Whatever the explanation, compelling ethical reasons are present to ensure that workers who undergo genetic monitoring or screening receive test results.

Whether an employer chooses to receive worker test results depends on the motivations for implementing genetic monitoring or screening programs. If genetic monitoring or screening is offered as a health promotion service (e.g., a voluntary sickle cell screening program), the employer might sponsor such programs without expecting to see the results. If genetic monitoring or screening is offered for economic or legal reasons, however, the employer will most likely want to see the results and may want to retain the information. Indeed, the OSH Act requires employers to keep medical records on their employees.

The OSH Act, however, has no specific language requiring occupational health professionals to protect the confidentiality of those records. Employers have unrestricted access to them and may, in certain circumstances, distribute genetic information to third-parties (10). Thus, employees might not want genetic monitoring and screening results from voluntary wellness programs to be disseminated to employers. Employees could feel that all genetic information should remain confidential under any circumstance, especially if it might be used to deprive them of a job, health insurance, or other benefit (see box 7-B).

The Communication and Interpretation of Test Results

How should test results be communicated to workers and employers?

Even if workers receive genetic monitoring and screening results, using them to make informed choices could be problematic unless the communication of genetic information is accompanied by appropriate interpretation. Results from genetic monitoring and screening need to be placed in context—unless their significance is properly communicated, there is much room for misunderstanding. Results delivered without adequate or accurate interpretation could harm workers by causing them extreme and, in some cases, undue concern about their health. In other situations, some workers who are found to be susceptible to workplace exposures may continue to work in an unhealthy environment unknowingly if the implications of the test results are misunderstood. While it is impossible to ensure that all workers make truly informed decisions, failure to communicate the results of genetic monitoring and screening tests in a clear, thorough, and responsible manner curtails employee autonomy by not enabling workers to make informed choices. Thus genetic counseling appears necessary for employees to fully understand the results of genetic monitoring or screening and to use this knowledge appropriately. Currently, however, employers are

Box 7-B—An International Survey of Attitudes of Medical Geneticists Toward Workplace Genetic Screening and Access to Results

A survey on mass genetic screening was sent to 1,053 medical geneticists in 18 nations, of whom 677 responded Geneticists strongly preferred voluntary over mandatory workplace screening, by a 72 percent majority. In the United States, there was consensus (>75 percent) that screening should be voluntary. Geneticists who thought screening should be voluntary cited the worker's autonomy or right to decide (74 percent), and the danger of stigmatization, discrimination in employment, or misuse of information by institutional third-parties (41 percent). Advocates of mandatory screening cited protecting the individual worker's health (64 percent), protecting public health (51 percent), and efficiency or cost-benefit arguments (22 percent). Nine percent of those who advocated voluntary screening and 12 percent of those who advocated mandatory screening based their responses in part on concern for economic interests of employers.

In advocating voluntary versus mandatory screening, a clear difference of opinion on whose welfare the respondent placed foremost was reported. Ninety-sewn percent who advocated voluntary screening and 58 percent who advocated mandatory screening placed the worker's welfare as most important. Three percent who advocated voluntary screening and 37 percent who believed in mandatory screening placed societal interests first. Only 1 percent placed the employer's welfare first.

Advocates of voluntary screening were more likely than supporters of mandatory screening to describe a conflict of interest between worker and employer; 34 percent described such conflicts, as opposed to 13 percent who advocated mandatory screening. A majority of both groups, however, described no conflicts.

Ninety-eight percent of respondents said the worker should have access to test results, including 86 percent who said the worker should be told the results even if he or she did not ask for them. When asked whether the employer should have access to genetic screening results, 81 percent said employers should have no access without the worker's consent, including 22 percent who believed that employers should have no access at all.

Thirty percent of respondents who gave reasons for their choices about access believed it would be to the worker's benefit if the employer had some form of access, e.g., employers could shift susceptible workers to less dangerous jobs. Only 6 percent of respondents, however, thought that working conditions in general would be improved. Nineteen percent described **potential economic discrimination, stigmatization, or other misuse of test results by employers. Ten percent based their responses on the economic interests** of the employer.

when asked whether government **health departments should have access, 68 percent said there should be** no access without worker consent. There was a strong consensus on this issue in six nations, including the United States.

These differences in perception indicate that geneticists-those in a position to conduct genetic screening tests--share concerns about how genetic screening might be used in the workplace. A large majority of geneticists ranked the interests of workers and society above those of employers in importance, but they disagree about how these interests can be best protected. Many geneticists believe that workplace screening should be voluntary and that workers should make autonomous decisions about whether to undergo genetic screening. Almost all geneticists believed workers should receive genetic screening results, but that employers' access should be restricted. They expressed concern that genetic screening results may be used to justify personnel actions that may stigmatize or discriminate against some workers.

SOURCE: D.C. Wertz and J.C. Fletcher, "An International Survey of Attitudes of Medical Genetics Toward Mass Screening and Access to Results," *Public Health Reports* **104(1):35-44, 1989.**



Photo credit: University of South Carolina School of Medicine

A genetic counselor discussing results with clients.

under no legal obligation to have genetic monitoring or screening results interpreted for workers by a qualified genetic counselor. If test results are shared with employees, the employer might suggest the worker have them interpreted by a genetic counselor, but is not required to provide one. (See ch. 8 for further discussion of genetic counseling.)

Employers, too, would likely benefit from professional interpretation of genetic monitoring and screening results, but might see no reason to obtain a genetic counselor's interpretation of test results. An employer might not want or need to know the exact levels of sensitivity or predictiveness for individual workers before taking personnel actions based on genetic tests. The employer could find it sufficient to rely on aggregate or imprecise data in making employment decisions without regard for false positive or false negative results. Although genetic monitoring and screening are not sensitive or predictive enough to identify every worker at risk of genetic disease, employers might still find the procedures beneficial on a population basis.

Without qualified interpretation of test results, however, employers might deny individuals jobs that would never cause them disease. This denial would then constitute unfair treatment of employees, and could reduce the efficiency of the workplace--thereby failing to serve the interests of the employer. Having a genetic counselor interpret genetic monitoring and screening results appears to be of both moral and economic value to employers.

ADDITIONAL CONSIDERATIONS

A number of factors either promote or violate the autonomy of workers and employers when ethical considerations of genetic monitoring and screening are analyzed. In some cases, genetic monitoring and screening programs appear to benefit both workers and employers; other programs likely function to the detriment of one or both. But genetic monitoring and screening in the workplace can affect societal interests as well. Because genetic monitoring and screening are likely to have impact beyond the workplace, societal interests must also be balanced against the interests of various parties.

Reducing the Incidence of Occupational Disease

Occupational disease might be prevented in three ways: increasing the safety of the work environment; identifying workplace-induced genetic changes early so as to minimize future damage; or removing susceptible employees from a hazardous environment. Genetic monitoring is intended to address the second goal; genetic screening the third. Some argue that the first goal, providing a safe workplace, is the employer's responsibility and that the use of genetic monitoring and screening to remove employees from high-risk jobs does not release employers from their obligation to improve the safety of working conditions.

Under the OSH Act, the employer is responsible for minimizing the potential for disease or physical harm in the workplace by providing the safest possible environment. When removing all risks is not possible, engineering protections may be required. If employers use genetic screening to identify individuals most likely to be affected by workplace conditions, they might consider it more expedient to relocate those workers rather than remove the hazards. Although ADA precludes excluding workers from jobs based on genetic characteristics, its coverage of genetic traits, susceptibilities, or disease is unclear. To minimize the costs of occupational illness, the most effective prevention could result from a safe workplace, either alone or in combination with genetic monitoring or screening.



Photo credit: American Philosophical Society

Eugenic and Health Exhibit, Kansas Free Fair, 1929.

Protecting Privacy

Protecting the privacy of workers undergoing genetic monitoring and screening is important not only to individuals, but to society as well. By protecting the privacy of workers and the confidentiality of genetic information, workers who otherwise would be unwilling to undergo genetic monitoring or screening in the workplace (even if such tests can protect their health) might choose to be tested. The value placed on the confidentiality of medical information is seen as early as the Hippocratic oath, and is confirmed in the Patient's Bill of Rights adopted by the American Hospital Association in 1973 and other principles and codes of medical ethics (2). The value society places on confidentiality is also seen in other contexts, such as the careful protection traditionally given to the records of adopted children.

Although a number of medical organizations have dealt with the issue of protecting patients' confidentiality in their codes of medical ethics (e.g., American Medical Association, World Medical Association), different views exist about whether medical procedures performed in the workplace are subject to the same constraints. Occupational health professionals might not consider the worker as a patient and thus not see obligations to workers being "as comprehensive or as stringent as the responsibilities that apply in a typical physician-patient relationship" (2). While law does not prevent workplace

physicians from notifying employers of employees' medical conditions, the American College of Occupational Medicine's Code of Medical Ethics emphasizes the importance of confidentiality of employees' medical information (see ch. 6). Similar viewpoints have been expressed by other groups (5), indicating a general interest in protecting the privacy of individuals and the confidentiality of medical information regardless of where it is obtained.

Society probably also has an interest in allowing employers access to genetic monitoring and screening results. If employers are prevented from examining results, they may unknowingly hire or retain workers who have genetic susceptibilities to workplace risk, which could eventually increase the costs of occupational illness to society. It could be argued that, if all medical testing results must remain confidential, genetic monitoring and screening in the workplace should not be considered medical testing or that these results should be considered an exception to the confidentiality rule.

No clear answer exists to whether a privacy right overrides the risk that might be presented to society in maintaining confidentiality of workplace test results. Currently, the matter is often resolved according to who requests or pays for the tests: when the employer pays for the test, the employer receives the results.

Fair Treatment of Individuals

Certain legislation expresses the societal belief that nondiscrimination promotes general well-being (see ch. 6). Title VII of the Civil Rights Act, for instance, states that denying jobs to qualified individuals for race, sex, or disability is prohibited (see box 7-C). Since a person's genetic endowment, whether or not it causes an obvious disability, is also beyond individual control, it might be unfair, although not expressly illegal, to use the results of genetic monitoring or screening as the basis for hiring and firing decisions. Some believe existing law does not protect workers from discrimination on the basis of genetic endowment. It might be appropriate to explicitly include genetic susceptibilities and traits among the conditions listed in Title VII or ADA (see ch. 6) if it is found that employers use the results of genetic monitoring or screening to stigmatize certain workers for genetic traits.

Some question whether the results of genetic monitoring and screening tests should be used as a basis for hiring or retention decisions if they show that members of certain racial, ethnic, or gender groups are more likely to be susceptible or potentially susceptible. It is not clear whether genetic monitoring or screening would be a socially acceptable means of reducing occupational illness regardless of its impact on such groups, or whether such testing would provide a means of justifying discrimination against such groups. Decisions to hire or fire members of racial, ethnic, or gender groups that already struggle for equality in the workplace, on the basis of the results of genetic monitoring and screening might be interpreted as discrimination (See box 7-D).

Economic Efficiency and Competitiveness

Capitalist economy depends on competition. One of the variables that determines successor failure for a business is management style, including hiring and firing policies and overall treatment of employees. Apart from preventing blatant discrimination in hiring practices, the law has largely left employers free to make decisions in this regard. This freedom is generally viewed as serving a societal interest by promoting economic efficiency and productivity within companies and competitive markets (9).

CRITERIA FOR WORKPLACE GENETIC MONITORING AND SCREENING PROGRAMS

Under ideal circumstances, genetic monitoring and screening could benefit workers, employers, and society by improving the health of the workforce. Workers would gain maximal information about risks of mutagenicity through genetic monitoring and screening and would be provided with protective measures or reasonable work alternatives when test results indicate such action is necessary. Employers would benefit by reducing the costs of occupational illness and increasing productivity.

To protect the interests of all parties two factors are necessary: a mechanism for deciding when it is appropriate to use genetic monitoring and screening in the workplace, and guidelines for how these results are to be applied. No guarantee exists that genetic monitoring or screening will be used to reduce occupational illness or that such testing will be conducted in an ethical manner. Therefore, guidelines for the use of genetic monitoring and screening in the workplace have been proposed.

Box 7-C-Sex Discrimination and Fetal Protection Policies

Some companies have fetal protection policies (FPPs) that deny women of childbearing age jobs to prevent harmful exposures to developing or future fetuses. Recently, several of these policies have been challenged, and courts have found that an FPP that applies only to women constitutes sex discrimination.

Because battery production involves exposure to lead (a known hazard to fetal development), Johnson Controls, Inc. has an FPP. Its policy denies all battery production jobs to women of childbearing age who lack medical evidence of infertility except those fertile women who prove they can keep their blood lead level below a specific minimum level.

Until 1982, Johnson Controls had a voluntary FPP that informed workers of the potential risks of lead exposure to fetal health during pregnancy and encouraged female workers to consult their doctors. The company based its voluntary policy on its view that fetal protection ''is the immediate and direct responsibility of the prospective parents . . . [it would] appear to be illegal discrimination" to have an FPP that treated all fertile female employees ''as though they will become pregnant.' The company found that the voluntary policy was ineffective because women refused to leave jobs which threatened exposure to hazadous amounts of lead.

Several court cases have been brought against Johnson Controls--one by a female employee m Johnson Controls' Globe Battery Co. plant in San Francisco, CA, who was denied a battery assembly job m 1983, although she was not pregnant or planning to be. A lower court ruled that Johnson Controls' FPP constitutes "overt gender-based discrimination'' founded in "unscientific stereotypic notions about women. " The decision was based in part on the facts that exposure to lead can affect fertile male workers as well as fertile women, and that Federal and State work safety agencies ban both male and female workers from job sites if their blood lead levels rise. Johnson Controls disputed the claim's scientific basis but in May 1990, the California Supreme Court upheld the ruling.

Another case has been brought against a Johnson Controls plant in Minnesota by the Auto Workers Union and eight Johnson Controls employees. The plaintiffs include a woman who was sterilized *to remain in* **a job she considered desirable, several women who had been transferred to lower-paying jobs, and a man who desired a leave of absence to lower his blood lead level before he became a father. The workers and union argued** Johnson Controls' FPP is explicit sex dismiminat ion because it singles out women for less favorable treatment on the basis of a factor that has nothing to do with their ability to do the job. Johnson Controls' FPP was upheld by the Circuit Court which said the plaintiffs failed to prove the FPP was discriminatory. The case is now before the U.S. Supreme Court, and a ruling is expected m 1991.

Other companies' FPPs have been challenge& General Motors (GM) has one "intended to protect fetuses that women may be carrying knowingly or unknowingly" and "to protect [GM] from possible lawsuits alleging that workplace lead exposures caused **birth defects. " This policy** *Was* challenged by a female iron pourer at GM's Defiance foundry in Cincinnati m a case currently under consideration by the **U.S. Court of Appeals, sixth** Circuit.

Neither case is new or unique, but both illustrate the ongoing problem with job discrimination and the confusion that can result in job bias litigation from introducing risk assessment technologies to the workplace. Scientific progress in identifying risks associated with exposure to hazardous workplace agents has been the basis for these policies, yet the teratogenic effects of exposures seem to be poorly understood by employers.

Whether employers would use genetic monitoring or screening results to justify FPPs is unclear, since exposure to lead and the detection of genetic sensitivities are not completely analogous. There is a crucial conceptual difference between Meeting intrinsic genetic traits that might confer risk and measuring the effects of external workplace agents on fetal development Detecting a susceptibility to worlplace explosures in a female worker does not necessarily idcntify risk to a future fetus because offspring would not be adversely affected unless the susceptibility was inherited from both parents, the trait was expressed, and workplace exposure could affect the fetus in utero. While genetic monitoring that identified genetic changes might better indicate actual risk to a future fetus, the gametes of both male and female workers would have to be affected, thus an FPP aimed at women would be clearly discriminatory.

SOURCES: Office of Technology Assessment, 1990; based on L. Denniston, "High Court To Consider Fetal *Safety:Workers'* Choice *at Center of Case,"* **Baltimore Sun,** p. *1*, Feb. 18, 1990; B. Egelko, "California Court Rebuffs Ban on Women From Jobs That Could Harm Fetuses," Associated Press, May 18, 1990; J. Nolan, Associated Press, Mar. **16, 1990; U.S. Congress, Office of Technology Assessment, *Reproductive*** *Health Hazards in the Workplace* OTA-BA-266 (Washington, DC: US. Government **Printing Office December 1985).**

Box 7-D-Using Workplace Genetic Screening as Power

Some persons believe political power and social status influence employers' uses of genetic screening. To illustrate this claim, two authors present a scenario in which the roles of employers (the party the authors believe are most likely to advocate occupational genetic screening programs) and workers are reversed.

''Imagine that an administrative committee, composed of some of the least powerful members of a population of workers--racial minorities, non-English-speaking immigrants, poorly educated youth-have suddenly been granted full authority to impose a genetic screening program on their more highly paid employers. The goal: to design and implement a test that will weed out 'genetically defective' business executives and mid-level managers. These genetic misfits are then to be efficiently eliminated from corporate payrolls in an effort to improve the company's lagging profits.

First this powerful committee might decide to provide corporate research funds to spur studies into human genetic variation in areas that might affect the job performance of managers. The search might encompass genes thought to influence the development of a wide range of diseases that are approaching epidemic levels in the ranks of executives, including alcoholism, drug abuse, heart disease, sexual dysfunction and mental illness, to name a few. In time, it is likely that ambitious genetics researchers in both private and public laboratories, flushed by the sudden influx of research grants, would find such DNA sequences or at least identify genetic markers that could be used to signal their presence m genetic screening tests.

Later, other researchers might suggest techniques to carry out low-cost screening programs on the chromosomes of these harried executives, who by now would almost certainly find themselves growing increasingly uneasy over rumors of the committee's benevolent plans to improve their genetic hygiene. As soon as these experimental genetic tests began to promise a degree of predictive value for the target occupational diseases, the committee, emboldened by the new scientific findings, might brashly demand that all managers submit to a series of genetic tests designed to ferret out their 'bad' genes. Those managers whose genetic profiles revealed any 'undesirable' DNA sequences might then be asked-for their own good health, of course, as well as for the economic health of the corporation-either to transfer to a less stressful position in the company or to seek more 'genetically suitable' employment elsewhere.

The pool of genetic information on these unfortunate would then be freely shared with other workers' committees controlling other firms, in the hope that epidemics of alcohol and drug addiction, heart disease and emotional disturbances could finally be controlled. No effort would be made to modify environmental factors that might be contributing to the deterioration of these 'executive diseases'—excessive work loads, social stresses, dietary practices and so forth, The diligent genetic screening task force would singlcmindedly devote its efforts to identifying what they perceived as disease-prone managers and plucking them unceremoniously from the workplace.

The utter improbability of this imaginary role reversal underscores the imbalance of power that traditionally exists between employers and employees in our society. But this thought experiment also reveals the potential for the abuse of genetic knowledge by any special-interest group, regardless of its ideology, whenever information is used to dictate important decisions to individuals, rather than to enlighten their own personal decisiomaking processes. "

SOURCE: D. Suzuki and P. Knudtson, "Genetic Screening" Genethics (Cambridge, MA: Harvard University Press 1989).

These guidelines call for the development of workplace genetic monitoring and screening pro**grams that produce maximal benefits to all parties** by **minimizing occupational illness without threatening** privacy and confidentiality, denying equality of opportunity, or stigmatizing workers:

- **Employers should demonstrate the need for a genetic monitoring or screening program** (14). Employers should be able to prove a high prevalence of genetic disease among the workforce and an increased risk of morbidity (12).
- Purposes for conducting **genetic monitoring or screening in the workplace should be attainable and clearly articulated before implemention. The purpose of any workplace** genetic monitoring or screening program should be to protect employee health and reduce the burdens of occupational illness to **workers, employers, and society (7,10).** This **zeal should be communicated to workers be**fore testing to avoid misunderstanding and heightened expectations for intervention that could be neither intended nor feasible. Only

scientifically valid tests should be used, and the ability of genetic monitoring or screening tests to meet these ends should be determined before implementing programs. Tests chosen should be subject to minimal misinterpretation and provide maximal, medically relevant information for protecting employee health (10).

- Participation of both individual workers and the workforce in general should be voluntary. For ethical reasons as well as purposes of efficacy, maximal involvement of the workforce in designing and implementing workplace genetic monitoring or screening programs is desirable (8,10,18). Voluntary participation requires that workers who choose not to undergo genetic monitoring or screening do not jeopardize employment opportunities (7). If possible, alternative protective measures should be provided for workers who do not wish to participate in diagnostic genetic monitoring or screening. Workers should be free to discontinue participation in monitoring. Voluntary participation recognizes the autonomy of workers: it provides opportunity for workers to gain information about job risks if they so choose, but does not compel participation.

- Any program of genetic monitoring and screening in the workplace should apply equally to all workers. Providing equal access to monitoring or screening lessens the possibility of such programs being used or perceived as devices to discriminate against certain workers (10). Particular attention should be given to ensuring that screening for genetic conditions normally concentrated in specific ethnic groups (e.g., glucose-6-phosphate dehydrogenase deficiency or sickle cell anemia) be made available to other members of the workforce on an equal basis and that consistent action be taken for all persons who test positive for a trait in order to avoid disparate impact of workplace testing policies.

- Informed consent should be obtained from any worker undergoing genetic monitoring or screening for any reason. Meaningful informed consent for genetic monitoring or screening should be solicited whether genetic monitoring or screening is performed at the worker's request, for research, or for diagnostic purposes. Informed consent forms should enumerate the purposes of the test, including a description of any ambiguities inherent in the test design, all projected uses of the results, and plans for disclosure of resulting data.

- Any worker undergoing genetic monitoring and screening in the workplace should have access to results. All results should be made available to workers who participate in genetic monitoring or screening programs, including those who are involved in preemployment testing (10). Since genetic monitoring does not clearly indicate risk to individuals, denying access might not limit employee autonomy, but the restricted access to results should be made clear to the employee before tests are performed, and employees should receive genetic monitoring results if they still want them. Genetic screening results should always be provided to workers.

- Professional interpretation of genetic monitoring and screening results should be provided for both workers and employers so that genetic monitoring and screening can be used in accordance with their intended ends. Genetic monitoring results should be interpreted by a genetic counselor so that statistical evidence of workplace hazards are completely understood. Genetic counseling should be provided for all workers who undergo genetic screening, especially when genetic screening indicates increased risk of genetic disease. Genetic screening results should also be conveyed to employers by a professional counselor, and "special care should be taken not to perpetuate past instances of misinformation and stigmatization of particular groups" (8).

- Genetic monitoring and screening results should be confidential. Workers should have the ability to restrict access to genetic monitoring and screening results. Ideally, the results of genetic monitoring and screening would be provided only to tested employees, and could only be provided to employers with the worker's explicit consent or without identifying individual subjects (8). In this regard, genetic monitoring and screening would be like any other form of medical testing service that individuals receive from their own physicians.

HOW MAY GENETIC MONITORING AND SCREENING RESULTS BE USED TO PROTECT WORKER HEALTH?

Once genetic monitoring or screening has been performed, what actions should be taken to protect worker health? If genetic screening identifies a susceptible individual, do employers have a responsibility to reduce the hazards in the workplace, or do they have a right to remove workers at risk? How can worker, employer, and societal interests be promoted equally in making these decisions?

This chapter and chapter 6 describe ethical and legal duties for employers to provide a safe work environment, but this obligation could be impossible to fulfill for persons genetically susceptible to workplace exposures. If engineering protections cannot provide adequate protection for these workers, removing them from sites of dangerous exposure could be the only recourse (16). Some workers are likely to view this preventive measure to their benefit; others, however, will take issue with what they perceive as restriction of their free choice and autonomous action.

Current employees who experience genetic changes or who are found genetically susceptible to occupational illness might be eligible for medical removal protection, which requires employers to transfer an at-risk employee to a safer job without loss of pay or benefits. Job applicants, however, might only be protected from genetic susceptibilities if employers install only genetically "safe" workers in hazardous environments: if genetically susceptible persons are denied employment in hazardous jobs altogether they will certainly be protected from exposure. An employment policy that excludes some workers from job opportunities based on genetic monitoring or screening results could be considered discrimination against handicap, where the disability is genetic susceptibility.

Some employees and job applicants might be willing to risk adverse health effects despite genetic monitoring and screening results. If freedom to make informed decisions about acceptable personal risks is a condition of autonomy, should autonomy ever by limited by preventing individuals from taking risks? The answer depends on whether other persons are affected. People are generally free to take risks in our society. Many people who engage in dangerous hobbies, for example, risk their health by doing so. When those risks affect others, however, there is usually cause to prevent them.

Workers who agree to work in hazardous conditions, or employers who hire workers with genetic susceptibilities, might be assuming risks not only for themselves but for others. Society might be responsible for medical care for workers if they become ill, and for disability payments if they cannot work. Family members can also suffer financially or emotionally if the worker is injured or becomes ill.

There could be health or safety risks involved for others as well. If a worker's decision to risk genetic disease threatens the well-being of other persons, there may be reason to curtail his or her autonomy in choosing to take chances. The safety of co-workers or consumers of a company's products or services could be threatened if genetic disease impairs an individual's job performance.

A similar dilemma about whether to deny jobs on the basis of predictive screening tests was a recent source of controversy in the passage of ADA. Both houses of Congress initially agreed the protections of ADA should not be extended to food service workers who have acquired immunodeficiency syndrome (AIDS). This decision was endorsed by the restaurant and food service industry, which shared congressional concern that restaurants would lose customers if patrons learned a chef or other employee had AIDS (1,6). The exclusive language was later removed from the bill as it became clear there is no scientific evidence that the handling of food by persons with AIDS presents a public health risk (1) (see box 7-E).

Since employees are free to take other risks, such as dangerous hobbies, despite the effects on others, should employees known to be genetically susceptible to workplace exposures be allowed to acceptor remain in jobs that increase the risk of disease? The answer depends on several conditions, including whether it is technically possible to reduce workplace hazards so that workers with predisposing traits can work safely, and whether alternative, acceptable forms of employment are readily available for those with a specific genetic predisposition (11). In other words, it might only be justifiable to prevent a worker from taking risks if the employer has already done everything possible to make the workplace safe and protect employees from harm.

Box 7-E—Protection of Others: A Case for Workplace Screening?

Workplace screening for HIV infection and genetic susceptibilities to occupational illness are somewhat analogous situations. Both types of screening tests are predictive rather than diagnostic tests intended to detect possible future health problems that do not affect a worker's job performance at the time the test is performed Employers might want to avoid hiring workers with HIV infection for similar reasons they might not want to hire a person with a genetic susceptibility to occupational illness: economic effect, stigma attached to the disease, or perceived risk to co-workers or the public. Like genetic screening, HIV screening provides personal information most workers want to be kept confidential.

Because HIV can only be transmitted through intimate contact or infected blood, it is generally acknowledged that protection of public safety cannot be used to justify mandatory AIDS screening in the workplace. In some cases, however, genetic susceptibilities may in fact present risk to others. If such is the case, would infringements of autonomy and privacy inherent in mandatory workplace genetic screening ever be justified by protecting public safety?

Some persons argue that the protection of others might just@ workplace genetic screening for nonoccupational illness. A common example used to illustrate this possibility is an airline pilot who develops Alzheimer's disease. As the early symptoms of the disease incrementally affect his or her judgment and memory, aircraft passengers could be endangered by the pilot's behavior. A gene for a disease, however, is not the disease itself, and should not be treated as one, since other factors can influence the gene's expression. If the development of a genetic disease, especially one that takes effect rapidly, can affect co-workers or the public, the potential for genetic disease could justify exclusion from job opportunities.

Significant risk to others must be ascertained before workplace genetic screening can be used for the protection of others. Employers should consider the predictive value of the test, how far in the future a detected trait would likely take effect, and the consequences of a trait becoming rnanifest. Identification of a genetic susceptibility to sudden heart failure might justify workplace genetic screening if expression of that trait could injure others and if no other ways of identifying the risk exist. For other illnesses, however, especially those that develop gradually and can be detected through other means, genetic screening might not be warranted Further discussion is needed to identify the conditions that should exist for genetic screening in the workplace to be justified by public safety considerations.

SOURCES: Office of Technology ***Assessment,*** 1990, based on AS. Leonard, "AIDS in the Workplace," H.L. Dalton, S. Burris, and the Yale AIDS Law Project **(eds.),AIDS and the Law:A***Guide for the Public (New Haven,CT:* Yale University Press, 1987); M.A. Rothstein, Medical Screening and the Employee Health ***Cost Crisis (Washington, DC:*** **Bureau of National *Affairs*, Inc., 1989); M.A.** Rothstein, "Screening Workers **for AIDS," H.L. Dalton, S. Burris, and**the **Yale AIDS Law Project (eds.), AIDS and the Law:*A Guide*** for **the** *Public (New Haven, CT: Yale* University Press, 1987),

Many jobs present risks of illness or injury, and the possible impact on others has seldom been accepted as reason to deny employment. It is impossible to organize society so that the individuals who make the decisions bear all of the risks themselves (15).

Should genetic screening be used in hiring decisions if they have a disparate impact on groups politically protected against workplace discrimination? Some maintain that such impact might be justified if it is generally accepted that it is necessary for the safety of the worker and there are no equally protective alternatives. Others argue that since "the law has traditionally viewed with disfavor any differentiation in treatment based on immutable characteristics like race, sex, alienage, and legitimacy . . . a person's genetic or environmentally-induced predisposition to occupational illness, which does not affect 'present ability' to perform the job, should not be permitted to result automatically in an adverse employment decision' (13). The tension between protecting the health of workers and avoiding discrimination illustrates the need for values to be balanced.

If the risk of occupational illness only affects the individual worker there may be no ethical reason to prevent employment on that basis. As long as co-workers and family cannot be harmed directly or indirectly, many argue that individual autonomy should not be limited. Some argue that genetically susceptible workers are responsible for their own health as long as they are informed of risks, even if alternative employment is available (4).

Employers could ask workers to sign waivers indicating they are aware of possible health risks and will not hold the employer liable. It has been argued, however, that this practice limits employee autonomy by limiting the range of options available to employees: forcing workers to relinquish benefits and protections normally provided by employers constitutes coercion (13). For many workers, a job is primarily a source of income and other benefits that provides security for themselves and their families and is essential to their well-being. Workers might be willing to risk their health in order to ensure continued income. Thus, a worker might feel pressure to keep a job even if it requires assuming health risks. On the other hand, waivers could provide a means for employers and employees to learn about possible health risks without employers being held liable for workers' autonomous decisions to accept health risks.

SUMMARY AND CONCLUSIONS

The interests of workers, employers, and society need to be addressed and balanced with respect to each other. Employees and employers will strive to maximize their autonomy and reduce their economic or personal costs, while certain social values might need to be protected. There is no consensus about how ethical issues related to genetic monitoring and screening in the workplace should be decided or whether any group's particular interests override another 's. Ethical arguments can be made for and against a number of different options.

Since genetic monitoring and screening in the workplace might, depending on circumstances, identify workplace hazards and function to benefit all the parties involved, the ideal solution would be to develop programs that minimize occupational illnesses while avoiding potentially harmful consequences from such testing, including the threat to privacy, confidentiality, and equality of opportunity, and the unfair stigmatization of employees. Striking balance among different interests poses a considerable challenge, since it is difficult to give equal emphasis to all the personal and social benefits and hazards that may derive from genetic monitoring and screening.

Some of the interests of different parties overlap considerably. Genetic monitoring can be ethically justified to the extent that it provides a verifiable and useful index of workplace risks and employers are willing to take action to improve the safety of the workforce based on the results. Genetic monitoring in the workplace currently might not be perceived as a threat to employee privacy. Although it indicates genetic damage in individuals, genetic monitoring cannot accurately predict specific health effects. If the proper conditions are fulfilled, genetic monitoring could mutually benefit employers, employees, and society by reducing the burden of occupational disease.

Issues related to genetic screening are less easily resolved, since genetic screening in the workplace is more controversial than genetic monitoring. On one hand, it can provide the most accurate and sensitive detection of risks to individuals. On the other hand, genetic screening results can be easily misused by employers. Employers could implement workplace genetic screening to protect their own interests without regard for the interests of job applicants and employees.

An additional problem with genetic screening in the workplace perceived as most serious is that employers can test for traits unrelated to workplace exposures, i.e., traits that have no medical relevance for the workplace. While identifying genetic susceptibility to occupational illness might motivate the employer to improve workplace conditions, genetic samples collected for that purpose could be put to other uses. Genetic screening for nonoccupational disease in the workplace does not protect workers against occupational illness, could violate the privacy and autonomy of job applicants and employees, and will not lower occupational health costs for society although it may lower health-related costs for employers.

Many of the standards suggested for an ideal workplace testing program are likely to be difficult to uphold while allowing the interests of workers, employers, and society to be met. It is not clear how conflicts of interest should be resolved, and there is little agreement about whether workplace hazard removal should be accomplished by denying employment to genetically susceptible individuals. For now, ethical questions surrounding genetic monitoring and screening in the workplace can only be answered on a case-by-case basis.

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Chapter 8

The Worker as a Person: Individual Uses of Genetic Information

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Chapter 8

The Worker as a Person: Individual Uses of Genetic Information

Our genetic identity is more than DNA sequences. Our genes carry much that is relevant to our past and our future. They also carry secrets. Everyone possesses a minimal number of deleterious genes, that may or may not be expressed, depending on their location, their phenotypic expression, the environment to which they are exposed, and the life choices of those who bear them.

Most often, individuals learn about their genetic identity in the context of family planning. Prospective parents may choose to undergo diagnostic tests so they can increase their reproductive choices. In other cases, individuals learn about their genetic identity because they, or a relative, are diagnosed with a genetic disease or syndrome. But in both cases, the individual requests to participate in testing and subsequent counseling, and understands, even if in rudimentary terms, why the tests are being done. At the least, the fact that tests are conducted in a medical setting provides a context in which certain assumptions and expectations can reasonably be held by the person being tested. These factors might be different if the workplace becomes the background for receiving genetic information.

New technical capabilities to diagnose and predict genetically based disease have opened new pathways for informed decisionmaking about ourselves and our family's health. But they have also created moral, ethical, and psychological dilemmas for which there are no easy solutions. In addition, genetic monitoring and screening tests often convey a probability, but not a certainty, that disease will appear, introducing difficult uncertainties into the lives of those tested. Other chapters in this report address the issues surrounding the application and use of tests (both monitoring and screening) in the employment setting. This chapter will address issues faced by the individual who undergoes testing-not as a worker—but as a person and a family member. It discusses the role of genetic information in family life and personal health and the need for sufficient and appropriate counseling for those who find themselves, or their families, at risk.

MONITORING v. SCREENING: ISSUES FOR THE INDIVIDUAL

Three approaches have been proposed to consider the various issues in genetic monitoring and screening (19). The frost is fatalistic, where the existence of a particular genetic vulnerability is recognized as a quirk of fate which could affect anyone and for which society cannot be held responsible. This approach most closely resembles the state of public thinking until recently. As a society, we are quickly moving away from this perspective.

The second approach is individualistic; i.e., society assists the individual to better understand the problem and find the best means of dealing with it. The burden, however, is on the individual to act or be acted on. Screening an individual for genetic traits and diseases, and removing the individual from an allegedly hazardous environment on the basis of test results reflects the individualistic approach. But, as discussed in chapter 5, there are technical and practical constraints to this way of thought because of the limits of the tests themselves and the uncertainty of cause and effect. Despite the technical constraints of testing, the individualistic approach is currently taken in the clinical genetics setting, the routine environment for genetic tests.

The last approach is social welfare activism. It applies the societal principles of justice and equity to the genetically afflicted individuals. This view holds that where conditions are found to be unequal, or natural differences contribute to inequalities, they should be rectified to benefit the least well-off person. The use of genetic monitoring to identify areas of potential risk for all individuals reflects the concept of social welfare activism. In this scenario, actions taken on the basis of test results are taken on the group, not the individual. No one is singled out.

The difference between the individualistic and social activism approaches lies in the locus of burden and the implications for action. In the individualistic approach, which involves screening, the burden of dealing with the test results is placed on the individual as a worker and a patient. In the social welfare approach, which also includes moni-

toring, the burden rests on the company to take action by lowering or removing risks. Testing becomes a source of surveillance data.

Whatever avenues society takes in applying genetic monitoring and screening tests to workplace decisions, it can never be overlooked that the focus of the tests—the person—is being provided with information which may have a significant impact on decisions unrelated to employment; these include marriage, procreation, and lifestyle. While positive test results could be the end of the story for the employer (having decided not to hire, to relocate, or to fire the individual), they are likely to be the beginning of the scenario for the individual, who must now decide what the findings mean in his or her private life.

THE NEED FOR SUFFICIENT AND APPROPRIATE COUNSELING

For many individuals, even considering whether to undergo genetic monitoring or screening constitutes a life crisis because of the possible outcomes. If the results are positive (for the trait, disease, or genetic change), the crisis obviously is exacerbated. How the results will affect the individual has much to do with the individual's own frame of reference, but also with the implications of the condition and its prognosis.

Psychological issues permeate every aspect of genetic consultation. Information received can be ego-threatening or even life-threatening, as individuals find that they are "flawed, "imperfect, " "defective," "inadequate,' or "abnormal, ' and may have the potential of transmitting these "flaws' to their progeny (16,17). How the information is obtained, communicated, retained, and eventually used by the person being tested involves a "series of complex, multidimensional processes with major rational and nonrational components" (17). In addition to the intrapsychic consequences of receiving genetic information, there are potential impacts on family. Genetic information affects not only the individual, but also the spouse, parents, grandparents, siblings, and children. Social and psychological stress, as well as future financial and emotional burdens, can strain family functioning (29).

In addition, genetic conditions found through screening are permanent and chronic and may evoke

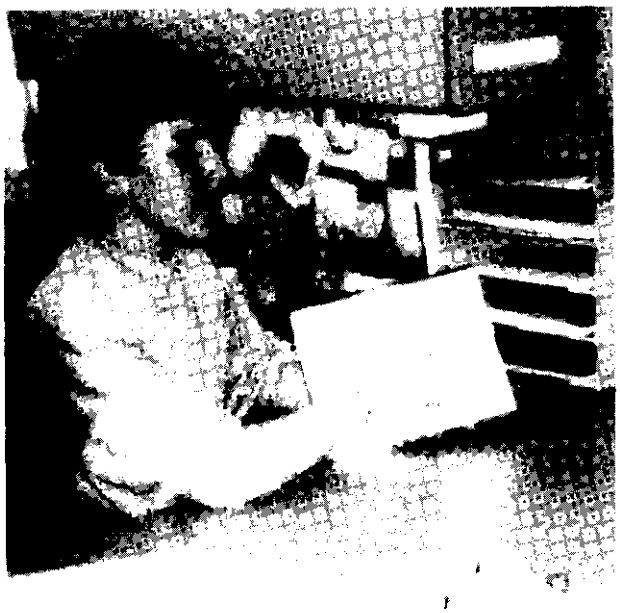


Photo credit: Diane Baker

A genetic counselor showing a chromosome chart to a client. Genetic counseling may assist individuals and families cope with positive test results.

labeling. The continuous, ever present diagnosis of genetic disease or potential for disease may elicit "chronic sorrow" (24) in those affected. In addition to coping with their own uncertain future, individuals may experience guilt or grief if they find they have unknowingly passed a deleterious trait to their offspring.

Obviously, the psychological impact of a positive diagnosis varies with its severity and treatability, and the fact that different families will react uniquely to similar situations. Support, counseling, and followup are likely to assist individuals and their families in coping with positive test results. The knowledge and skills of a properly trained counselor can help the individual understand the diagnosis, recurrence risk, prognosis, relevant preventive and therapeutic measures, and also aid in communicating important information to other family members. When these goals are accomplished, genetic counseling is usually perceived as a valuable experience by the counselee and the counselor (22).

When it is not possible to make a specific diagnosis, or to give an accurate recurrence risk or more than a very general prognosis, as will be the case in many predictive tests, interactions between the testee and the tester are even more complex. Until research progresses, it is likely that non-

specificity of diagnosis and prognosis will predominate in workplace genetic monitoring. Employers undertaking such programs should anticipate the complexity of interpretation and communication of test results.

Pretest Counseling

Professionals in the fields of health and education are usually the first to see families who are seeking information about genetics. Helping a client to cope with the question "why is this happening to me?" is one of the objectives of pretest counseling. Another objective is helping a client understand the test—what it is and is not, as well as why it is being done. When employees are tested at the workplace by someone insensitive to counseling objectives, the workers may be confused throughout the entire process.

In routine genetic counseling, the client discusses why he or she chooses to be tested and discusses with the counselor the implications of the possible outcomes. The counselor prepares the individual for both positive and negative test results. It is also the time to discuss risk reduction strategies, if relevant.

Understanding Risk

One of the genetic counselor's tasks is to communicate risk to the client-a job not easily performed (13). A decision to be tested will be influenced by a person's perception of the chance that the test will be positive. The interpretation of numerical risk varies depending on: prior perception of the magnitude of the risk; anxiety state of the client at the time of the test; familiarity with the outcome (whether there is an affected relative); how treatable the condition is; and belief that the outcome with which the individual is familiar is representative of all such outcomes (15).

The perception of risk may be a more important determinant of decisionmaking than the actual risk. The way risks are posed by the counselor may, in fact, influence the client's choices. When confronted with the risk of genetic disease in their offspring and when making reproductive decisions, people tend to place greater weight on their ability to cope with a disabled or fatally ill child than on precise numerical risks. For example, for some couples, a risk of 10 percent could be perceived no differently than a risk of 50 percent if they believe that they cannot cope with the situation. In prenatal counseling, regardless of actual risk, parents overwhelmingly perceive the chance of recurrence as either O or 100 percent-it either will or will not happen. By processing rates in this way, individuals simplify probabilistic information and shift their focus to the implications of being at risk, and the potential impact of what could occur ***(20).***

In addition to the subjective factors that influence the interpretation of risk already discussed, the understanding of risk in arithmetic terms is usually deficient. Comprehension of the concepts of probability and risk will influence the client's understanding of the genetic information provided by testing (16). In a Maryland study of 190 predominantly White, middle-class women, over one-fifth thought that "1 out of 1,000" meant 10 percent, and 6 percent thought it meant greater than 10 percent (5).

The way risks are framed also influences choices (21). The decision to have a genetic screening test can be different if the risk is presented as a 25 percent chance of having an affected child rather than a 75 percent chance of having a normal child. Presenting risks in personal terms may improve the chance that action will be taken (13).

Most studies of counseling have focused on cases where the patient already has an affected child or relative and is familiar with the disorder. Little is known about the effect of counseling prior to genetic screening in people with no previous family history of the condition for which they are being tested. It is likely that their misperceptions could be great. Pretest counseling is all the more imperative in these cases, as is the need for informed consent.

Obtaining Informed Consent

The following text presents the routine consent process in contrast to that which we will find in the workplace. (See ch. 6 for further discussion of informed consent.) In the routine clinical genetics setting, very few situations arise in which genetic monitoring or screening can be performed by a health care provider without informed consent. Before any invasive procedure (including the taking of samples such as blood, urine, or saliva) the individual should be informed of the following:

- purpose of the test,
- risk of the test itself,
- validity of the test (the possibilities of false results),

- implications of a positive result (medical and social),
- nature of the condition for which the test is being conducted,
- options available to reduce the burden of disease in the event of a confined positive test result, and
- alternatives if the individual decides not to have the test.

Most of these, or analogous elements, are specified in the informed consent statutes of 21 States (l). Informed consent is not obtained when a disclosure is incomplete, constructed to prejudice the subject toward a particular action, or obtained under pressure.

The process of obtaining informed consent in the medical sense may not be practiced in the workplace. Consent may be obtained for using the results to make hiring and employment decisions but the future or current employee may not receive the information needed to obtain explicit consent for medical intervention.

Posttest Counseling

When attending a genetics clinic for reasons other than prenatal genetic screening, people have historically come because they have had an affected relative, usually a child. They tend to be familiar with the disorder. The affected relative, rather than a test, served as the indicator of potential disease for others. As an increasing number of genetic screening tests are administered to healthy individuals with no apparent family history of genetic disease, counselors will have to spend more time describing the disorder to those with positive test results.

Studies have shown that test results should be reported in person, by the same person who provided the pretest counseling (9). If the test results are positive, prior contact may have alerted the counselor as to whom else should be informed, whose help might be needed on behalf of the client (i.e., financial or emotional support), and important information about the client's lifestyle and family (as well as financial and insurance information).

Followup counseling and support is also strongly advised. News of a positive result impedes a person's ability to accept advice on both emotional and practical levels. Faced with positive results, most individuals are unable to take advice until they overcome the shock and possible denial that their fate or their children's fate could suddenly shift in a negative direction. Information about treatments and the importance of changing lifestyle is best assimilated several days after the test results are communicated. Focusing on medical facts at this stage could convey to the individual that the psychological issues he or she is dealing with are unimportant or irrelevant (38).

Even in the best of all worlds, where consistent counseling has been provided all through the process, the effectiveness of counseling is sometimes questionable. An analysis of nine studies on counseling published since 1970, concluded, "many parents of children with a genetic disorder have an inadequate understanding of the genetic implications of the disease, even after one or more genetic counseling sessions" (10). One survey found that more than half of the 87 percent of people who came to a genetic counseling center with inaccurate knowledge of risk were still misinformed after counseling (13).

The task of communicating genetic information is formidable. Counseling programs are continually trying to educate counselors to improve the process (35). A major impediment to satisfactory counseling has been a profound lack of understanding of basic genetics. Anyone administering tests necessarily takes on the role of educator as well as practitioner and examiner.

THE ROLE OF GENETIC INFORMATION IN FAMILY MANAGEMENT AND PERSONAL HEALTH

A person's genetic constitution (genotype) determines the broad limits of his or her potential, whereas the expression of that potential (phenotype) is dependent in an important way on the environment with which the genes interact. The assumption that there is always a one-gene-disease relationship is fallacious. There are numerous variables such as general health, diet, medication, and stress that contribute to or interact with the genetic trait, in addition to workplace exposures, to produce a disease state.

The harmful manifestations of some genetic diseases can be prevented or ameliorated by the administration of drugs or special diets, or by the

elimination of harmful environmental agents. To be optimally effective, intervention must take place early, frequently before symptoms of the disease appear. Predictive tests have been unavailable for most single-gene diseases, but with the use of recombinant DNA technology many are being developed (see ch. 5).

For most genetic diseases, the basic defect is not known and effective interventions are not yet feasible. Although linkage studies or direct DNA analysis will eventually reveal the defect, there will be long delays between the time the gene is located and the time when effective interventions are available. In the meantime, predictive tests for those at risk could be developed and widely disseminated. Healthy individuals could learn of their fate as potential patients and face several options, depending on the prognosis for the disease and the availability of effective intervention.

When Intervention Is Available

A considerable amount is known about the pathogenesis of some multifactorial conditions, such as diabetes mellitus, coronary artery disease, and lung cancer. If it were possible to identify individuals with genetic susceptibilities to these conditions, the pathogenic process might be interrupted (if the person at risk adopts risk-reducing behaviors). In contrast to highly penetrant single-gene disorders, however, it is doubtful that all persons found to have a susceptibility-conferring genotype would eventually manifest the disease, even if they possessed other predisposing alleles or were exposed to harmful environmental agents. Unless one can be certain that disease will appear, potentially harmful interventions should not be used on those who may never become sick in the first place. Avoidance of dispensable habits, however, such as smoking or a high fat diet, would be safe plans of action (see box 8-A).

Individuals found to be at risk for non-insulin dependent diabetes could be counseled about the importance of weight control. Counseling people found to be at risk for colon cancer to increase fiber intake, or to have periodic colonoscopic testing could ensure early treatment. Those at risk for melanoma could be advised to protect themselves from sunlight.

In all these cases, individuals can be informed of the likelihood that specific actions they can take, could modify the prognosis delivered with the test results. When positive test results are based on monitoring, rather than screening, the individual's choices are not as clear (see ch. 4). At that point, the patient as a person may wish to be removed from the potentially hazardous exposure, but the patient as a worker may have no choices.

When Intervention Is Unavailable

For many disorders, neither drugs nor diets nor lifestyle changes have yet been found that markedly improve the outcome. This greatly complicates the personal burdens of threatening medical information. Examples of such disorders with a late onset are Huntington's disease and Alzheimer's disease (see box 8-B). Other disorders can be treated with some benefit, but the outcome is not always good and the management of the disease may be costly. Maple syrup urine disease, hemophilia, bipolar affective disorder, and schizophrenia fall into this category.

The psychological sequelae of facing the uncertainties of untreatable illness are devastating. There is a growing body of literature related to coping behaviors associated with testing positive for HIV antibodies. One of the most psychologically unacceptable notions which confronts the individual at risk is to be the passive victim of a totally random event (36). Another aspect of detecting a late onset disorder is the possibility of self and social stigmatization, and the increased opportunity for discrimination (16).

When the Test Results Are Inconclusive

In the case of screening for genetic disease, most tests are fallible. Some of the problems are specific to the method employed and some to the laboratory performing the test. Others result from genetic heterogeneity and incomplete penetrance. Failure to correctly interpret monitoring and screening test results poses a significant problem for the patient.

In the case of genetic monitoring, the uncertainty is probably even more pronounced. Because of the lack of causal linkages between exposures and clinical prognosis, the clinician is left with little on which to base a prognosis. If the results reveal chromosomal damage, there is little reliable and valid information available that would allow individuals to make informed choices. For example, they can be told that there appear to be causal linkages between cancer and their condition, but that there is

Box 8-A—Screening for Coronary Artery Disease

Coronary artery disease (CAD) is a major public health problem. Myocardial infarction, secondary to CAD, causes 30 to 35 percent of all deaths in men between ages 35 and 50 and is responsible for more than half a million deaths per year in the United States. CAD results from atherosclerosis, a slow, progressive disease of the arteries that begins early in life and may go undetected until the first heart attack which maybe fatal.

A strong association between hyperlipidemia and the risk to develop CAD has been demonstrated. There is evidence for the existence of three monogenic forms, as well as of polygenic and nongenetic forms, of hyperlipidemia. Familial hypercholesterolemia, familial hypertriglyceridemia and familial combined hyperlipidemia are transmitted as autosomal dominant traits and are well-established entities. In most cases of autosomal dominant transmission of CAD, the individual has symptoms that lead to the diagnosis.

Several different genetic factors have been associated with CAD. Only 1 percent of those classified as hyperlipidemic have a clear-cut monogenic cause. Nongenetic factors, e.g., cigarette smoking, high cholesterol diets, obesity, physical inactivity, stress, and diabetes mellitus, may also contribute to the disease state. Most cases, therefore, are heterogeneous or multifactorial and would be prime candidates for some type of predictive tests. Intervention could be started well before the appearance of heart disease.

Research using restriction fragment length polymorphisms has demonstrated an association between a 3.3 kilobase band and inherited apolipoprotein abnormalities that could predispose an individual to CAD. Tests at the DNA level may ultimately prove better predictors of CAD than lipid or apofipoprotein measurements. These tests may provide risk information prior to elevated lipid levels. When such tests become widely available, persons at risk could begin a prevention program including lowering dietary levels of cholesterol or taking drugs that bind cholesterol-like compounds in the intestine or inhibit cholesterol biosynthesis.

SOURCES: R.T. Acton, R. Bamberg, R.C.P. Go, et al., ''Utilization of Genetic and Other Laboratory Test Results To Predict and Reduce the Risk of Disease," *Proceedings of the Society of Prospective Medicine, 1988;* J.L. Goldstein, W.R Hazzard, H.G. Schrott, et al., "Hyperlipidemia in Coronary Heart Disease," *Journal of Clinical Investigation 52:1544, 1973;* A.G. Motulsky and H. Boman, ''Screening for the Hyperlipidemias,' Genetic Counseling, H.A. Lubs and F. de la Cruz (eds.) (New York, NY: Raven Press, 1977); J.M. Ordovas, E.J. Schaefer, D. Salem, et al., ''Apolipoprotein A-I Gene Polymorphisms Associated With Premature Coronary Artery Disease and Familial Hypoalphalipoproteinemia' ' New *England Journal of Medicine* 314:671-677, 1986; J. Stamler, "Epidemiology of Coronary Heart Disease," Medical *Clinics of* North *America* 57:5, 1973; G.L. Vega and S.M. Grundy, "Treatment of Primary Moderate Hypercholesterolemia With Lovastatin (Mevinolin) and Colestipol," ***Journal of the American** Medical Association 257:33-38, 19S7.*

no certainty that they are going to develop cancer. For individuals trying to cope with uncertain medical prognoses "(e.g., cancer, multiple sclerosis, or Hodgkin's disease) the loss of certainty in one's future (having a family, children, grandchildren, retirement, etc.) is often just as destructive to mental well-being as the certainty of death from a definitive prognosis.

When the Results Affect Reproductive Futures

In the past 15 years, genetic screening tests have most frequently been used for prenatal diagnosis and family planning. Tests intended to detect disorders in offspring appear to be viewed differently than tests undertaken to identify personal risk. A 1986 Office of Technology Assessment (OTA) poll found that a majority of Americans who think human gene manipulation is morally wrong in the abstract approve of its use to save lives and heal sick children. In addition, a large majority of those polled (77 percent) say they approve of human genetic alteration to stop children from inheriting nonfatal birth defects or to reduce the risk of developing a fatal disease later in life (32).

Those identified as being carriers of autosomal recessive disorders (e.g., Tay-Sachs disease, thalassemia, and sickle cell anemia) currently have several options in family planning. They can proceed with an unmonitored pregnancy knowing that they have a 25 percent chance of having an affected child; if a prenatal diagnostic test is available, they can avail themselves of amniocentesis or chorionic villus sampling to determine whether the fetus is affected, at which point they can decide whether to continue or terminate the pregnancy; they can choose to become pregnant by alternative methods, or not to become pregnant at all.

Adequate and timely information is a key factor in helping families make their choices. Prospective parents need to understand the prognosis for an affected child before making a decision. For exam-

Box 8-B—Huntington's Disease

Huntington's disease is a chronic, progressive, degenerative disorder, beginning usually between the ages of 30 and 50 years. It is characterized by uncontrollable, spasmodic movements in the face and extremities, as well as gradual loss of mental faculties, ending in dementia. The disease is lethal and incurable; death usually occurs on average 15 to 17 years after disease onset. The disease is transmitted as an autosomal dominant trait; offspring of an affected individual have a 50 percent chance of developing the disease. The test for the Huntington's gene is most often performed on an asymptomatic individual. If someone has the gene, that person will definitely develop the disease. Symptoms for the disease usually begin past the typical childbearing years, between ages 35 to 45.

The test provokes considerable anxiety among those at risk who elect to take it. Not all of those at risk elect to be tested, even though there is a 50 percent chance that they will receive good news. Prior to the availability of a predictive test for Huntington's disease, surveys indicated that between 56 and 85 percent of those at risk would avail themselves of the test. In a survey conducted after the test became available, less than 14 percent of the sample population at risk elected to take the test.

In another survey, 66 percent of the sample population at risk said they wanted the test. Of that group, 15 percent said they might commit suicide if the test were positive. Of the group that chose not to be tested, 30 percent feared they might be suicidal and therefore did not want their fears confirmed. For some people, uncertainty appears to be preferable to certainty.

A recent study on the psychological reaction of people being tested for the disease found no clear increase in psychiatric illness among people who tested positive for the Huntington's gene. People's reactions to their test results ranged from ''extreme joy and relief to disappointment, sadness and demoralization. " This study suggests that people cope well with this type of information if they are carefully screened, counseled, and provided followup care. In addition, those who test positive should be given appropriate long-term monitoring.

SOURCES: Office of Technology Assessment, 1990; based on C. Mastromauro, R.H. Myers, and B. Berkman, "Attitudes Toward Presymptomatic Testing in Huntington's Disease," *American Journal of Medical Genetics 26:271-282, 1987;* K.A. Quaid, J. Brandt, and S.E. Folstein, "The Decision To Be Tested for Huntington's Disease, " *Journa/ of the American Medical Association 257:3362 (letter), 1987;* B. Teltscher and S. Polgar, "Objective Knowledge About Huntington's Disease and Attitudes Toward Predictive Tests of Persons at Risk," *Journal of Medica1 Genetics 18:31-39,* 1981; A. Tyler and P.S. Harper, ''Attitudes of Subjects at Risk and Their Relatives Toward Genetic Counseling in Huntington's Chorea" *Journal of Medical Genetics 20179-188,* 1983.

pie, in one study, at least **89 percent of 333 couples identified as at risk for having children with Tay-Sachs disease used prenatal diagnosis (14). Tay-Sachs is a progressive, fatal disorder that results in death usually before a child's fifth birthday.** On the other hand, couples at risk for sickle cell anemia might not seek prenatal diagnosis, possibly because the disease is partly manageable and, therefore, many women would not abort an affected fetus (see chs. 3 and 5).

In the case of a late onset autosomal dominant disorder (e.g., Huntington's disease, or adult polycystic kidney disease), adults at risk face a double dilemma. Before the availability of predictive tests, individuals at risk (who knew of their risk status) could forego childbearing as the only way of avoiding passing on the trait. Now that those at risk can find out whether they will most likely develop the disease, they are presented with new options. If not at risk, they can freely reproduce without the burden of passing the gene to their children. If found



Photo credit: Woody Guthrie Publications

Woody Guthrie: A famous American folksinger who died of Huntington's disease.



Photo credit: Diane Baker

An employee's genetic information can play an important role in his or her family planning.

to be carriers of the gene, they can elect to have prenatal diagnosis to determine whether their offspring will also inherit the fatal gene. However, this is complicated by the fact that many do not know they are at risk until they have already had children.

The availability of these genetic screening tests is recent enough that very little is known about how high risk people who are tested deal with the psychological aftermath. Clearly, counseling and other support services should be offered in conjunction with any test.

When the Results Affect Other Family Members

In the case of genetic monitoring, it is unlikely that positive results will directly affect other members of the existing family (with the exception of the unborn). Obviously, other family members can be secondarily affected by any consequences of potential or real deteriorating health of a loved one.

In genetic screening, there is a real possibility that test results will affect other family members. In the usual genetic counseling setting, the person being tested (the proband) is routinely advised of risks to other family members. For example, if the client is found to be a carrier for an autosomal recessive disorder, e.g., Tay-Sachs or sickle cell disease, the counselor informs the client that siblings each have a 50 percent chance of also being carriers. In most cases, the counselor suggests that the proband contact his or her siblings and suggest that they consult with their personal physician or come to the same clinic. The counselor cannot confirm that the proband has informed relevant family members. Unauthorized disclosure of medical information could result in legal action.

The issue of disclosure of medical information to others, e.g., insurers and employers, is discussed in chapter 6. Disclosure of medical information to relatives raises different issues. Not all families are emotionally and psychologically secure. Sibling relationships could impede full disclosure. Sharing highly personal medical information that involves reproductive and health futures may cause personal embarrassment or emotional stress for family members.

The question of duty to warn the proband's spouse also arises as a consequence of genetic screening. For example, a woman informed that she is a carrier of an X-linked condition might not wish to inform her husband or prospective husband that their male offspring will have a 50 percent chance of being at risk.

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research took the position that physicians may release genetic information to relatives without the patient's or client's consent provided certain conditions are met. They are:

- reasonable efforts to elicit voluntary consent to disclosure have failed;
- high probability exists both that harm will occur if the information is withheld and that the disclosed information will actually be used to **avert** harm;
- identifiable individuals will suffer serious harm; and
- appropriate precautions are taken to ensure that only the genetic information needed for diagnosis and/or treatment of the disease in question is disclosed (26).

A different view was taken by the Committee for the Study of Inborn Errors of Metabolism of the National Academy of Sciences. It held that "under current law, genetic screeners would be ill advised to contact relatives without the screenee's explicit consent" (8).

AVAILABILITY OF AND ACCESS TO GENETIC SERVICES

Tests are already available for a multitude of conditions with a genetic component. There are numerous tests available to diagnose a preexisting genetic condition in an individual or in utero. Several States require genetic screening for certain genetic conditions in the newborn period (e.g., phenylketonuria, sickle cell anemia) (30). In addition, tests are available to identify carriers of autosomal recessive conditions such as Tay-Sachs disease. Traditionally, these tests have been used almost exclusively within the disciplines of pediatrics and obstetrics.

In the next decade, it is estimated that tests will be available to identify genetic predispositions to certain disease, such as cancer or heart disease (31). In a 1987 survey of firms developing tests, half of the respondents felt that within 5 years, demand for genetic testing would outstrip current laboratory capabilities (31).

Comprehensive diagnostic, treatment, and management services are offered to high risk or symptomatic individuals and their families at approximately 20 clinical genetic service centers throughout the United States (33). Most (63 percent) are located at university-affiliated medical centers, with some centers operating satellite clinics in rural areas. However, genetic counseling services are not readily available to everyone, particularly those unable to pay for the tests themselves.

In examining the ability of workplace monitoring and screening programs to provide adequate followup services, the following should be considered. Genetics consultations tend to require longer office-visit time than most other specialties because of the need for detailed family histories and thorough physical examinations. Considerable time may be spent explaining the diagnosis for several family members as well as providing counseling (2). In addition, there are a number of other potential barriers-geographic, financial, linguistic, cultural, and educational-to the provision of followup services. Perhaps the greatest barriers to be overcome are those related to language and cultural differences (23). Bilingual genetic counselors will be needed in increasing numbers as more immigrants come to the United States.



Photo credit: University of South Carolina School of Medicine

Genetics consultations can require longer office-visit time because of the need for gathering detailed information about the client. This genetic counselor is discussing the client's chromosome profile with her.

As tests become available to a growing number of presumably healthy Americans, the administration of diagnostic tests and subsequent treatment for an increasing number of individuals will have to be assumed by medical professionals in other areas of primary care. There are doubts within the medical community about the adequacy of medical genetics education in medical schools for students not pursuing pediatrics or obstetrics. At the very least, primary care providers need to be equipped to discuss tests results and make necessary referrals. This requires a basic understanding of genetics. Yet, in a 1985 survey, only 21 percent of U.S. medical schools were considered to have good or excellent instruction in human genetics. Forty-seven percent of the schools responding were considered to have either nonexistent or poor human genetics teaching (27).

An OTA survey of companies developing predictive tests revealed that they had little confidence in the ability of primary care physicians to inform their patients about genetic screening, arrange for tests, and interpret test results (31). There is ample evidence that physicians have difficulty interpreting results of laboratory tests more familiar to them and less complicated than genetic tests (3,6,25).

Adequate genetic services are not always provided in the most likely setting-hospitals. In a study of Huntington's disease counseling in Veterans' Administration Hospitals, less than 1 percent of

the hospitals had a formal policy regarding the provision of genetic counseling (18).

While physicians are likely to be required to administer most genetic monitoring and screening tests, they are not the only health care professionals qualified to provide genetic services. Nurses, social workers, and master's level genetic counselors frequently participate in counseling and followup programs for individuals seeking genetic services. There are currently 15 programs in the United States and Canada offering a master's in genetic counseling (34). For many years, there has been some recognition that genetics is an important feature of the nursing curriculum (4) and, yet, when nurses have been surveyed about their genetic knowledge, important gaps have been noted (37). This has important implications for job site genetic monitoring and screening, as occupational health nurses are likely to be involved.

The American Board of Medical Genetics has certified more than 1,000 providers of genetic services, of which approximately half are clinical geneticists (M.D., D. O., or D.D.S.) (28). However, certification does not necessarily test one's counseling ability. Nonphysician genetic counseling personnel have been trained since 1969 and play a critical role in delivering services in an already overburdened system. One of the rate-limiting steps in the widespread use of genetic monitoring and screening tests will be the availability of adequately trained personnel to interpret results and provide followup services.

Cost of Counseling and Additional Tests

If an employer proceeds with monitoring or screening and then refers the worker to an outside source for additional testing or followup, unless the employer is willing to pay for those services, the costs of further testing or followup may deter some employees from proceeding. When tests are coupled with prenatal diagnosis or when multiple family members need to be evaluated for linkage studies, the bill can be well over $1,000. For example, the cost for predictive testing for Huntington's disease currently ranges from $2,800 to $4,000. This includes genetic and psychological counseling, a neurological examination, as well as posttest counseling (7).

Presently, some Blue Cross/Blue Shield Plans (BC/BS) and State Medicaid programs reimburse for genetic services, although services covered and amounts reimbursable vary. Reimbursement by Medicaid is frequently less than the full charge. This is particularly true for genetic counseling, which is sometimes not reimbursed at all (12). Fewer than half of BC/BS plans reimburse for carrier screening tests, and genetic counseling is covered by less than 60 percent (11). Twenty-three of the thirty-five health maintenance organization plans provide genetic counseling as a covered benefit.

Deficiencies in reimbursement for genetic counseling in both BC/BS and Medicaid programs are in part due to the absence of an American Medical Association code for genetic counseling (which is used by insurers to guide payment) and the policy of third-party insurers of not reimbursing nonphysician genetic counselors. Nonphysician genetic counselors are likely to be a needed source for referral of individuals identified through screening and monitoring programs. The fact that genetic consultations are frequently excluded in part, or in full, from insurance coverage is a disincentive for individuals pursuing further interpretation of their test results.

As part of the OTA survey on genetic monitoring and screening practices in the workplace, questions concerning genetic counseling were asked. The following section describes these results.

Use of Genetic Counseling: Survey Results

Corporate health officers in companies (Fortune 500 and non-Fortune 500 companies) that have conducted any form of genetic monitoring or screening were asked:

> Has an employee ever been referred for genetic counseling by your company's medical staff as a result of any medical or genetic testing?

Health officers in 10 percent of those companies that had ever done genetic monitoring or screening reported that one or more employees in their companies had been referred to genetic counseling as a result of medical testing (table 8-l). Half of these companies were currently conducting some form of genetic monitoring or screening, and the other half had only tested in the past. Nearly all of the companies referring employees to genetic counselors (8 out of 9) had 10,000 or more employees.

OTA found that 6 percent of the companies that had conducted genetic monitoring or screening employed a genetic counselor. No companies re-

Table 8-l-Genetic Counseling Referrals

Q. 26. Has an employee ever been referred for genetic counseling by your company's medical staff as a result of any medical or genetic testing?

(Base: Health Officers in companies that have ever done genetic monitoring or screening)

Unweighed base	Total percent (59)
Yes	10
NO	80
Don't know[a]	5
No answer	5

a volunteered response.

SOURCE: Office of Technology Assessment, 1990.

ported contracting with a genetic counselor (table 8-2).

Table 8-2 -Company Employment of Genetic Counselors

Q. 25. Does your company employ or contract with a genetic counselor?

(Base: Health Officers in companies that have ever done genetic monitoring or screening)

Unweighed base	Total percent (59)
Employ	6
Contract with	0
Neither	89
No answer	5

SOURCE: Office of Technology Assessment, 1990.

SUMMARY AND CONCLUSIONS

Individuals who have just learned about a genetic condition through employment genetic monitoring or screening face a double dilemma. Workers may have found that they are unemployable in certain job positions (including their current one) and that their future health or that of family members may be in jeopardy.

How individuals react depends on their own life circumstances as well as the diagnosis and prognosis. Because a probability, but not a certainty, that disease may result if difficult uncertainties are introduced into the lives of those tested. The information provided prior to administration of the test can help to prepare individuals for the outcome. In addition, a genetic counselor can help the person being tested understand the concept of risk. When the test results are positive, posttest counseling and followup are essential.

An important aspect of human communication is the context in which it occurs. Workplace testing is an atypical setting for receiving information of such personal importance. The absence of referrals to trained professionals and reimbursement for the costs of additional tests or counseling may be prohibitive factors influencing an individual's ability to obtain additional information. Current resources to provide counseling may be strained as more tests are developed and made commercially available.

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Chapter 9

Genetics in the Workplace: Perceptions and Practice

The use of genetic monitoring and screening in the workplace is a multifaceted issue that has drawn scientists, ethicists, lawyers, genetic counselors, and occupational health care providers into an ongoing debate. Yet what is the extent of actual use of genetic monitoring and screening by U.S. employers and unions? Except for a 1982 Office of Technology Assessment (OTA) survey, evidence about past, present, and future genetic monitoring and screening of workers by U.S. companies and unions is anecdotal (5).

To assess the current practice of genetic monitoring and screening by U.S. employers, OTA commissioned Schulman, Ronca, & Bucuvalas, Inc. to conduct a followup survey in 1989 of current Fortune 500 companies, the 33 largest unions, and the 50 largest utilities. The comparable population surveyed by OTA in 1982 was included in this population to provide trend data. (See app. C for a discussion of the 1982 survey.) The 1989 survey was designed to include a representative sample of all other companies with 1,000 or more employees so that broader estimates of the use and pattern of genetic monitoring and screening in the workplace could be made. This chapter discusses Americans' perceptions toward genetic tests in general, examines employer practices, and reports how genetic monitoring and screening in the workplace have changed since the 1982 OTA survey.

WORKER PERCEPTIONS OF GENETIC MONITORING AND SCREENING

Assessing worker attitudes, about genetic monitoring and screening was not possible for this report. Other recent studies, however, have examined attitudes (e.g., regarding risk v. benefit) and understanding of the general American public toward science and technology (2,3,4). Specifically, the results of a 1986 OTA nationwide survey on public perceptions of human genetics could shed light on the general attitude of Americans toward genetic tests (4). For example, in response to the question:

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

Eighty-nine percent of the American populace said they approved, while 9 percent said they disapproved of having such tests available through physicians (table 9-l).

The 1986 OTA survey did not probe American attitudes toward genetic tests and their availability through employers, but approval likely would be lower than tests through private physicians. In fact, a November 1985 *Business* Week-Lou Harris nationwide survey posed the question:

> Even though they might not be able to cure a genetic disease, scientists will be able to test people to find out if they are likely to come down with one-as much as 20 years before it happens. Do you feel that an employer should have the right to make [sic] such tests before hiring someone, or not?

Eighty-nine percent of adult Americans answered that employers should not have the right to use such tests for hiring decisions. Furthermore, 82 percent of respondents felt an employer's knowledge of a job applicant's potential to have a serious disease in the future was not acceptable grounds for that candidate to be denied work. The survey also asked:

> Using the same kind of [genetic] testing, an employer may soon be able to tell how vulnerable an employee is to having a heart attack or stroke as a result of being put in a stressful work situation. Do you feel an employer should be able or not to bar people who do poorly on such tests from certain kinds of jobs?

Table 9-l—Availability of Genetic Tests From Physicians[a]

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

	Percent
Approve	89
Disapprove	9
Not sure	2

a percentages are presented as weighted sample estimates. The unweighed base from which the sampling variance can be calculated is 1,273.

SOURCE: Office of Technology Assessment, 1987.

Thirty-five percent of Americans felt employers should be able to exclude individuals from certain jobs based on the results of such a test. And 21 percent of respondents felt that insurance companies would be justified in using genetic tests to refuse life or health insurance coverage. The *Business Week*-Lou Harris poll found that if genetic testing was not linked to employment or insurance decisions, about 50 percent of respondents were willing to be tested for incurable and fatal diseases they would develop later in life (l).

Similarly, the 1986 OTA survey explored the kinds of genetic tests Americans would be inclined to use, if available. Two-thirds of the public said they would take a test to determine whether they are likely to develop a fatal disease later in life, if such a test becomes widely available (table 9-2). Greater than 8 of 10 Americans (83 percent) reported they would use a genetic test before having children, if such a test would tell them whether their children would probably inherit a fatal genetic disease (table 9-3). And, perhaps in a measure of how workers would accept genetic monitoring and screening to benefit their own health outlook, the 1986 OTA survey found members of the general public said they were less likely to take tests to determine their own proclivity to a fatal genetic disease than to prevent heritable diseases in their offspring.

In general, the overall rate of acceptance by Americans of biotechnology, including human genetic applications, increases with the likelihood of personal benefit (4). Thus, worker attitudes toward genetic monitoring and screening to benefit personal health could be higher, if the testing were perceived to be in the individual's self-interest, not linked to corporate interests and employment decisions.

Table 9-2—Using Genetic Tests for Personal Health[a]

Question: If genetic tests become available that would indicate whether or not a person was likely to develop a fatal disease later in life, would you personally take such a test or not?

	Percent
Would take test	66
Would not take test	29
Not sure	4

a percentages are presented as weighted sample estimates. The unweighed base from which the sampling variance can be calculated is 1,273.

SOURCE: Office of Technology Assessment, 1987.

Table 9-3—Using Genetic Tests Before Having Children[a]

Question: If genetic tests become available that would indicate whether or not it was likely that your children would inherit a fatal genetic disease, would you personally take such a test before having children or not?

	Percent
Would take test	83
Would not take test	15
Not sure	3

a percentages are presented as weighted sample estimates. The unweighed base from which the sampling variance can be calculated is 1,273.

SOURGE: Office of Technology Assessment, 1987.

STUDY DESIGN

The 1989 OTA survey was designed to provide comparability to the 1982 survey in terms of the populations sampled and the questionnaire content. At the same time, the survey was designed to go beyond the 1982 survey by sampling additional populations (non-Fortune 500 companies with 1,000 or more employees) and expanding the questionnaire content. (See app. B for a discussion of the survey methodology.)

Definition of Genetic Monitoring and Screening

For purposes of the 1989 survey, genetic monitoring and screening were defined for respondents as follows:

> By *genetic monitoring, we* mean periodically examining employees to evaluate modifications of their genetic material via tests such as cytogenetic or direct-DNA tests. By *genetic screening, we* mean screening job applicants or employees for certain inherited characteristics. Screening tests may be biochemical tests or direct-DNA tests. They can be used to indicate a predisposition to an occupational illness if exposed to a specific environmental agent, or they could be used to detect any inherited characteristic such as Huntington's disease. In contrast to periodic monitoring, screening tests are generally performed one time per characteristic.

In addition, the series of questions on genetic monitoring and screening practices were preceded by this explanation:

> The following questions concern cytogenetic monitoring and/or biochemical genetic screening that may have been conducted by your company on one or more employees or job applicants. By

conduct, we mean perform, contract for, or arrange for the test as part of a routine or ongoing program.

The 1982 survey defined genetic monitoring and screening in a similar but less detailed fashion. Unlike the 1989 survey, the 1982 survey had no item covering the use of genetic monitoring or screening for diagnosis. The 1982 survey defined biochemical genetic screening as tests that screen "healthy, asymptomatic individuals." The 1989 survey contained no such requirement. Other differences in question wording are described in the following section.

The Questionnaire

The scope of the 1982 survey questionnaire was limited to measures of the frequency of past, present, and anticipated genetic monitoring and screening; which tests were used and under what circumstances; how the results were used; and the criteria against which tests have been measured to determine acceptability for use. Nearly all of these questions were repeated in the 1989 survey to measure change in corporate practice over time.

In order to flesh out the details of the survey data, OTA added questions that explored the use of genetic monitoring and screening in more depth. The additional questions not covered by the 1982 survey specifically asked about genetic monitoring and screening tests that may have been conducted as part of a voluntary wellness program, at the request of the employee, or for diagnosis. These questions were not part of the 1982 survey. Including the results of the new questions produced a broader definition of genetic monitoring and screening. Questions were also added to cover current use of direct-DNA monitoring and direct-DNA screening tests.

The wording of the trend questions on the 1989 survey instrument concerning current and past use of genetic monitoring and screening tests was changed slightly from 1982 to make the language more specific. For example, the survey asked whether genetic monitoring or screening tests were conducted "for research or any other reason," a phrase not present in the 1982 survey. Questions on genetic monitoring and screening practices were changed from asking about monitoring and screening of "employees or potential employees" to monitoring and screening of "any employees or job applicants. OTA believes the increased specificity attained an accurate measure of genetic monitoring and screening in 1989, established a firm base for future comparisons, and preserved general comparability to the 1982 survey.

The 1989 questionnaire was also modified to provide increased details on the use of specific genetic monitoring and screening tests. The 1982 survey asked about current or past use of four general types of biochemical genetic screening tests. In comparison, the 1989 survey asked about current use of 16 specific biochemical genetic screening tests. Similarly, the 1982 survey asked about current or past use of five types of cytogenetic monitoring tests, while the 1989 survey asked about current use of seven types of cytogenetic monitoring tests.

Health officers in companies that had conducted any genetic monitoring or screening tests were asked which specific tests their companies had conducted. It should be noted that some health officers who reported that their companies had never used genetic monitoring or screening, including testing as part of a voluntary wellness program, at employee request or for diagnosis, *did* report that their companies had conducted a specific genetic screening test. For example, some health officers who reported no corporate experience with genetic monitoring or screening also reported that their companies were testing for sickle cell trait. Thus, counting affirmative answers to specific genetic screening tests further expanded the number of companies reporting any use of genetic monitoring or screening.

GENETIC MONITORING AND SCREENING: U.S. CORPORATIONS AND UNIONS

Before presenting the trend data from 1982 to 1989, there will first be a discussion of current, past, and combined use of genetic monitoring and screening. Following those sections, the overall and future use of genetic monitoring and screening in 1989 and 1982 will be discussed.

Current Use of Genetic Monitoring

The one company reporting current use of cytogenetic monitoring in 1989 was a petroleum firm with more than 10,000 employees (table 9-4). No health officer from Fortune 500 companies surveyed in 1989 reported conducting direct-DNA monitoring, either at the time of the survey or in the past.

Table 9-4-Current Use of Genetic Monitoring by Fortune 500 Companies

Q.15. Is your company currently conducting *cytogenetic monitoring* of any employees or job applicants, for research or any other reason?

Q.18. Is your company currently conducting *direct-DNA monitoring* of any employees or job applicants, for research or any other reason?

(Base: Health officers)

	Number of companies currently conducting	
	Cytogenetic monitoring	Direct-DNA monitoring
Total	1	0
Type of business		
Electrical utility	0	0
Pharmaceutical	0	0
Other chemical	0	0
Petroleum	1	0
Electronic	O	0
Other manufacturing	0	0
Nonmanufacturing	0	0
Number of employees		
Less than 5,000	O	0
5,000-9,999	0	0
10.000 or more	1	0

SOURCE: Office of Technology Assessment, 1990.

Table 9-5-Current Use of Genetic Screening by Fortune 500 Companies

Q.13. Is your company currently conducting *biochemical genetic* screening of any employees or job applicants, for research or any other reason?

Q.17. Is your company currently conducting *direct-DNA screening* of any employees or job applicants, for research or any other reason?

(Base: Health officers)

	Number of companies currently conducting	
	Biochemical genetic screening	Direct-DNA screening
Total	12	0
Type of business		
Electrical utility	0	0
Pharmaceutical	0	0
Other chemical	4	0
Petroleum	1	0
Electronic	O	0
Other manufacturing	2	0
Nonmanufacturing	5	0
Number of employees		
Less than 5,000	1	0
5,000-9,999	2	0
10,000 or more	9	0

SOURCE: Office of Technology Assessment, 1990.

Questions relating to direct-DNA monitoring were not asked in 1982.

Current Use of Genetic Screening

The OTA survey found that in 1989, 12 companies reported current biochemical genetic screening. Of these 12 companies, 4 represented the chemical industry, 1 represented the petroleum industry, 2 represented other types of manufacturers, and 5 represented other nonmanufacturing companies. None of the 12 companies was an electric utility, pharmaceuticals firm, or electronics firm (table 9-5). Companies conducting genetic screening were disproportionately large fins, including 9 with 10,000 or more employees, 2 with 5,000 to 9,999 employees, and 1 with less than 5,000 employees. No health officers reported current use of direct-DNA screening by their companies. Questions relating to direct-DNA screening were not asked in 1982.

Past Uses of Genetic Monitoring

The 1989 survey asked health officers whether their companies had conducted genetic monitoring tests in the past 19 years, for research or any other reason. Five health officers in Fortune 500 companies reported that their companies had conducted cytogenetic monitoring in the past 19 years of any employees or job applicants, for research or any other reason (table 9-6). All 5 companies that formerly conducted cytogenetic monitoring reported no current use of genetic monitoring or screening, and all 5 had 10,000 or more employees. One was a chemical company, one was another type of manufacturer, and the other three were nonmanufacturing fins. None of the five was an electric utility, pharmaceutical company, petroleum company, or electronics firm.

Past Uses of Genetic Screening

A total of eight health officers in the Fortune 500 companies reported that their companies had conducted biochemical genetic screening of any employees or job applicants in the past 19 years (table 9-7). This included four health officers in Fortune 500 companies that reported they were currently conducting biochemical genetic screening.

The 8 health officers who reported that biochemical genetic screening was conducted by their companies in the past 19 years were disproportionately from large companies, with 7 in companies with 10,000 or more employees, and 1 in a company with 5,000 to 9,999 employees. Four were in the chemical

Table 9-6—Past Use of Genetic Monitoring Tests by Fortune 500 Companies

Q.16. Has your company conducted any cytogenetic *monitoring* of any employees or job applicants, for research or any other reason in the past 19 years?
(Base: Health officers)

	Number of companies conducted in past
	Cytogenic monitoring
Total	5
Type of business	
Electrical utility	0
Pharmaceutical	0
Other chemical	1
Petroleum	0
Electronic	0
Other manufacturing	1
Nonmanufacturing	3
Number of employees	
Less than 5,000	0
5,000-9,999	0
10,000 or more	5

SOURCE: Office of Technology Assessment, 1990.

Table 9-7—Past Use of Genetic Screening Tests by Fortune 500 Companies

Q.14. Has your company conducted any *biochemical genetic screening* of any employees or job applicants, for research or any other reason in the past 19 years?
(Base: Health officers)

	Number of companies conducted in past
	Biochemical genetic screening'
Total	8
Type of business	0
Electrical utility	
Pharmaceutical	0
Other chemical	4
Petroleum	0
Electronic	0
Other manufacturing	2
Nonmanufacturing	2
Number of employees	
Less than 5,000	0
5,000-9,999	1
10,000 or more	7

'NOTE: Includes companies currently conducting genetic screening.
SOURCE: Office of Technology Assessment, 1990.

industry, two were in other manufacturing companies, and two were in nonmanufacturing firms.

Combined Genetic Monitoring and Screening: 1989 Survey Results

A total of 20 health officers reported that their companies had conducted cytogenetic monitoring or biochemical genetic screening, either currently or in the past 19 years. This includes 12 health officers who reported that genetic monitoring or screening was currently conducted, and 8 who reported that genetic monitoring or screening had been conducted in the past 19 years, but not currently (table 9-8).

Six Fortune 500 health officers reported that their companies had conducted cytogenetic monitoring, either currently or in the past 19 years. One was in a company currently conducting cytogenetic monitoring, while five were in companies that had conducted cytogenetic monitoring in the past 19 years, but no longer conducted such monitoring.

Sixteen Fortune 500 health officers reported that their companies had conducted biochemical genetic screening, either currently or in the past 19 years. Twelve health officers reported their companies currently conducted genetic screening, while four were in companies that conducted genetic screening in the past 19 years, but not at the present time.

Overall Use of Genetic Monitoring and Screening in 1989 and 1982

Trend data on the use of genetic monitoring or screening can be obtained by tabulating comparable questions in the 1989 and 1982 surveys. These are general questions dealing with the use of genetic monitoring or screening, and do not include items added in 1989 on genetic monitoring or screening as part of a voluntary wellness program, at the request of an employee, or for diagnosis. Using this narrow definition, the 1989 survey found a total of 20 health officers in the Fortune 500 sample who reported that their companies had conducted genetic monitoring or screening, either currently or in the past 19 years. In comparison, the 1982 survey found 18 health officers in the Fortune 500 companies who reported current or past use of genetic monitoring or screening (table 9-9). These figures suggest little change between 1982 and 1989 in the number of companies that had used genetic monitoring or screening in the workplace.

In the 1982 survey, six health officers (1.6 percent) reported their companies currently conducted genetic monitoring or screening. In 1989, 12 health officers (5 percent) reported their companies currently conducted genetic monitoring or screening. (These numbers do not directly correlate because of different sized survey populations in 1982

Table 9-8-Combined Testing: Current v. Past Monitoring and Screening by Fortune 500 Companies

(Base: Health officers)

	Number of companies
Conducted genetic monitoring or screening for research or any other reason, at present or in past 19 years	20
Currently conducting genetic monitoring or screening	12
Conducted monitoring or screening in past only	8
Conducted genetic screening for research or any other reason at present or in past 19 years	16
Currently conducting genetic screening	12
Conducted genetic screening in past only	4
Conducted cytogenetic monitoring for research or any other reason at present or in past 19 years	6
Currently conducting cytogenetic monitoring	1
Conducted cytogenetic monitoring in past only	5
Currently conducting direct-DNA screening for research or any other reason	0
Currently conducting direct-DNA monitoring for research or any other reason	*0*

SOURCE: Office of Technology Assessment, 1990.

and 1989.) The increase in the number of "current users" in 1989 could reflect slight differences in question wording between the two surveys.

Of the six companies that reported current use of genetic monitoring or screening in 1982, two were in the chemical industry, two were electric utilities, and two were in the electronics industry. In 1989, 12 companies reported current use of genetic monitoring or screening. Of those, all 12 conducted genetic screening, while one also conducted cytogenetic monitoring, Of the companies reporting current use of genetic screening four were in the chemical industry, one in the petroleum industry, two were other types of manufacturers, and five were other nonmanufacturing companies. None of the 12 companies was an electric utility or electronics firm. The petroleum firm was the only company also reporting current use of cytogenetic monitoring of any employees or job applicants in 1989.

No health officer from Fortune 500 companies surveyed in 1989 reported conducting direct-DNA monitoring or direct-DNA screening, either at the time of the surveyor in the past. No question related to direct-DNA monitoring and direct-DNA screening was asked in 1982.

Table 9-9—Use of Genetic Monitoring or Screening: 1989 v. 1982 Survey Results

(Base: Health officers)

	Number of companies	
	1989	1982
Conducted genetic monitoring or screening for research or any other reason, at present or in the past*	20	18
Currently conducting genetic monitoring or screening	12	6
Conducted monitoring or screening in past only	8	12

*Defined as past 19 years in 1989 survey and past 12 years in 1982 survey.
SOURCE: Office of Technology Assessment, 1990.

In summary, in the 1989 survey 12 companies reported current use of genetic monitoring or screening, while 8 companies reported conducting genetic monitoring or screening in the past but were no longer conducting such tests. The ratio of current to past monitoring and screening was reversed in 1982, with 6 companies indicating current use of genetic monitoring or screening and 12 companies indicating past but not current use of monitoring or screening. overall, OTA found that 20 companies had used genetic monitoring or screening in 1989, as compared to 18 companies in 1982.

General Use of Genetic Monitoring and Screening Tests

A total of 27 health officers in Fortune 500 companies reported current or past use of genetic monitoring or screening tests of any employees or job applicants, for any reason, including research, as part of a voluntary wellness program, or for diagnosis (table 9-10). In addition, one personnel officer from a company not represented by the health officers who returned surveys reported use of genetic monitoring or screening. Thus, a total of 28 companies in the 1989 Fortune 500 sample reported current or past use of genetic monitoring or screening tests.

Health officers reporting any experience with genetic monitoring or screening included 17 who reported that their companies were currently conducting genetic monitoring or screening, and 10 who reported that their companies had conducted genetic monitoring or screening in the past, but were not currently conducting either. (Of those 17 companies, 5 are currently testing.) None reported current or past

Table 9-10-Summary Data on Use of Genetic Monitoring and Screening: 1989 Results Among Fortune 500 Companies

(Base: Health officers)

	Number of companies
Conducted genetic monitoring or screening for research or any other reason, at present or in past 19 years, *including as* part of a voluntary wellness program, at the request of the employee, or for diagnosis	27
Currently conducting genetic monitoring or screening	17
Conducted monitoring or screening in past only	10
Conducted direct-DNA screening or direct-DNA monitoring. currently or in the past	0

SOURCE: Office of Technology Assessment, 1990.

use of either direct-DNA monitoring or direct-DNA screening by his or her company.

However, a number of health officers who reported no current or past use of genetic monitoring or screening tests, including testing for voluntary wellness programs, at employee request, and for diagnosis, did report use of specific genetic screening tests listed in the survey. Thus, responses to general questions on genetic monitoring and screening appeared to somewhat understate the prevalence of these tests. Total use of genetic monitoring and screening is discussed in the next section.

Total Use of Genetic Monitoring or Screening

A total of 33 health officers from the Fortune 500 companies reported that their companies had used any type of genetic monitoring or screening, either currently or in the past (table 9-11). In other words, 13 percent of the health officers from Fortune 500 companies responding to the survey reported that their companies had used some type of genetic monitoring or screening, either currently or in the past. This measure of genetic monitoring or screening included testing as part of a voluntary wellness program, at the request of the employee, or for diagnosis. It also included health officers who reported that their companies conducted one or more specific biochemical genetic screening tests or cytogenetic monitoring tests.

Counting all health officers from Fortune 500 companies who reported that their companies had conducted genetic monitoring or screening, in one

Table 9-1 l—Total Prevalence of Genetic Monitoring or Screening: 1989 Survey Results Among Fortune 500 Companies

(Base: Health officers)

	Number of companies with any current or past use of genetic monitoring or screening
Total	33
Number of employees	
Less than 5,000	3
5,000-9,999	3
10,000 or more	27
Type of business	
Electrical utility	0
Pharmaceutical	3
Other chemical	11
Petroleum	3
Electronic	0
Other manufacturing	5
Nonmanufacturing	11

SOURCE: Office of Technology Assessment, 1990.

form or another, produced the most accurate measure of the total- use of genetic monitoring or screening in 1989. It appears likely that the 1982 survey probably understated the prevalence of genetic monitoring and screening at that time, because that questionnaire included a more limited set of items on the use of genetic monitoring and screening. As the results from the 1989 survey indicate, a fuller battery of questions likely detected all forms of genetic monitoring and screening.

Twenty-seven of the thirty-three health officers surveyed in 1989 who reported that their companies had conducted genetic monitoring or screening were in large companies with 10,000 or more employees. Of the 33, 11 were in chemical companies, 3 were in pharmaceutical fins, 3 were in petroleum companies, 5 were in other manufacturing companies, and 11 were in nonmanufacturing firms.

The findings of the 1989 survey suggest that the 1982 survey may have underestimated the actual prevalence of workplace use of the technology at that time. The 1989 survey asked about past and present use of genetic monitoring and screening in a number of different contexts—screening to identify increased susceptibility to workplace risk, as part of a voluntary wellness program, at the request of the employee, and for diagnosis—in addition to the set of questions used in 1982. When all reports of genetic monitoring and screening were taken into account, the number of companies that had used genetic monitoring or screening increased to 33 from

18 companies in 1982. The larger number of companies identified as using genetic tests appeared to be almost entirely the result of additional questions about the use of genetic monitoring or screening, rather than changes in industry practices. Using the comparable measures, the number of companies that had ever conducted genetic monitoring or screening had only increased from 18 in 1982 to 20 in 1989.

Future Use of Genetic Monitoring and Screening

If there has been little or no real growth in the number of companies conducting genetic monitoring and screening in the workplace, what do companies foresee for the future? The 1982 OTA survey found that 4 companies (1.1 percent) anticipated using the tests in the next 5 years, and 55 companies (15 percent) stated they would ' 'possibly" use the tests in the next 5 years. In order to avoid classifying an indefinite response as a positive response to future genetic monitoring or screening, the 1989 survey provided the response categories "yes," "no," and "not sure' for the same questions.

OTA found one Fortune 500 company that anticipated cytogenetic monitoring, one company that anticipated direct-DNA monitoring, and four companies that anticipated biochemical genetic screening. No company anticipated using direct-DNA screening in the next 5 years. Twenty-seven companies in 1989 indicated they were not sure whether they anticipated cytogenetic monitoring, and 27 were not sure whether they anticipated direct-DNA monitoring. For biochemical genetic screening, 25 companies were not sure whether they anticipated using it, and 23 were not sure about future direct-DNA screening (table 9-12).[1] In 1982, 55 companies said they would possibly use such test in the next 5 years. Although this number cannot be directly compared to the current survey, the 1989 OTA survey appear-s to indicate fewer companies anticipate using genetic monitoring or screening.

Intervening events offered another possible explanation for the absence of expected growth since 1982 in industry adoption of the technology of genetic monitoring and screening in the workplace. Specifically, the experience of other employers with genetic monitoring and screening-publicity, criticism, employee problems—might have dissuaded some prospective users from adopting the technology. However, the survey found fewer than 10 cases among Fortune 500 companies that had never used genetic monitoring or screening in the past, reporting that they had chosen not to use such tests as a result of the experiences of other companies.

Genetic Monitoring for Other Reasons: 1989 Survey Results

Questions added to the 1989 survey covered applications of genetic monitoring that had not been specifically covered in the 1982 survey. Some health officers reporting that their companies conducted genetic monitoring and screening for these purposes, however, did not report that their companies conducted genetic monitoring or screening "of any employees or job applicants, for research or any other reason.

One health officer reported past use of cytogenetic monitoring at employee request and one reported past use of cytogenetic monitoring as part of a voluntary wellness program. One health officer reported current use of cytogenetic monitoring for diagnosis and one reported past use of cytogenetic monitoring for diagnosis (table 9-13).

Genetic Screening for Other Reasons: 1989 Survey Results

Questions added to the 1989 survey covered applications of genetic screening that had not been specifically covered in the 1982 survey. Current use of genetic screening was reported by two companies for voluntary wellness, eight companies at employee request, and seven for diagnosis (table 9-14). These figures may overlap, since health officers were asked to report all types of genetic screening conducted by their companies. Past use of genetic screening for voluntary wellness was reported by four health officers, while five health officers reported past use of genetic screening at employee request, and three health officers reported past use of genetic screening for diagnosis.

[1]These numbers cannot be added because of cross counting; nor do they directly correlate to th55 companies because Of question wording. In retrospect, those who chose 'possibly' in 1982 might not have meant to indicate that genetic monitoring or screening was anticipated, they simply could not rule out the possibility they would use it in the future.

Table 9-1 2—Consideration To Conduct Genetic Monitoring and Screening in the Next Five Years: Health Officers

Q.33. Does your company anticipate conducting any biochemical genetic screening, for any reason, in the next 5 years?

Q.34. Does your company anticipate conducting any cytogenetic monitoring, for any reason, in the next 5 years?

Q.35. Does your company anticipate conducting any *direct-DNA screening,* for any reason, in the next 5 years?

Q.36. Does your company anticipate conducting any *direct-DNA monitoring,* for any reason, in the next 5 years?

(Base: Health officers)

	Percent			
	Yes	No	Not sure	No answer
Biochemical genetic screening	4	218	25	3
Cytogenetic monitoring	1	219	27	3
Direct-DNA screening	0	224	23	3
Direct-DNA monitoring	1	218	27	4

SOURCE: Office of Technology Assessment, 1990.

Specific Types of Cytogenetic Monitoring Conducted in 1989

As with genetic screening, the 1989 survey asked health officers in companies that had conducted cytogenetic monitoring to list which specific types of monitoring were being conducted. The survey covered seven categories of cytogenetic tests. For each test conducted, health officers were asked to give the reason their companies were conducting the test. The only cytogenetic tests reported were those testing for chromosomal aberrations and sister chromatid exchanges. No health officer reported testing for mutations by assaying the DNA, enzymes/proteins, hypoxanthine-guanine phosphoribosyltransferase (HPRT) mutation rate, DNA adduct formation, or by using other cytogenetic tests (table 9-15).

Only two reasons were reported for cytogenetic monitoring: 1) testing as part of a voluntary research program, and 2) testing as part of followup diagnosis. No health officers reported conducting cytogenetic monitoring as part of routine health surveillance, as part of a voluntary wellness program, or at employee request. Moreover, only one health officer reported conducting cytogenetic monitoring for followup diagnosis. Genetic monitoring for a voluntary research program was reported by three health officers in companies monitoring for chromosomal aberrations and three in companies monitoring for sister chromatid exchanges.

Table 9-13-Prevalence of Genetic Monitoring for Voluntary Wellness Programs at Employee Request and for Diagnosis: Fortune 500 Companies

Q.19. Has your company conducted any of the following tests (biochemical genetic screening, cytogenetic monitoring, direct-DNA screening, direct-DNA monitoring), as part of a voluntary wellness program, at the request of an employee, or for diagnosis? (MARK ALL THAT APPLY)

(Base: Health officers)

	Number of companies	
	Cytogenetic monitoring	Direct-DNA monitoring
As part of voluntary wellness program		
Currently	0	0
In past 19 years	1	0
No	113	114
Not sure	3	2
No answer/not applicable	132	133
At *the request of the employee*		
Currently	0	0
In past 19 years	1	0
No	111	111
Not sure	4	4
No answer/not applicable	133	134
For diagnosis		
Currently	1	0
In past 19 years	1	0
No	107	108
Not sure	9	9
No answer/not applicable	131	132

SOURCE: Office of Technology Assessment, 1990.

Specific Types of Genetic Screening Tests Conducted in 1989

The 1989 survey asked health officers in companies that had ever done biochemical genetic screening tests to list which specific genetic screening tests were being conducted, and for each, to indicate the

Table 9-14-Prevalence of Genetic Screening for Voluntary Wellness Programs, at Employee Request and for Diagnosis: Fortune 500 Companies

Q.19. Has your company conducted any of the following tests (biochemical genetic screening, cytogenetic monitoring, direct-DNA screening, direct-DNA monitoring), as part of a voluntary wellness program, at the request of an employee, or for diagnosis? (MARK ALL THAT APPLY)

(Base: Health officers)

	Number of companies	
	Biochemical genetic screening	Direct-DNA screening
As part of voluntary wellness program		
Currently	2	0
In past 19 years	4	0
No	127	113
Not sure	3	3
No answer/not applicable	113	133
At the request of the *employee*		
Currently	8	0
In past 19 years	5	0
No	116	111
Not sure	6	4
No answer/not applicable	114	134
For diagnosis		
Currently	7	0
In past 19 years	3	0
No	116	108
Not sure	12	9
No answer/not applicable	111	132

SOURCE: Office of Technology Assessment, 1990.

purpose of the test. A total of 16 specific biochemical genetic screening tests were covered by the 1989 survey.

Genetic screening tests cited most frequently as being conducted by Fortune 500 companies included: contact dermatitis, sickle cell trait, allergic respiratory disease, serum alpha-l-antitrypsin deficiency, alpha and beta thalassemias, and glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. Other genetic screening tests cited by one or two health officers included methemaglobin reductase deficiency, aryl hydrocarbon hydroxylase inducibility, slow v. fast acetylation, histocompatibility markers, other immune system markers, Bloom syndrome, and xeroderma pigmentosum. None reported conducting biochemical screening tests for Fanconi syndrome, ataxia-telangiectasia, or other heterozygous chromosomal instabilities (table 9-16).

The 1989 survey asked whether the specific biochemical screening tests were being conducted on a routine basis for health surveillance, as part of a voluntary research program, as part of followup diagnosis, as part of a voluntary wellness program, or at the request of an employee. Obtaining a followup diagnosis and responding to an employee request were the two reasons given most often for conducting biochemical genetic screening. Followup diagnosis was cited by 13 health officers in companies testing for contact dermatitis, 11 in companies testing for allergic respiratory disease, 7 in companies testing for serum alpha- 1-antitrypsin deficiency, 6 in companies testing for sickle cell trait, and 6 in companies testing for alpha and beta thalassemias. Genetic screening at employee request was listed by 12 health officers in companies testing for sickle cell trait and 5 in companies testing for allergic respiratory disease. In addition, testing as part of routine health surveillance was reported by six health officers in companies testing for allergic

Table 9-15—Types of Cytogenetic Monitoring Conducted in 1989 by Fortune 500 Companies

Q.21. Which of the following types of cytogenetic monitoring are being conducted by your company of any employees?

(Base: Health Officers in companies that have conducted cytogenetic monitoring)

	Number of companies				
	Routine health surveillance	Voluntary research program	Followup diagnosis	Voluntary wellness program	At employee request
Chromosomal aberrations	0	3	1	0	0
Sister chromatid exchanges	0	3	0	0	0
Mutations by assaying the DNA	0	0	0	0	0
Mutations by assaying the enzyme/protein	0	0	0	0	0
HPRT mutation rate	0	0	0	0	0
DNA adduct formation	0	0	0	0	0
Other (specify)	0	0	0	0	0

SOURCE: Office of Technology Assessment, 1990.

Table 9-16-Types of Biochemical Genetic Screening Conducted by Fortune 500 Companies

Q.20. **Which of the following types of biochemical screening tests are being conducted by your company of any employees or job applicants? For each test conducted, mark whether the testing is being done on a routine basis for health surveillance, as part of a-voluntary research program, as part of followup diagnosis, or only at the request of an employee.**

(Base: Health officers)

	Number of companies				
	Routine health surveillance	Voluntary research program	Followup diagnosis	Voluntary wellness program	At employee request
Sickle cell trait	1	0	6	3	12
Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency	0	1	3	2	3
Methemaglobin reductase deficiency	1	0	0	1	0
Serum alpha-1 -antitrypsin deficiency	1	0	7	2	4
Alpha and beta thalassemias	0	0	6	2	4
Aryl hydrocarbon hydroxylase (AHH) inducibility	0	0	0	1	0
Slow v. fast acetylation	0	0	0	1	0
Allergic respiratory disease	6	1	11	1	5
Contact dermatitis	5	1	13	1	4
Histocompatibility markers (HLA).	0	0	0	1	0
Other immune system markers	0	0	1	0	1
Bloom syndrome	0	0	0	1	0
Fanconi syndrome	0	0	0	0	0
Ataxia-telangiectasia	0	0	0	0	0
Xeroderma pigmentosum	0	0	1	0	0
Other heterozygous chromosomal instabilities	0	0	0	0	0

SOURCE: Office of Technology Assessment, 1990.

respiratory disease and five health officers in companies testing for contact dermatitis.

As previously noted, some health officers who reported that their companies conducted *specific* biochemical genetic screening tests did *not* report that their companies had conducted genetic monitoring or screening, at present or in the past 19 years, including testing for voluntary wellness programs, at employee request, or for diagnosis. Each of the following genetic screening tests was reported as being currently conducted by more than one health officer who reported no current or past genetic monitoring or screening tests: sickle cell trait, serum-1-antitrypsin deficiency, allergic respiratory disease, and contact dermatitis (table 9-17). In addition, each of the following tests was reported as being currently conducted by one health officer who had reported no current or past use of genetic screening or monitoring: G-6-PD deficiency, alpha and beta thalassemias, and xeroderma pigmentosum.

Reasons for Conducting Genetic Monitoring and Screening

Personnel officers in the Fortune 500 companies that conducted genetic monitoring or screening were asked: "To the best of your knowledge, which of the following were important factors in the decision to conduct genetic monitoring or screening of employees in your company?" Six possible reasons for conducting genetic monitoring or screening were listed. Only six personnel officers responded to this set of questions.

Four of the six personnel officers in companies conducting genetic monitoring and screening reported that cost-benefit analysis was an important factor in the decision by their companies to conduct genetic monitoring or screening of employees (table 9-18). Four personnel officers also reported that the evidence of a possible association between chemical exposure and illness in epidemiological studies was an important reason in the decision by their compa-

Table 9-17-Specific Biochemical Genetic Screening Tests Reported by Companies Reporting No Genetic Monitoring or Screening Among Fortune 500 Companies

Q.20. Which of the following types of biochemical screening tests are being conducted by your company of any employees or job applicants?

(Base: Health officers in companies reporting *no* monitoring or screening)

	Number of companies				
	Routine health surveillance	Voluntary research program	Followup diagnosis	Voluntary wellness program	At employee request
Sickle cell trait	0	0	1	1	2
Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency	0	0	0	1	0
Methemaglobin reductase deficiency	0	0	0	0	0
Serum alpha-1-antitrypsin deficiency	0	0	1	1	1
Alpha and beta thalassemias	0	0	0	1	0
Aryl hydrocarbon hydroxylase (AHH) inducibility	0	0	0	0	0
Slow v. fast acetylation	0	0	0	0	0
Allergic respiratory disease	0	0	4	0	1
Contact dermatitis	0	0	4	0	1
Histocompatibility markers (HLA)	0	0	0	0	0
Other immune system markers	0	0	0	0	0
Bloom syndrome	0	0	0	0	0
Fanconi syndrome	0	0	0	0	0
Ataxia-telangiectasia	0	0	0	0	0
Xeroderma pigmentosum	0	0	1	0	0
Other heterozygous chromosomal instabilities	0	0	0	0	0

SOURCE: Office of Technology Assessment, 1990.

nies to conduct genetic monitoring and screening of employees.

In addition, three personnel officers reported that the legal consequence of a failure to test was an important reason in the decision to conduct genetic monitoring or screening. One personnel officer reported that evidence of a possible association between chemical exposure and illness in animal studies was an important factor, and one personnel officer reported that union or employee initiative was an important factor in the decision to conduct genetic monitoring or screening. None of the six personnel officers reported "something else" as an important factor in the decision to conduct genetic monitoring and screening.

Actions Taken as a Result of Genetic Monitoring or Screening

The survey found relatively few instances of negative personnel decisions as a result of genetic monitoring or screening. Only one corporate personnel officer for the Fortune 500 companies reported ever rejecting a job applicant, primarily or partly, based on the results of a genetic screening test. Similarly, a single corporate health officer reported ever suggesting an employee seek a job elsewhere, as a result of a genetic monitoring or screening program. (In 1982, a comparable two companies reported that they had suggested an employee seek a job elsewhere.)

No instances were reported by personnel officers from Fortune 500 companies in the 1989 survey of cases in which employees were transferred or terminated, primarily or partly, based on the results of genetic monitoring or screening. Health officers in three Fortune 500 companies, however, reported that their companies, as a result of a genetic monitoring or screening program, had transferred or placed employees in different jobs within their companies. This is comparable to the five companies that reported transferring employees in the 1982 survey.

Although instances of genetic monitoring and screening were rare, the health officers in Fortune 500 companies that had done it were at least as likely to report that the genetic monitoring and screening

Table 9-18-Factors in the Decision To Conduct Genetic Monitoring or Screening of Employees Among Fortune 500 Companies

Q.13. To the best of your knowledge, which of the following were important factors in the decision to conduct genetic monitoring or screening of employees in your company? (Base: Personnel officers answering question)

	Number of personnel officers		
	Unweighed base	Important	Not important
Cost-benefit analysis	(6)	4	2
Evidence of a possible association between chemical exposure and illness in animal studies	(6)	1	5
Evidence of a possible association between chemical exposure and illness in epidemiological studies	(6)	4	2
Legal consequence of failure to test	(6)	3	3
Union/employee initiative.	(6)	1	5
Something else (please specify)	(1)	o	1

SOURCE: Office of Technology Assessment, 1990.

had resulted in changes in the workplace, as had resulted in changes in workers. A number of health officers reported that, as a result of genetic monitoring and screening programs, their companies had:

- recommended personal protection devices (five in 1989, compared to three in 1982);
- implemented engineering controls (four in 1989, compared to two in 1982);
- implemented a research program (four in 1989, compared to one in 1982); or
- discontinued a product or changed materials in a product (two in 1989, compared to one in 1982).

In Summary, only a small proportion of companies had conducted any form of genetic monitoring or screening, and such monitoring and screening, in most cases, had not generated personnel action against employees or changes in the workplace. The findings of the 1989 survey are virtually identical to the 1982 survey in these areas.

The 1989 survey finds little evidence that companies anticipate the use of any kind of genetic monitoring or screening in the foreseeable future. Personnel officers in this representative, national sample of companies with 1,000 or more employees were asked whether or not they anticipated that their companies would conduct biochemical genetic screening, DNA-based screening, cytogenetic monitoring, or DNA-based monitoring within the next 5 years, either on a mandatory or voluntary basis. The survey found only 2 percent of companies with 1,000 or more employees anticipated any form of mandatory genetic monitoring or screening within the next 5 years, while another 3 percent said they anticipated conducting some form of genetic monitoring or screening on a voluntary basis.

Survey Results without Certain Tests Included

In the original 1982 survey, certain **tests were** included in the basic definition of biochemical genetic screening tests. The 1989 survey, however, did not contain those specific tests in the definition of biochemical genetic screening. Instead, they were added to a later question that asked which types of biochemical screening tests were conducted by the company of employees or applicants. This means that the proportion of the 1989 survey findings concerning the prevalence of biochemical genetic screening attributable to certain tests (the nongenetic tests) can be identified. Two tests were identified in the 1989 survey that were included in the 1982 survey as being nongenetic tests—allergic respiratory disease and contact dermatitis.

A variable from the responses to the question asking which types of screening tests were conducted was constructed from the health officer's questionnaire. (Note: This could only be done for the long survey forms returned by mail, not the short forms conducted by telephone, which were identical to the 1982 survey-but which yielded no genetic testers.) If the respondent said yes to either allergic respiratory disease or contact dermatitis in this question, but no to other tests in this question, the respondent was labeled "nongenetic only. " Re-

spondents saying yes to either of these tests, in addition to other tests in the question, were labeled "both." Those responding yes to other tests in this section, but not to either of the two nongenetic tests, were labeled "genetic only. "

This constructed variable was run against the two questions about biochemical genetic screening—whether companies were currently screening and what their past screening history was—as well as against the general banner, which included all of the definitions of genetic monitoring and screening.

There were a total of 10 cases (weighted) in which genetic screening tests of allergic respiratory disease or contact dermatitis were reported, but none of the other biochemical genetic screening tests were specified. This includes 5 (weighted) of the 18 (weighted) cases in which respondents are identified as "current users' of genetic monitoring and screening. The other 5 cases were only picked up in the "total test' variable, which includes individuals reporting any of the tests from the question, regardless of whether they reported that they were conducting "genetic tests. '

If these are not genetic screening tests, then the prevalence of genetic screening is even less (29 percent less for both the traditional definition and the expanded definition) than previously estimated in 1982, when these tests were explicitly part of the question. In 1989, there were five respondents that said they were conducting biochemical genetic screening, and apparently these were the only tests they reported conducting (contact dermatitis and allergic respiratory disease).

Survey Results of the 1,000+ Companies: Current Use

Less than one-half of 1 percent of companies with 1,000 or more employees reported they were currently conducting cytogenetic monitoring of any employees or job applicants, for research or any other reason. Such cytogenetic monitoring was currently conducted by no company with 1,000 to 4,999 employees, 2 percent of companies with 5,000 to 9,999, and 2 percent of companies with 10,000 or more employees.

Three percent of health officers in companies with 1,000 or more employees reported that their companies were currently conducting biochemical genetic screening of any employees or job applicants, for research or any other reason. Seven percent of companies with 10,000 or more employees reported current genetic screening, compared with 4 percent of those with 5,000 to 9,999 employees and less than 3 percent of companies with fewer than 5,000 employees (table 9-19).

No health officer in a company with 1,000 or more employees reported currently conducting direct-DNA monitoring of any employees or job applicants, for research or any other reason. Similarly, none reported currently conducting direct-DNA screening of any employees or job applicants.

Survey Results of the 1,000+ Companies: Past Use

OTA found that few companies have ever conducted genetic monitoring and screening of workers and job applicants for any purpose. Six percent of health officers in companies with 1,000 or more employees reported that their companies had conducted genetic monitoring or screening tests within the past 19 years, for research or any other reason. This included companies that had conducted genetic monitoring or screening as part of a voluntary wellness program, for diagnosis, or at the request of the employee. It also included reported use of specific genetic screening tests listed in the survey.

Larger companies were most likely to have conducted genetic monitoring or screening tests of job applicants or employees. Seventeen percent of health officers from companies with 10,000 or more employees reported that their companies had used genetic monitoring or screening tests, of some kind, in the past. By contrast, use of genetic monitoring or screening was reported by only 5 percent of health officers from companies with 5,000 to 9,999 employees and 4 percent in companies with 1,000 to 4,999 employees.

UNIONS AND GENETIC MONITORING AND SCREENING

A total of 10 unions responded to the OTA survey, out of the 33 unions that were mailed the survey. This response rate of 30.3 percent was close to the 36.4 percent response rate (4 out of 11) reported for the 1982 survey. Unions responding to the 1989 survey represented workers in a wide variety of occupations. The 10 unions ranged in size from 1 with less than 100,000 members to 2 with more than 1 million members each. A total of 5.1 million

Table 9-19—Current Use of Genetic Monitoring or Screening Tests Among Companies With 1,000 or More Employees

Q.13. Is your company currently conducting biochemical genetic screening of any employees or job applicants, for research or any other reason?
Q.15. Is your company currently conducting cytogenetic monitoring of any employees or job applicants, for research or any other reason?
Q.17. Is your company currently conducting direct-DNA screening of any employees or job applicants, for research or any other reason?
Q.18. Is your company currently conducting direct-DNA monitoring of any employees or job applicants, for research or any other reason?
(Base: Health Officers)

		Percent of companies currently conducting			
		Biochemical genetic screening	Cytogenetic monitoring	Direct-DNA screening	Direct-DNA monitoring
Total	(546)	3	•	o	0
Type of business					
Electrical utility	(39)	1	0	0	0
Pharmaceutical	(22)	5	0	0	0
Other chemical	(47)	7	0	0	0
Petroleum	(5)	o	0	0	0
Electronic	(21)	2	0	0	0
Other manufacturing	(1 79)	4	•	o	0
Nonmanufacturing	(233)	3	1	0	0
Number of employees					
Less than 5,000	(272)	3	o	0	0
5,000-9,999	(99)	4	2	0	0
10,000 or more	(167)	7	2	0	0

less than 1%.
SOURCE: Office of Technology Assessment, 1990.

members were represented by the 10 unions responding to the survey.

Genetic Monitoring and Screening conducted by Unions

None of the 10 unions responding to the survey reported that it now conducted genetic screening, cytogenetic monitoring, direct-DNA screening or direct-DNA monitoring of members or potential members, or had conducted such tests in the past. However, one union did report that it conducted tests for allergic respiratory disease and contact dermatitis as part of a voluntary research program. The same union wrote under "other' cytogenetic tests that it does conduct a "review of ailments & material safety data sheets." The respondent also reported that the union had conducted genetic monitoring or screening of its members based on job exposures. Three reasons were given as important factors in the union's decision to conduct genetic screening: evidence of a possible association between chemical exposure and illness in epidemiological studies; union-employee initiative; and "individual rights & privacy.' It should be noted that the respondent wrote: "Union does not conduct any genetic monitoring or screening tests." On the other hand, the respondent also indicated that the union had conducted genetic monitoring or screening of its members based on job exposures.

A second union reported arranging biochemical genetic screening tests and cytogenetic monitoring tests for a union member, at the request of the member, in the past 19 years. These tests were for allergic respiratory disease, contact dermatitis, histocompatibility markers, other immune system markers, other heterozygous chromosomal instabilities, and chromosomal aberrations. The respondent explained:

> Our own medical staff consists of two physicians on retainer, who also have faculty appointments at university medical schools. So far as I know, they have not conducted genetic monitoring and screening tests themselves. In rare cases, they have referred patients for testing to assist in diagnosis.

A third union respondent reported no genetic monitoring or screening but was 'not sure' whether the union was currently conducting biochemical genetic screening tests. Thus, a total of two unions appeared to have some limited experience in conducting one or more genetic monitoring or screening tests, or arranging these tests for their members. This

limited experience in conducting genetic monitoring and screening was consistent with the prevalence of genetic monitoring and screening reported by large companies, particularly since one union only arranged for genetic monitoring and screening without conducting it itself. None of the unions responding to the survey employed or contracted with a genetic counselor.

Genetic Monitoring or Screening Conducted by Companies

Three of the ten unions responding to the survey reported that companies had conducted genetic monitoring or screening tests of their members. All three unions reported that such tests were based on job exposures. One union reported that the company conducted genetic monitoring of its members to identify increased individual susceptibility to workplace risk. A second union reported that company genetic monitoring or screening were also based on family history and cofactors (e.g., smoking). A third union reported that company genetic monitoring or screening were also based on ethnic-racial background. (This was the same union that had referred a few members to outside doctors for genetic monitoring or screening.)

In addition, two union respondents reported that they did not know whether companies had conducted genetic monitoring or screening of their members. One respondent was unable to answer the survey question on whether companies had conducted genetic monitoring or screening of its members, as well as many other questions, because "there are 15,000 employers with enormous variations in size, practice and policy. No general conclusions can be drawn.

None of the 10 unions reported that genetic monitoring or screening were used by a company, primarily or partly, to reject a union member applying for a job. One union was not sure whether a company had used genetic monitoring or screening to reject a job applicant.

However, one union did report that a company had transferred or terminated a union member based on the results of genetic monitoring or screening. This case took place 1 to 2 years ago. The job action involved hypersensitivity to isocyanates. Consistent with limited union experience in job terminations involving genetic monitoring and screening, no union reported that biochemical and cytogenetic tests were used as rejection categories in statistical data on the reasons for job terminations. However, it should be noted that only one union reported maintaining statistical data on the reasons for job terminations, using medical but not genetic criteria as rejection categories.

Union Positions on Genetic Monitoring and Screening

Four unions reported having a formal policy related to the use of genetic screening of employees or job applicants. Two of these unions also had a formal policy related to the use of genetic monitoring of employee health.

The only union to report making recommendations to companies as a result of genetic monitoring and screening was one whose members reported genetic monitoring or screening by companies and which had also referred a few of its members to outside doctors for genetic monitoring or screening. Specifically, the union recommended that the company(ies) implement engineering controls, provide personal protection devices, implement a research program, and discontinue a product or change materials in a product. The union also recommended that a company change its workplace practice or exposure level due to the results of genetic monitoring in establishments where the union is not represented. No other union responding to the survey reported having made recommendations for company changes in the workplace as a result of genetic monitoring or screening.

One union reported having engaged in contract negotiations covering the topic of genetic monitoring and/or screening. It reported that companies had conducted genetic monitoring of its members. The union had a formal policy for the use of genetic screening, but not monitoring. The union respondent took the following position:

> We assume that, as with many types of employer surveillance of workers, genetic monitoring and screening are going on without any formal notification to workers or the union, much less any request for consent. Notification and consent (including provision of payment for scientific peer review by trade union medical consultant) should be mandated. Furthermore, employer genetic testing should be limited to monitoring, and screening prohibited. Questions of suitability of an employee for continued work should be resolved by worker and private physician, in a confidential manner, No individual's

results should be reported to employers directly—only the collective results. In other words, employer-sponsored health research on workers should be conducted according to the same rules as any NIH-sponsored research, complete with Human Subjects Review Board oversight and doctor/patient confidentiality. Just because an employer pays for it does not justify the abandonment of these fundamental concepts.

Answers to survey questions showed that for some unions, the perceived acceptability of genetic monitoring or screening depended on the circumstances. Unions were divided on the acceptability of genetic monitoring or screening of employees or job applicants by employers:

- to make a clinical diagnosis of a sick member—five found it generally acceptable, four found it generally unacceptable;
- to monitor chromosomal changes associated with workplace exposures-five found it generally acceptable, four found it generally unacceptable; and
- to inform members of their increased susceptibility to workplace hazards-four found it generally acceptable, five found it generally unacceptable.

In contrast, genetic monitoring or screening was viewed as generally unacceptable: to establish links between genetic predisposition and workplace hazards (seven unions); to establish evidence of preemployment health status for liability purposes (eight unions); and to exclude members with increased susceptibility to workplace hazards (eight unions). Consistent with union opposition to using genetic monitoring and screening to exclude members with increased susceptibility to workplace hazards, eight unions viewed health examinations to identify job applicants with genetic susceptibility to workplace exposures as unacceptable.

Unions took issue with the idea that employers should have control over the use of genetic monitoring and screening tests. All nine unions expressing an opinion disagreed with each of these three statements:

- The employer should have the option of deciding how to use the information obtained through genetic monitoring and screening.
- The decision to perform genetic screening of job applicants and employees should be the employers.
- The decision to perform genetic monitoring of employees should be the employers.

One union qualified disagreement to the above three items by explaining that employers and unions should both have a say, but that the decision whether to perform genetic monitoring and screening was the employer's.

Unions also showed a general consensus on two other questions. Nine unions disagreed-with eight expressing strong disagreement-that ' 'it's fair for employers to use genetic screening to identify individuals whose increased risk of occupational disease poses a threat for greater costs to the employer. " Eight unions agreed strongly that "genetic screening in the workplace represents a potential threat to the rights of employees." However, there was no consensus among the unions on the desired role of government concerning genetic monitoring and screening. Five unions agreed strongly or somewhat with the statement that "government agencies should provide guidelines for genetic screening of job applicants and employees,' but four disagreed strongly. Similarly, six unions agreed that "government agencies should provide guidelines for genetic monitoring of employees," but three disagreed strongly. The survey asked:

> If an employer becomes aware that an employee has a genetic susceptibility to serious illness if he or she is exposed to substances in the workplace, do you think the employer should exclude that employee from those jobs for which he/she is at increased risk, or do you think the employer should allow the employee to take those jobs, if he/she waives corporate liability?

Three unions thought the employee should be excluded, while two thought the employee should be allowed to take the job. Another two unions said that the employee should be allowed to take the job, but there should be 'no waiver of liability' or no waiver of liability "to the point of no coverage. ' One union said the decision depended on the nature of the exposure, and the availability of work. Two union respondents did not answer the question. One of these respondents criticized the question as inherently biased because it did not offer the responses of "preventing risks by ameliorating the conditions and reducing exposure' or 'transferring susceptible

workers to other jobs with guarantees of pay and job security.'

Unions and the Future of Genetic Monitoring and Screening

None of the 10 unions was currently considering conducting, or anticipated conducting, biochemical genetic screening, cytogenetic monitoring, direct-DNA screening or direct-DNA monitoring, for any reason in the next 5 years.

One respondent was not sure whether the union anticipated conducting cytogenetic monitoring in the next 5 years, and was also not sure whether the union anticipated conducting any direct-DNA monitoring over that period. This union was "not opposed to genetic monitoring as research, or in diagnosis, where the investigation focuses on the relationship between workplace exposure and genetic damage." This union's medical staff had referred a few patients for genetic monitoring or screening to assist in diagnosis.

Another union respondent did not answer the question on whether the union anticipated conducting any biochemical genetic screening in the next 5 years. However, it should be noted that the respondent commented that "employer genetic testing should be limited to monitoring, and screening prohibited. Questions of suitability of an employee for continued work should be resolved by worker and private physician, in a confidential manner.'

Many of these unions viewed genetic screening in the workplace as a threat to the rights of employees and were strongly opposed to employers having control over the decision to perform genetic monitoring or screening of employees. Half of the unions regarded genetic monitoring or screening as generally acceptable to diagnose sickness and monitor chromosomal changes resulting from workplace exposures. However, most were opposed to genetic screening to link genetic predisposition to workplace hazards, exclude members with increased susceptibility from risk situations or establish evidence of preemployment health status for liability purposes.

Given these views, unions may be expected to object to large-scale use of genetic monitoring or screening mandated by employers without union involvement and consent. The survey suggests that some unions might approve of genetic monitoring or screening, but only for limited purposes, under carefully controlled circumstances agreed on by unions and management.

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Appendixes

Appendix A
Basic Tenets of Human Genetics

Basic Human Genetics

The chemical bearer of genetic information is DNA, which takes the structural form of a double-stranded helix (figure A-l). DNA is composed, in part, of four chemical subunits called bases. These four bases—guanine (G), adenine (A), thymine (T), and cytosine (C)-are the coding units of genetic information. The bases normally pair predictably-A with T, and G with C (figure A-2)—to form the DNA double helix structure. The order and organization of the base pairs determines all genetic information. Genes, which are segments of DNA, come in many different sizes ranging from 1,000 to 1 million base pairs in length. A mutant gene results in an altered amino acid sequence, which can alter the protein in such a way that clinical symptoms arise.

Genes are organized in microscopically visible bundles called chromosomes (figure A-3). The chromosomal constitution of each individual is derived equally from mother and father. In humans, 23 chromosomes are contributed by each parent in the gamete (egg or sperm), resulting in a total of 46 chromosomes-22 pairs of autosomes and 1 pair of sex chromosomes (two X chromosomes for females and an X and a Y for males). The entire complement of genetic material in this set of chromosomes, about 3.3 billion base pairs-50,000 to 100,000 structural genes—is called the human genome. Only about 2 percent of the genes have been identified along the chromosomes.

The physical location of a gene on a chromosome is called its locus. Some genes have been mapped and cloned and can be identified directly at their locus. But it is the exception that the direct link between one gene, one locus, and one disease can be made. Most diseases are multifactorial and polygenic; i.e., several genes in combination with specific environmental factors act together to produce the disease state.

Because chromosomes come in pairs, there are two copies of a gene at each locus, one inherited from each parent. Different "versions" of a gene at a particular locus are called alleles. When two or more alleles of a gene are found at a particular locus in the population, the genetic variants are referred to as polymorphisms. Polymorphisms (i.e., common genetic differences between people) play an important role in diagnosing genetic diseases.

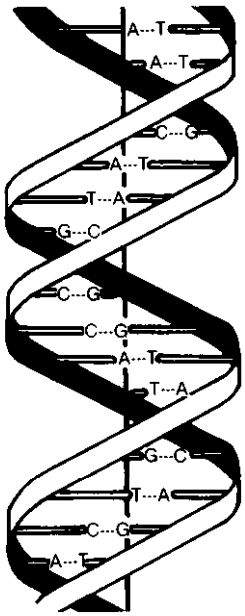
The term 'mutation' refers to a change in the sequence or number of nucleotides in a gene. Mutations arise through a number of mechanisms: through environmental agents as mentioned previously, or through normal cellular processes. Not all mutations cause disease, although that is the reference in which the term is commonly used. Mutations that form in germline cells that produce eggs and sperm are inherited by offspring, whereas those that occur in somatic cells remain only in the descendants of those cells in the affected individual. This distinction is critical in distinguishing between monitoring and screening. Genetic screening can detect traits that are caused by mutations in both somatic **and** germ cells, whereas monitoring generally detects mutations that have occurred in that population of somatic cells being tested and cannot be extrapolated to other tissues.

Genetics and Disease

The link between familial factors and certain health conditions has long been recognized. A useful classification of the genetic basis of disease is disorders caused by:

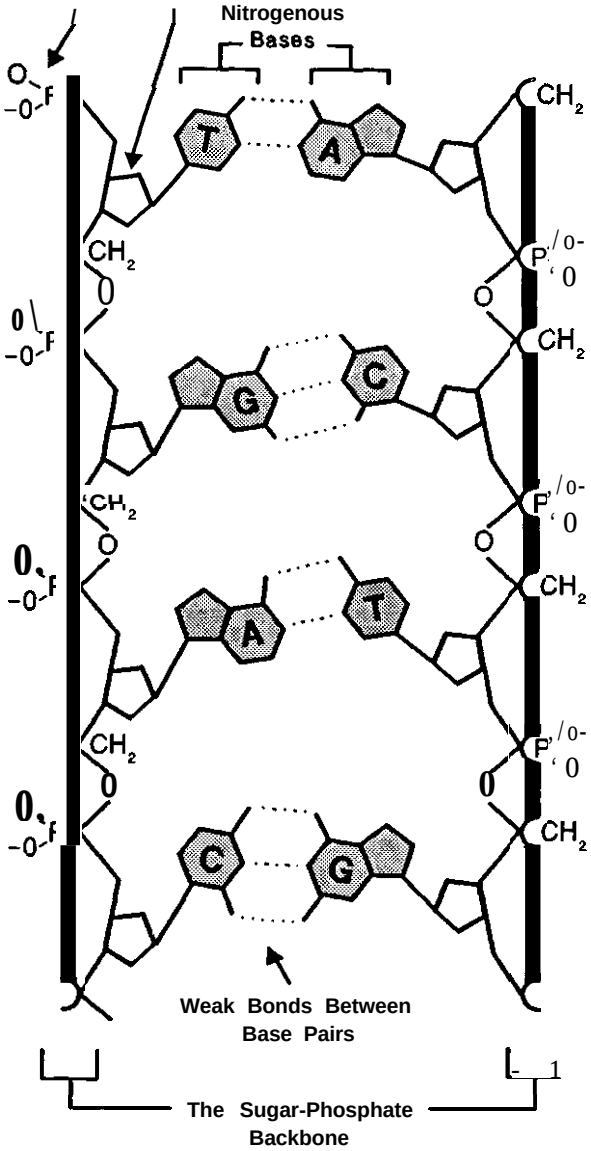
. a single mutant gene (monogenic);
. chromosomal aberrations;
- genetic predisposition combined with environmental interaction (multifactorial); and
- changes in the somatic cells (cancer, aging, autoimmune disease, and some congenital malformations).

Figure A-I—The Structure of DNA



SOURCE: Office of Technology Assessment, 1990.

Figure A-2—DNA Base Pairing



The four bases of DNA, guanine (G), adenine (A), thymine (T), and cytosine (C) form the four letters of the genetic code. The pairing of the four bases is A with T, and G with C, It is the sequence of bases along the strand of DNA encodes the genetic information.

SOURCE: Office of Technology Assessment, 1990.

Single Gene Disorders

A gene can be altered by a "point" mutation (i.e., a change in only a single base pair) resulting in an altered protein or function for which it codes. Thus, a gene can have several functional and dysfunctional variants, all of which are referred to as alleles. Each individual carries two sets of genes, one from each parent. If the two members of a pair of genes are the same, the individual is considered to be homozygous for that locus. If the two members of the pair are different, the individual is said to be heterozygous for the locus. Such an individual has the trait, but not necessarily the disease. Heterozygotes for certain traits, therefore, make two kinds of gene products from their two genes. If only one functional gene is needed to produce sufficient protein activity, the individual will be normal for that trait and the mutant allele will be considered recessive. If, however, the one mutant allele is sufficient to produce a defect in the individual, the trait is considered dominant.

Most often, single gene mutations, whether transmitted recessively or dominantly, cause a defect in enzymes that may cause "inborn errors" of metabolism and transport. These errors result from lack of a functional enzyme and may result in:

- diseases resulting from absence of the end product;
- diseases resulting from the accumulation of substrates or metabolizes;
- diseases resulting from interference with regulatory mechanisms; and
- diseases where there is an inborn error of membrane transport.

Single gene mutations can also cause amino acid substitutions that produce "hemoglobinopathies' (hemoglobins with abnormal functions). Sickle cell anemia is a common form of hemoglobinopathy. The mutant gene in this disease causes an abnormality in hemoglobin which distorts the red blood cells, resulting in small blood vessel blockage and subsequent oxygen deficit.

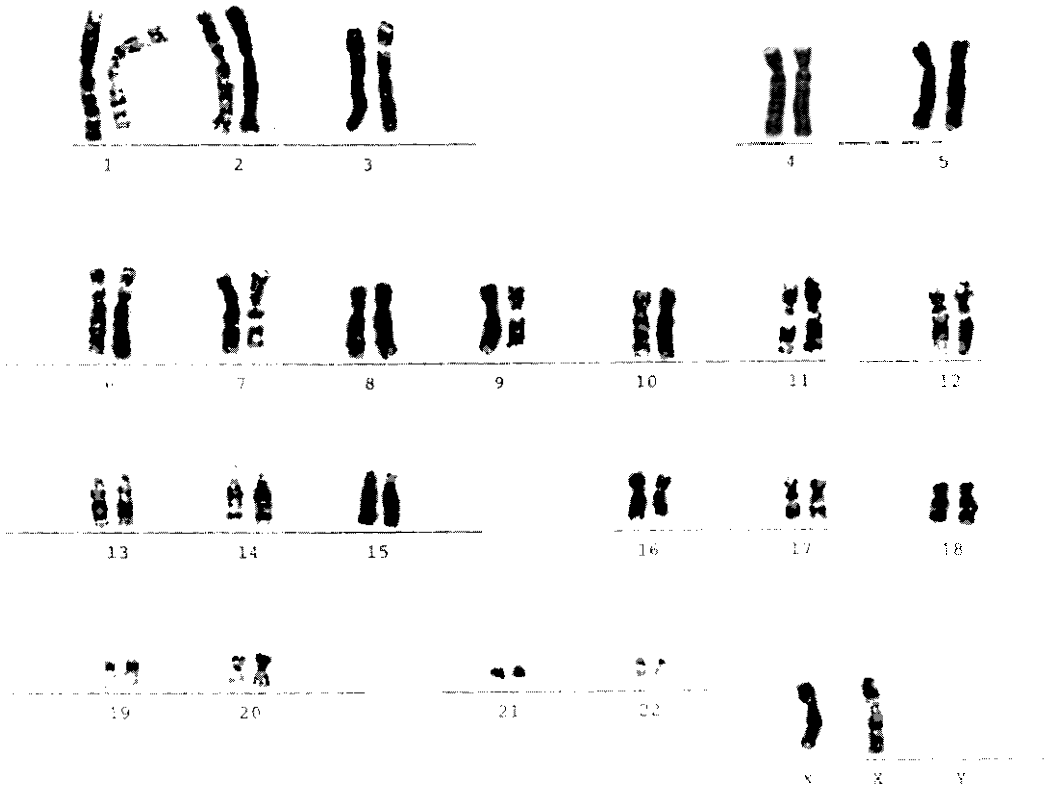
Some 400 gene products of the approximately 3,000 known single gene disorders have been identified (5). The nature of the mutations involved, however, has only been determined in 45 of these disorders (see table A-l). Better understanding of the nature of the mutation leads to increased capabilities for diagnosis, both prenatally and in children and adults and, in a few disorders, has resulted in improved treatment for affected individuals.

Critical to diagnosis and treatment has been understanding the mode of inheritance of the mutant gene. The three modes of inheritance are discussed below. Figure A-4 illustrates the various modes of inheritance for single gene disorders. The figure represents a pedigree or family tree, the standard tool used by geneticists tracking the history and mode of inheritance of genetic disease in families.

Autosomal Dominant Inheritance

If the mutant gene is located on one of the autosomes (not a sex chromosome) and it is dominant, every affected

Figure A-3-Chromosome Complement of a Normal Human Female



SOURCE: The Genetics & IVF Institute, Fairfax, VA.

individual has an affected parent, except for cases arising from a fresh mutation. If that affected individual has an unaffected spouse, each of their children will have a 50 percent chance of inheriting the mutant gene and having the disease. Offspring of affected persons who have not inherited the mutant gene will not have affected offspring.

Examples of genetic disease inherited in this manner are Huntington's disease, adult polycystic kidney disease, and Marfan syndrome. Except for eases where the disease has appeared as a fresh mutation in an individual, families with dominantly inherited genetic disease are more likely to know they are at risk because of the appearance of the disease in preceding generations. More problematic are those diseases with a late onset, such as Huntington's, because individuals might not know they are affected until they already have children.

Autosomal **Recessive Disorders**

Recessive deleterious genes produce disease only in the homozygote, that is, persons with two copies of the mutant gene. Affected individuals have received one mutant gene from each parent. Most often both parents are asymptomatic heterozygotes, unaware that they carry the mutant allele until they either produce an affected offspring or undergo testing for heterozygote or 'carrier' status. There is infrequently a family history of the disease because of the small likelihood that two individuals heterozygous for the same trait would meet and have children. Recessive disorders are more common than dominant disorders. Even if both parents are carriers of the trait, each child has a 1 in 4 chance of inheriting the mutant gene from both parents, producing the homozygous or disease state. Statistically, each child also has a 50 percent chance of inheriting one mutant gene from either parent, thus, becoming a carrier. Each child also has a 25 percent chance of inheriting the normal gene from both parents.

Examples of some common autosomal recessive disorders are cystic fibrosis, sickle cell anemia, phenylketonuria, and beta-thalassemia.

Sex Linkage

Theoretically, if the mutant gene is on one of the sex chromosomes, the X or the Y, the pattern of inheritance differs. In reality, the Y chromosome is very small and contains few genes. There are no known diseases trans-

Table A-I-Some Known Hereditary Disorders for Which Gene Has Been Cloned

Acatalalasemia	Hereditary congenital hypothyroidism
Alpha 1 -Antitrypsin deficiency	Hers' disease (glycogen storage disease VI)
Alpha-Thalassemia	Homocystinuria
Antithrombin III deficiency	Hypobetalipoproteinemia, premature atherosclerosis
Argininosuccinic aciduria	Isolated familial growth hormone deficiency
Atransferrinemia	Lecithin-cholesterol acyltransferase disease
Beta-thalassemia	Lesch-Nyhan syndrome
C2 deficiency	Lipid adrenal hyperplasia deficiency
C3 deficiency	McArdle's disease
C4 deficiency	Medium-chain acyl-CoA dehydrogenase deficiency
Carbamylphosphate	Mucopolysaccharidosis VII
Chronic granulomatous disease	Ornithine transcarbamylase deficiency
Citrullinemia	Osteogenesis imperfecta
Color blindness	Phenylketonuria
Congenital adrenal hyperplasia	Phosphoglycerate kinase deficiency
Diabetes mellitus due to abnormal insulins	Porphyria cutanea tarda
Duchenne muscular dystrophy	Propionic acidemia type I
Dysfibrinogenemias	Propionic acidemia type II
Dyslipoproteinemia	Pyruvate carboxylase deficiency
Ehlers-Danlos syndrome type IV	Renal tubular acidosis with osteopetrosis
Ehlers-Danlos syndrome VII A2	Retinoblastoma
Elliptocytosis-1	Sandoff's disease
Elliptocytosis-2, spherocytosis	Severe combined immuo-deficiency from adenosine deaminase deficiency
Fabry's disease	Sickle cell anemia
Factor VII deficiency	Tay-Sachs disease
Factor X deficiency	Thrombophilia from plasminogen activator deficiency
Factor XIII deficiency	Thrombophilia from plasminogen variant
Familial hypercholesterolemia	Thrombophilia from protein C deficiency
Familial hypoparathyroidism (one form)	Triosephosphate isomerase deficiency
Fructose intolerance	Tyrosinemia type II
Fucosidosis	X-linked icthyosis
Gaucher's disease	von Willebrand's disease
Glucose-6-phosphate dehydrogenase deficiency	
Gyrate atrophy	
Hemophilia A	
Hemophilia B	

SOURCE: S.E. Antonarakis, "Diagnosis of Genetic Disorders at the DNA Level," New *England Journal of Medicine* 320:153-163, 1989.

mitted via the Y chromosome. The X chromosome, however, is much larger and contains numerous genes, many of which are known to cause disease when in the mutant form. Genes on the X chromosome can also be dominant or recessive, but the fact that females have two X chromosomes, and males have only one X and one Y leads to differences in the patterns of inheritance. Figure A-4 illustrates the characteristic pedigree for X-linked disease, usually being transmitted by an asymptomatic female to each of her sons with a 50 percent probability. Daughters of the unaffected carrier mother each have a 50 percent chance of also being unaffected carriers. Sons who do not inherit the abnormal gene are unaffected and cannot transmit the gene.

Examples of X-linked disorders are Duchenne muscular dystrophy and hemophilia.

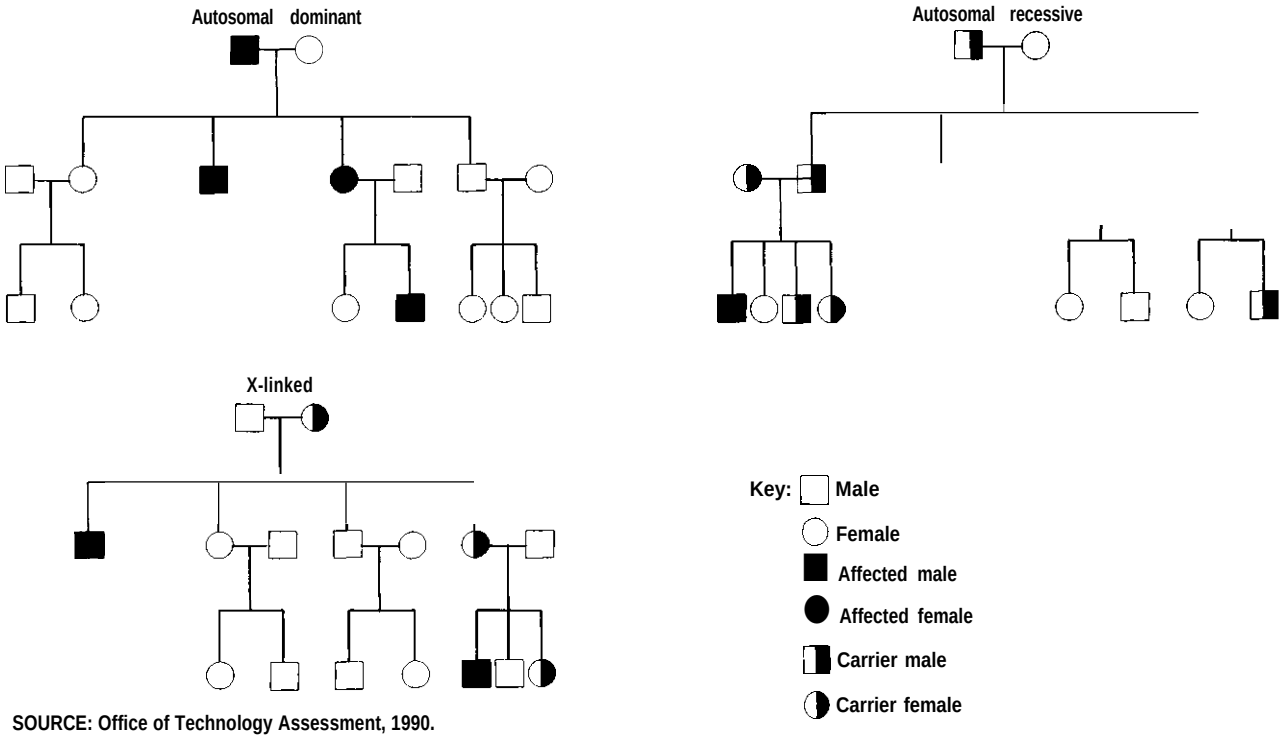
Confounding Factors in Mendelian Patterns

Not all mutant genes display the regularity of transmission implied by the previous discussion. Several irregularities can complicate accurate genetic diagnoses and are described in the following sections.

Mutation-As mentioned earlier, for two reasons, family history does not usually forewarn individuals that they are at risk for genetic disease. First, many diseases are transmitted in an autosomal recessive manner, meaning the chances are very low that two carriers for the same disease will meet, procreate, and have an affected child. Second, naturally occurring mutation rates exist for all diseases. For example, "Fragile X Syndrome and Duchenne muscular dystrophy have high mutation rates which explains why these diseases persist despite the fact that those who have them rarely procreate.

Variable Expressivity--Variable expressivity is the term used for the variation in severity of effects produced by the same genes in different people. The physical presentation of effect of a gene is referred to as the "phenotype." Thus, one genotype often gives rise to a range of phenotypes in different individuals. For example, the neurofibromatosis gene may cause multiple disfiguring tumors in one patient but only skin discoloration and a few insignificant tumors in another patient.

Figure A-4-Modes of Inheritance of Single Gene Disorders



SOURCE: Office of Technology Assessment, 1990.

Heterogeneity-The same or similar physical characteristics can be produced by different genes or loci. Thus, several different genotypes can produce similar phenotypes. In most genetic diseases, heterogeneity appears to be the rule rather than the exception.

Penetrance—To further complicate matters, a gene that expresses itself clinically in one person can produce no detectable effect in another. The failure to reach the "clinical surface' in an individual is called "nonpenetrance." The gene is silent. At the population level, the gene is said to have reduced penetrance. Reduced penetrance is most easily detected in the case of dominant traits, when an individual who must carry the mutant genes, based on pedigree or DNA analysis, does not have the disease or trait.

Phenocopies--Sometimes the effect of a gene is simulated by an environmental agent in an individual not carrying the mutant gene. For example, congenital deafness can be caused by a recessive gene or by the drug streptomycin.

Multifactorial Inheritance

Combinations of genes encode complex aspects of the human phenotype, such as the immune response and cholesterol metabolism. Defects in one or more of these genes can cause diseases that may be exacerbated by environmental factors such as viruses, chemicals, and radiation; thus the term "multifactorial disease. " Multifactorial diseases are far more common than single gene disorders. They include coronary artery disease, diabetes mellitus, multiple sclerosis, schizophrenia, epilepsy, allergic rhinitis, asthma, some forms of arthritis, and some forms of emphysema, to name a few (4).

Identification of the genes that make an individual "susceptible" to disease state is especially compelling because of the possibility of prevention. An individual identified to be at risk can avoid known exogenous risk factors such as diet or infectious agents, or watch for the developments of symptoms for treatment at an early stage.

Chromosomal Disorders

Sometimes genetic disease is caused by structural aberrations in the chromosomes. Chromosomal aberrations (CAs) are gross structural changes visible under the light microscope that arise from errors in cell division. During the two types of cell division in humans —mitosis and meiosis—' 'mistakes" can occur resulting in too much, too little, or rearranged chromosomal material in the daughter cells. Errors in the number or structure of chromosomes can result in maldevelopment of the fetus and subsequent disorders in liveborn infants.

In some cases, CAs can be caused by environmental agents such as radiation, chemicals, or viruses (2,3,6,8). These environmental insults have been associated less

with errors in number than with breakage of the chromosomes. Such breakage can interfere with the genetic signals necessary for normal cell growth and repair (e.g., it is well-documented that large doses of ionizing radiation cause chromosomal breakage correlated with certain forms of cancer) (1,7).

Errors in chromosome number and structure can present clinical disorders in a variety of forms, from before conception to the advanced stages of disease. The spontaneous frequency of CAs (both structural and numerical) in newborns is about 6 per 1,000. Chromosomal analysis of human spontaneous abortuses shows that about 50 percent are chromosomally abnormal. In addition, persons exposed to ionizing radiation and certain chemicals have increased frequencies of CAs in their lymphocytes. Many forms of cancer are associated with increased frequencies of aberrations. And, several human hereditary conditions, such as ataxia telangiectasia and Fanconi's anemia, are associated with increased frequencies of CAs as well as increased incidence of cancer.

Genetic evaluation at the chromosomal level, rather than the biochemical or molecular level, is referred to as "cytogenetics. Cytogenetic approaches to genetic screening are most reliably used in prenatal diagnosis for women of advanced maternal age, and for the diagnosis of certain forms of cancer and certain hereditary traits. The use of cytogenetic tests for monitoring populations exposed to genotoxic agents and ionizing radiation is discussed in chapter 4.

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Appendix B
Survey Methodology

Study Design

The survey was conducted for the Office of Technology Assessment (OTA) from March 24 to July 15, 1989, by Schulman, Ronca, & Bucuvalas, Inc. (SRBI). The core of the 1989 survey remained a national survey of the 500 largest U.S. industries, 50 largest utilities, and 33 major unions. The 1989 survey contained comparable questions to core survey items from the 1982 OTA survey. (See table B-1 for a summary of the methodology of the 1989 and 1982 surveys.)

Sampling Design

The purpose of the sampling design was to provide comparability with OTA's 1982 survey, while expanding the ability to generalize the results to a broader population. The 1989 survey results were based on four samples. First, all Fortune 500 companies were selected to provide information on genetic monitoring and screening at large corporations in the United States. The procedure for specifying this population was to use the Fortune 500 listing of manufacturers and utilities from the previous year. This procedure, which was identical to the procedure used in the 1982 survey, produced an independent census of the current Fortune 500 population rather than a panel of previously surveyed organizations.

Second, the 50 largest private utility companies in the United States were surveyed to provide coverage of large utilities. This sampling was based on the most recent *Fortune Magazine* listing prior to the survey. As with the Fortune 500 listing, this produced a current census of the 50 largest utilities.

Third, a sample of large unions was developed by OTA to provide broad coverage of a wide variety of unions. The 1982 sample of unions was based on 11 unions with the largest number of members working for Fortune 500 companies, identified from the 1979 Directory of National Unions and Employees Association published by the U.S. Department of Labor. This publication was discontinued in the early 1980s, so no comparable list was available for the 1989 survey. A broader sample of unions was desired, in any case, since the 1989 survey had been expanded to include a cross-section of medium and large companies with 1,000 or more employees. Therefore, a sample of 33 large unions was identified by OTA for the 1989 survey.

Fourth, the 1989 survey added a stratified cross-section sample of large- and medium-sized companies with at least 1,000 employees that did not belong to the Fortune 500 group, to provide results projectable to the universe of companies with 1,000 or more employees. Public organizations, such as nonprofit groups and governmental organizations, were excluded. The number of employees in the company was defined as the total number of persons employed company-wide in the United States, rather than the number of employees at company headquarters or at a particular establishment.

The sample of companies with 1,000 or more employees was stratified by company size. The sample was divided into four size strata: companies with 10,000 or more employees, companies with 5,000 to 9,999 employees, companies with 2,500 to 4,999 employees, and companies with 1,000 to 2,499 employees. Companies were randomly selected within each strata from Dun & Bradstreet lists. The final sample consisted of 100 companies with 10,000 or more employees, 100 companies with 5,000 to 9,999 employees, 300 companies with 2,500 to 4,999 employees, and 350 companies with 1,000 to 2,499 employees. Such division by size allowed the survey to oversample the largest companies and obtain a relatively high sampling incidence of these firms.

Table B-I-Summary of Methodology

Samples	
Fortune 500 companies . .	Sampled in 1989 and 1982.
50 largest utilities	Sampled in 1989 and 1982.
Unions	33 unions in 1989 and 11 unions in 1982.
Companies with 1,000+ employees	1,000 sampled in 1989. Not sampled in 1982.
Designated respondent	
Private companies:	
Chief health officer	Designated respondent in 1989 and 1982. Received version of questionnaire for health officers.
Chief personnel officer. .	Designated respondent in 1989 only. Received different questionnaire version for personnel officers.
Unions:	
Union president	Designated respondent in 1989 and 1982.
Followup methodology	
Reminder letters	Sent in 1989 and 1982.
Remailing questionnaires to nonresponders	Sent to all nonresponders in 1989 and 1982.
Telephone followup to nonresponders	All Fortune 500 and utilities in 1989. Only 200 largest companies in 1982.
Actual telephone interviews with non-responders to mail survey	Done as a last resort in 1989 and 1982.

SOURCE: Office of Technology Assessment, 1990.

In addition, companies with certain standard industrial code (SIC) groups were oversampled to obtain sufficient numbers of oversampled companies and permit analysis of certain types of SIC groups. The oversampled SIC groups covered pharmaceuticals (SIC 2834), other chemical companies (rest of SIC group 28), petroleum (SIC group 29), semiconductors (SIC 3674), other electronics companies (SIC 3675-3679), and electric utilities other than the 50 largest utilities (SIC 4911 and 4931). A target subsample size of 50 companies was adopted for each of the oversampled industry groups. In order to achieve this subsample size, a sufficient number of companies with 1,000 or more employees in each oversampled group were randomly selected to supplement the core cross-section sample so that the final sample included 50 companies in the oversampled group. In cases where there were 50 or less U.S. companies in an oversampled group with 1,000 or more employees, all companies in that group with 1,000 or more employees were included in the final sample.

Questionnaire Development

A survey questionnaire was developed by the contractor in concert with OTA according to the detailed research objectives set forth by OTA. The OTA advisory panel reviewed the questionnaire at the March 1989 panel meeting after a pretest was conducted between February 17 and March 1, 1989. The findings of the pretest were used to revise the questionnaire.

The 1989 survey contained comparable questions to core survey items from the 1982 survey. This provided OTA with the necessary comparability to the 1982 survey so that changes in the workplace over time could be assessed. However, the method was altered to increase the usefulness of the information. The central components were:

1. The content of the questionnaire was broadened to include the use of genetic monitoring and screening in the workplace in the context of other types of employee testing. The survey was expanded to deal with attitudes of employers toward the proper and improper uses of genetic monitoring and screening in the workplace. The survey also covered more areas related to the applications of genetic monitoring and screening in personnel matters, as well as applications for employee health.

2. As in 1982, the survey was directed to the chief health officer, to answer questions dealing with the medical applications of genetic monitoring and screening. A different questionnaire was also directed to the chief personnel officer focusing on personnel applications (e.g., recruitment, placement, advancement, and retention) of genetic monitoring and screening.

3. The universe of Fortune 500 companies was supplemented by a sample of non-Fortune 500 large- and medium-sized employers so that the extent of genetic monitoring and screening in the workplace could be examined more broadly.

4. Telephone recontact was attempted with all nonrespondents in the Fortune 500 and 50 largest utility companies.

5. The identity of companies returning questionnaires was anonymous in 1982. In order to improve tracking of the sample and prevent duplicate responses, the 1989 survey used questionnaires with identification numbers on peel-off labels. The respondent was encouraged to leave the label on the questionnaire when it was returned, but this was voluntary. All labels were removed after receipt of the questionnaires, making the data both anonymous and confidential.

Confidentiality

The 1982 survey used a postcard system to verify which companies had returned questionnaires. Each questionnaire was sent to the company along with a postcard. Substantially more questionnaires were returned (n=373) than postcards (n=307). This raised the possibility that more than one survey was completed by the same organization, since respondents are normally more likely to return a postcard without a questionnaire, so that he or she would not be subject to followup. In fact, a few organizations returned more than one questionnaire in 1989, i.e., the original questionnaire and a questionnaire sent in a followup mailing. These were identified and removed from the 1989 sample.

Because there appeared to be a problem with the use of a separate postcard to track anonymous questionnaire returns, a respondent identification number was proposed for the 1989 questionnaires. This permitted improved sample tracking and allowed identification of duplicate returns. Due to concerns about the anonymity of the questionnaires, a compromise solution was to affix the identification number to the 1989 questionnaires on 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, which explained it would be removed after receipt. After SRBI received the questionnaires, the peel-off labels were removed, making the data both anonymous and confidential.

Nine out of ten survey participants left the peel-off label on the questionnaire. The peel-off labels were removed from 11 percent of the health officer questionnaires, and 10 percent of the personnel officer questionnaires returned to SRBI. Only 5 of 59 health officers reporting any type of genetic monitoring and screening removed the label before returning it.

Table B-2—Sample Disposition for 1989 Survey: Fortune 500 and 50 largest utilities

Sample mailing and eligibilitv	Number
Drawn sample.	550
Companies ineligible before mailing: merged/out of business/bought by other company in sample.	3
Companies mailed questionnaires	547
Companies ineligible to complete survey	18
Merged/out of business/bought by other company in sample.	15
Noncontactable by mail and telephone, no forwarding address and nonlocatable	3
Companies eligible to complete survey.	529
Participation in survey	
Total questionnaires received during field period. .	453
Health questionnaires received.	250
Personnel questionnaires received	203
Companies returning at least one questionnaire during field period	325
Companies returning both questionnaires	128
Companies returning only health questionnaire .	122
Companies returning only personnel questionnaire	75
Companies returning questionnaires after close of field period	5
Total companies returning questionnaires	330
Nonparticipation in survey	
Companies refusing to participate	150
Too busy to complete survey	41
Participation against company policy	51
Company too decentralized for someone to do survey	5
Other refusals.	53
Companies in callback status: had been remailed questionnaires	45
Other companies not returning questionnaires. . . .	4
Completion rate (Total companies returning questionnaires/ eligible companies).	62.4%

SOURCE: Office of Technology Assessment, 1990.

Field Procedures

The field procedures used in this study included:

. an advance letter, produced on OTA stationery and signed by OTA Director John H. Gibbons, sent to the Chief Executive Officer (CEO) of each sampled company and union Presidents prior to mailing the questionnaire;
- a first mailing of the questionnaire with a cover letter to the CEO, asking that one questionnaire be directed to the firm's chief executive for health affairs and a second one to the chief personnel officer;
- a followup letter to individuals whose replies were not received within 2 weeks of the first mailing;
- a second questionnaire mailing approximately 3 weeks after the followup letter;
- a telephone followup of all Fortune 500 companies and the 50 largest 'utility companies that did not return both questionnaires; and
- telephone interviews after repeated telephone followup and remails.

Sample Disposition

A total of 330 organizations in the Fortune 500 and 50 largest utilities categories completed and returned at least one questionnaire for the 1989 survey (see table B-2). An additional 21 organizations in these groups were classified as ineligible for the survey because they had merged, were no longer in business, or had been bought by another Fortune 500 company or by one of the 50 largest utilities. The overall response rate among the 529 eligible organizations was 62.4 percent.

By comparison, the 1982 survey on genetic monitoring and screening reported a 65.2 percent response rate among the Fortune 500 companies, 50 largest utilities and 11 unions, based on 366 organizations returning questionnaires. One four-page questionnaire was mailed to CEO's and directed to chief health officers in 1982. In 1989, two questionnaires totaling 20 pages were mailed to CEO's, including a 12-page instrument for chief health officers and an 8-page questionnaire for chief personnel officers.

The 62.4 percent response rate was achieved after repeated followup telephone calls and remails of the questionnaires. A total of 150 companies refused to participate in the 1989 survey, or 28 percent of the Fortune 500 companies and 50 largest utilities. These telephone followup efforts were not conducted among the additional sample of companies with 1,000 or more employees because response rate comparability was not sought. A somewhat lower response rate was obtained from this group as a result (see table B-3).

Table B-3-Sample Disposition for Survey: Non-Fortune 500 Companies

Sample mailing and eligibility	Number
Drawn sample ... ,	1,039
Companies ineligible before mailing: merged/out of business/bought by other company in sample. .	*0*
Companies mailed questionnaires.	*1,039*
Companies ineligible to complete survey: merged/ out of business/bought by other company in sample.	40
Companies eligible to complete survey.	999
Participation in survey	
Total questionnaires received during field period. .	667
Health questionnaires received.	301
Personnel questionnaires received	366
Companies returning at least one questionnaire during field period	460
Companies returning both questionnaires	207
Companies returning only health questionnaire.	94
Companies returning only personnel questionnaire	159
Companies returning questionnaires after close of field period	10
Total companies returning questionnaires	470
Nonparticipation in survey	
Companies refusing to participate .,.	22
Companies requesting mail to different address . .	19
No response after two mailings	488
Completion rate (Total companies returning questionnaires/ eligible companies)	47.O%

SOURCE: Office of Technology Assessment, 1990.

Appendix C

1982 Survey of the Use of Genetic Testing in the Workplace

There have been conflicting accounts of the extent of genetic testing and the use of its results. In testimony given before Congress in the fall of 1981, the corporate medical director of a large chemical company stated that except for sickle cell trait tests, his company" . . . is not conducting genetic screening of its employees, and I am not aware of any other company which is" (2). However, a series of articles in the New York Times in February 1980 alleged a widespread corporate practice of such testing on American workers (3). Furthermore, a May 1981 survey of east coast industrial physicians indicated that preemployment, preplacement, and periodic testing for sickle cell anemia, hemoglobin disease, and glucose 6-phosphate dehydrogenase (G-6-PD) deficiency was being conducted in some large east coast companies (l).

None of these or other accounts examined by OTA has been based on a rigorous, scientifically valid assessment of the use of genetic testing. Therefore, in an attempt to dispel the confusion and speculation and to provide necessary data for policy analysis, OTA surveyed major U.S. industrial companies, utilities, and unions about their use of this technology.

Purpose

The survey was designed to determine:

- the frequency of past, present, and anticipated genetic screening and cytogenetic monitoring* in the workplace and whether they had been conducted on a routine, special, or research basis;
- which tests were used and under what circumstances;
- how the results of the tests were used; and
- the criteria against which tests have been measured to determine acceptability for use.

The survey did not attempt to establish the number of workers involved in these tests; that information would have required a much more extensive effort.

"The questionnaire used the term biochemical genetic testing to refer to genetic screening and the term cytogenetic testing to refer to cytogenetic monitoring.

Study design

The survey was conducted for OTA from February **25** to June 8, 1982, by the National Opinion Research Center (NORC), a nonprofit survey research corporation affiliated with the University of Chicago. NORC sent confidential questionnaires to the chief executive officers of the 500 largest U.S. industrial companies, * the chief executive officers of the 50 largest private utility companies, * * and the presidents of the 11 major unions that represent the largest numbers of employees in those companies.** * For further information on the study design and other aspects of survey methodology, see appendix A. The NORC report to OTA on the survey is in appendix B.

"Identified by Fortune 500 listing of U.S. companies engaged in manufacturing/mining; Fortune, vol. 103, No. 9, May 4, 1981,

" "Identified by Fortune Magazine List C; *Fortune, vol.* 103, No. 9, May 4, 1981.

" " "identified in Directory of National Unions and Employees Association (1979) by the U.S. Department of Labor.

By the June 8, 1982, cutoff date, 366 organizations had answered the questionnaire, a 65.2 percent response rate, and 26 organizations had specifically declined to do so, a 4.6 percent refusal rate. Those who declined generally gave either no reason for refusal or the reason of corporate policy not to respond to surveys. (See table 1.)

Table 1 .—Frequency of Response to Survey by 6/8/82 By Type of Response (based on 561 organizations)

Type of response	Number	Percent
Participated	366	65.20/o
Refused to participate:	26	4.60/o
Policy not to reply to surveys	(10)	
Not interested, no time.	(3)	
Object to methodology	(1)	
Phone refusal—no reason	(12)	
Unknown	169	30.1 %
Total	561	

SOURCE National Opinion Research Center, survey conducted for OTA, 1982,

Results

Overall rates of testing

Of the **366** organizations responding, 6 (1.6 percent) were currentl, conducting genetic testing, * 17 **(4.6** percent) used some of the tests in the past 12 years, 4 (1.1 percent) anticipated using the tests in the next 5 years, and 55 (15 percent) stated they would possibly use the tests in the next 5 years. Most of these organizations are in manufacturing/mining (particularly chemicals) or are utility companies. Of those organizations that have tested in the past 12 years, five are currently doing so. (See table 2.) Because the questionnaire instructed respondents to include any instance of testing, positive responses can include isolated instances of testing as well as long-term testing programs. Among the six companies currently testing, two are in the chemical industry, two are utilities, and two are in the electronics industry. Half of those that tested in the past are chemical companies. Of the four organizations that anticipate the use of genetic testing, two are conduct - ing testing at present, one has done so in the past, and one has never had such a program. None of the four responding unions reported any testing. These results are set forth in more detail in tables 3, 4, and 5.

Table 2.—2 x 2 Contingency Table for Organizations Engaged in Genetic Testing (past testers by current testers)

		Past testers		
		Yes	No	Total
Current testers	Yes	5	1	6
	No	12	348	360
	Total	17	349	366

SOURCE National Opinion Research Center, survey conducted for OTA, 1982.

Types of testing genetic screening and cytogenetic monitoring

Organizations that reported some genetic screening were asked whether they had ever tested employees for genetic traits associated with: (A) any red blood cell and serum disorders, (B) liver detoxification systems, (C) immune system markers, or (D) heterozygous chromosomal instabilities. For each of the four broad categories A through D, the questionnaire listed several examples. Of those who have ever tested, 14 of the organizations had tested in category A, 3 in category B, 5 in category C, and none in category D. Organizations that have used red blood cell and serum disorder tests, category A, often used more than one type of test. The most frequently used test in this category was that for sickle cell trait, for which 10) organizations have tested. The G-6-PD and serum alpha-l antitrypsin deficiency tests were the second most frequently used. (See table **6** for a summary of the frequency of individual genetic screening tests.)

For each test, companies were asked about the circumstances under which the tests were done (that is, routinely, for research, or for other reasons) and the type of employee tested. Respondents generally said they tested routinely or for unspecified reasons. (See table 6.) Employees most often were selected on the basis of ethnicity and race for sickle cell trait testing and on the basis

"Genetic screening and/or cytogenetic monitoring

Table 3.—Distribution of Organizations By Type, Indicating Current, Past, and/or Future Use of Genetic Testing (based on 366 responses)

	Testing					
	Current		Past		Future	
Organization type (number of respondents)	Yes	No/NA[a]	Yes	No/NA[a]	Yes/Poss.	No/NA[a]
Manufacturing/mining companies (322)	4	318	16	306	49	273
Private utility companies (31)	2	29	1	30	9	22
Unions (5)	O	5	0	5	0	5
Unknown (8)	0	8	0	8	1	7
Total (366)	6 (1.6%)	360	17 (4.6%)	349	59 (16.1%)	307

[a]A combination response. Further breakdown is impossible since the category (current, past, future) is a summary of responses to two questions dealing with genetic screening and cytogenetic monitoring. In the case of No/NA, most responses were No; for Yes/Poss., most responses were possibly. See table 4 for further breakdown.

SOURCE: National Opinion Research Center, survey conducted for OTA, 1982

Table 4.—Frequency of Current, Past, and/or Future Use of Genetic Testing, By Type (based on 366 responses)

	Testing									
	Current			Past			Future			
Type of test	Yes	No	N/A	Yes	No	N/A	Yes	Poss.	No	N/A
Genetic screening	5	350	11	12	342	12	1	53	292	20
Cytogenetic monitoring	2	354	10	6	348	12	3	49	294	20

SOURCE: National Opinion Research Center, survey conducted for OTA, 1982

Table 5.—Distribution of Companies by Classification," Indicating Current, Past, and/or Future Use of Genetic Testing (based on 366 responses)

	Genetic testing					
	Current		Past		Future	
Main industrial classification (number of respondents)	Yes	No/NA[b]	Yes	No/NA[b]	Yes/Poss.	No/NA[b]
Chemical (37)	2	35	8	29	11	26
Utilities (33) '...	2	31	1	32	10	23
Petroleum (18)	0	18	0	18	4	14
Pharmaceuticals (9)	0	9	0	9	3	6
Rubbers/plastics (4)	0	4	0	4	3	1
Metals (16)	0	16	0	16	2	14
Others (249)	2[c]	247	8	241	26	223
Total (366)	6 (1.60/ii)	360	17 (4.6%)	349	59 (16.1 °/0)	307

[a]Maln Industrial classification baaed on the first listed response of respondent to question concerning the major Industrial classificatlon of their company.
b ,combination response. Further breakdown impossible since the category (current, past, future) is a summary of two questions: 1) genetic screening, 2) Cytogenetic _monitorlng. In the case of No/NA, most responses were No; for Yes/Poss. most responses were possibly. See table 4 for further breakdown.
[c]Both of these companies report electronics as their main industrial classification

SOURCE: National Opinion Research Center, survey conducted for OTA, 1982.

of job category for other types of tests. No organization reported basing a genetic screening test on an employee's sex. (See table 7.)

Of the organizations that reported cytogenetic monitoring, four had tested for chromosomal aberrations and two for sister chromatid exchanges (SCE). None reported having tested for mutations by assaying either deoxyribonucleic acid (DNA) or enzymes. Most frequently, no reason was given for chromosomal aberration testing. The two companies that did SCE testing said it was for research purposes. (See table 6.) Job category was the only employee-related characteristic used to determine who would be tested. (See table 7.)

Table 6.—Genetic Testing Ever[a] Conducted By Purpose and Type of Test (based on 18 responses)

	Genetic screening						Cytogenetic monitoring	
Purpose	Sickle cell	G-6-PD	SAT	Methemoglobin reductase	Unspecified red blood cell/serum disorder	Unspecified liver detox	Unspecified immune system markers	Chromosomal aberrations	Sister chromatid exchanges
Routine . . .	5	3	1	0	1	1	4	1	0
Research . .	1	0	2	1	2	1	0	1	2
Other	6	2	2	1	2	1	3	3	0
Total number of respondents utilizing test[b]	10	4	4	1	3	3	5	4	2

a in the past 12 years.
[b]since categories above are not mutually exclusive, total can be lest/more than sum of categories.
SOURCE: National Opinion Research Center, survey conducted for OTA, 1982.

Table 7.—Genetic Testing Ever[a] Conducted By Criteria and Type of Test (based on 18 responses)

	Genetic screening						Cytogenetic monitoring	
Criteria	Sickle cell	G-6-PD	SAT	Methemoglobin reductase	Unspecified red blood cell/serum disorder	Unspecified liver detox	Unspecified immune system markers	Chromosomal aberrations	Sister chromatid exchanges
Job category	1	2	2	0	2	1	1	2	1
Ethnicity/race	7	0	0	0	0	0	0	0	0
Sex	0	0	0	0	0	0	0	0	0
Total number of respondents utilizing test[b]	10	4	4	1	3	2	4	4	2

a In the past 12 years.
b since categories above are not mutually exclusive, total can be less/more than sum of categories.
SOURCE National Opinion Research Center, survey conducted tor OTA, 1982.

Recipients were asked about the factors considered in the decision to implement testing and the criteria employed in selecting specific tests. Data from epidemiological studies, data from animal studies, and other reasons such as employee protection were the highest ranked factors involved in decisions to implement genetic testing for both genetic screening and cytogenetic monitoring. (See table 8.) The predictive value of a test, its specificity, scientific consensus, and other factors such as research findings were the factors cited most frequently as criteria for selecting a specific genetic test. These responses were similar for both genetic screening and cytogenetic monitoring. (See table 9.)

Table 8.—Genetic Testing Ever[a] Conducted By Reasons for and Type of Testing (based on 18 responses)

	Type of testing	
Reasons for deciding to implement testing	Genetic screening	Cytogenetic monitoring
Data epidemiologic studies	6	2
Data animal studies	4	2
Legal consequences of not testing	3	0
Union employee initiative .	3	0
Cost-benefit analysis	2	0
Other[b]	4	3

a In the past 12 years.
Includes reasons related to protecting employees, research findings.
SOURCE: National Opinion Research Center, survey conducted for OTA, 1982,

The types of testing carried out by current testers were compared with those of past testers. For genetic screening, current testers are using a slightly greater variety of tests (tests for red blood cell and serum disorders, liver detoxification systems, and immune system markers) than

Table 9.—Genetic Testing Ever[a] Conducted By Criteria for Test Selection and Type of Testing (based on 18 responses)

Criteria[b]	Type of testing: Genetic screening	Type of testing: Cytogenetic monitoring
Predictive value of test[c]	5	1
Specificity of test[d]	5	1
Scientific concensus	4	2
Sensitivity of test[e]	3	0
Cost of test	2	0
Other[f]	4	3

[a] In the past 12 years.
[b] A respondent may have based its selection for a test on one or more of the above criteria.
[c] Predictive value of test: the likelihood that the disease status of the individual will be correctly identified by the test; i.e., a disease-free individual will have negative test result, a diseased individual will have positive test result.
[d] Specificity of test: ability of test to correctly identify individuals without disease.
[e] Sensitivity of test: ability of test to correctly identify individuals with disease.
[f] Includes research findings (general).

SOURCE: National Opinion Research Center, survey conducted for OTA, 1982.

past testers and at a slightly higher proportion of usage. Of the six current testers, five are testing for red blood cell and serum disorders, three for liver detoxification systems, and two for immune systems markers. Eight of twelve past testers had tested for red blood cell and serum disorders, none had tested for liver detoxification systems, and two had tested for immune system markers. In fact, however, because of the small numbers involved, the only notable difference between current and past testers may be the current use of tests for liver detoxification systems. In any event, testing for red blood cell and serum disorders continues to be the most frequently used test. (See table 10.)

A different pattern of use emerges for cytogenetic monitoring. Of the six current testers, one is testing for chromosomal aberrations and one is testing for sister chromatid exchanges. For the 12 past testers, 3 tested for chromosomal aberrations and I tested for sister chromatid exchanges. This may reflect the change in the state of the art concerning the science of sister chromatid exchanges. (See table 10.) In any event, the number of tests remain small and caution is advised in interpreting these data.

Actions taken as a result of testing

Responses concerning the way in which the results of genetic screening or cytogenetic monitoring were used varied greatly, ranging from actions involving an employee to changing or discontinuing a product. Of the **18** companies that reported taking some action, 8 reported that they had informed an employee of a potential problem. Five respondents reported transferring the "at-risk" employee. Two suggested that the employee seek another job as a result of testing. One discontinued or changed a product. The complete list of actions taken appears in table 11.

Generalizability of the survey

Can the results of this survey be generalized to the population of Fortune 500 companies, large utility companies, and major unions? An answer to this involves two additional questions: Are the responses equally distributed among the groups

Table 10.—Distribution of Type of Testing By Status of Tester (based on 18 responses)

Type of testing	Status of tester: Current N-6 Yes	Current N-6 No/NA	Current N-6 Percent using	Past N-12 Yes	Past N-12 No/NA	Past N-12 Percent using	Total
Genetic screening:							
Red blood cell and serum disorders	5	1	830/o	8	4	67%	18
Liver detoxification systems	3	3	50%	0	12	O%	18
Immune system markers	2	4	33"/0	2	10	1O%	18
Heterozygous chromosomal instabilities	0	6	0%	0	12	O °/o	18
Cytogenetic monitoring:							
Chromosomal aberrations	1	5	17"/0	3	9	25%	18
Sister chromatid exchange	1	5	17%	1	11	8%	18
Mutations by assaying DNA	0	6	00/0	0	12	O °/o	18
Mutations by assaying enzymes	0	6	0%	0	12	O%	18
Other	1	5	17"/0	0	12	O%	18

SOURCE: National Opinion Research Center, survey conducted for OTA, 1982.

Table 11 .—Actions Taken by Respondents That Have Ever[a] Used Genetic Testing (based on 18 responses)

Type of action[b]	Number of companies
Informed employee of a potential problem	8
Transferred employee	5
Personal protection device	3
Other action	3
Suggested employee seek other job	2
Installed engineering control	2
Implemented research program	1
Discontinued/changed product	1

a In the past 12 years.
b A respondent may have taken more than one action.
SOURCE National Opinion Research Center, survey conducted for OTA, 1982.

represented in the survey? Are characteristics of the respondents different from the nonrespond - ents? These two questions are discussed in turn.

By the close of the survey, a discrepancy in response rate among the groups represented in the survey became apparent. The large corporations had the highest response rates: 68 percent for utilities and 61.5 percent for the top 200 companies in the Fortune 500 listing; the unions and small corporations had the lowest response rates: 36.4 percent for unions and 44 percent among the bottom **300** companies in the Fortune 500 listing. (See app. A.) The variation in response pattern was most probably due to the followup efforts that focused on the top 100 companies of the Fortune 500 listing and organizations in selected industrial classifications such as utilities. Thus, the results of this survey may be more applicable to the larger manufacturing/mining and utility companies than to smaller manufacturing/mining companies and unions.

Analysis of selected characteristics of respondents compared with nonrespondents is limited to the Fortune .500 companies. Respondents and nonrespondents were compared on the following characteristics: geographic location, size of organization, and type of industry. Rates of response and nonresponse did not differ greatly geographically. (See app. A.)

For size of company, however, the rate of nonresponses did differ widely from the rate of responses. For example, 53 percent of the nonrespondents were in the smallest companies, compared with 32 percent of the respondents. Again, because larger companies were used in followup efforts, the response rates may reflect these efforts. (See app. A.)

Rate of nonresponse did not vary greatly from rate of response with respect to industry classification. Eleven industries had a slightly higher rate of response than predicted. Of these industries, five (chemicals, petroleum refining, rubber and plastic products, metal manufacturing, and pharmaceuticals) were the key industries selected for followup activities and the rates from the remaining six (glass/concrete, electronics, measuring equipment, motor vehicles, aerospace, and office equipment) may be explained by such factors as the effect of followup based on size of company or chance. (See app. A.)

Thus, the results of the survey may be more representative of the larger manufacturing/mining corporations and private utility companies as identified in Fortune magazine listings; however, the respondents do not appear to differ greatly from the nonrespondents in geographic location or type of company.

Comments on survey

Respondents were encouraged to write explanatory notes or other comments on the questionnaires and on the post cards. Thirty-one respondents did so. (See app. C for complete text of comments.) Three current testers sent in comments. Two of these respondents said testing was being done for reasons of health evaluation—preplacement and/or routine monitoring; one respondent said that such testing should not be interpreted to mean a large-scale testing program or a problem exists.

Comments were received from two companies that had tested in the past. Both respondents referred to testing for sickle cell trait, one at the request of the State health department, and the other at the request of the employer for employees of child-bearing age as part of the company's preventive medical program.

Seven organizations that anticipate future testing but that have not conducted any testing to date provided comments. The comments ranged

from addressing animal research to questionnaire improvement to any future testing being dependent on "practical utility. "

Comments received from 19 organizations that have never tested or that do not plan to test in the future focused on three major points. The first was the genetic testing was not relevant to the products or processes to which their workers were exposed. The second was that these tests were not sufficiently developed for use. The third point was that the organization was satisfied with its current conventional industrial hygiene practice and standard medical surveillance of its workers.

Caveats

In evaluating the results of the survey, several caveats must be considered. First, since the questionnaire instructed respondents to include any instances of testing, positive responses can include isolated cases as well as long-term testing programs. Second, the questionnaire was not structured to provide information on the number of workers tested. Positive responses indicate only the existence of testing, not its extent. Third, since approximately one-third of the population did not respond and the number of organizations testing is very small, any generalizing of these results to the study population as a whole is not warranted. Fourth, the level of effort employed in completing each questionnaire is unknown. For example, holding companies which have autonomously operating subsidiaries may or may not have included the activities of those subsidiaries in their responses. Fifth, a limitation of an anonymous questionnaire is that respondents cannot be contacted about missing information or unclear responses. Approximately 3 percent of the respondents failed to answer every item in the core questions. Eight returned questionnaires did not provide enough information to allow the respondents to be classified as a Fortune 500 company or 'as a utility. Sixth, the use of post cards for followup has pitfalls: respondents may return post cards but not questionnaires or vice versa; NORC received 293 post cards and 366 questionnaires. This may have resulted in duplication of information or minimized the effect of followup.

Conclusions

The survey of major U.S. industrial companies, utilities, and unions has shown that genetic testing currently is being used by a few companies, that its use has declined in the past 12 years, but that it may be used by many more companies in the future. The responses cannot be generalized to the survey population or to all U.S. companies and labor unions. However, it is clear that 17 organizations have used genetic testing in the past 12 years, 5 of the 17 and 1 other currently are doing so, and 59 organizations have expressed an interest in using these tests. None of these organizations is a union. The extent of testing by these organizations is unknown.

Further, of the 18 companies that have ever conducted genetic testing in the past 12 years, more companies have conducted genetic screening (17 companies) than cytogenetic monitoring (8 companies). Tests for sickle cell trait were the most frequently used type of genetic screening and tests for chromosomal aberrations were the most frequently used type of cytogenetic monitoring. Research was the least frequently mentioned purpose for testing. Respondents generally tested routinely or for other unspecified reasons. The type of employee chosen for testing was based most often on ethnicity and race for sickle cell trait testing, and job category for other types of tests. Sex was never stated as a criterion used in determining the test of choice. Actions taken on the results of the tests ranged from informing the employee of a potential problem (eight companies) to discontinuing or changing the product (one company).

Data from epidemiological and animal studies were the most frequently cited factors in the decision to implement testing of those companies that tested. A cost-benefit analysis was the least impor-

tant factor. The predictive value and specificity of a test were the most important criteria in the selection of the specific genetic screening test, while research findings were most important in the selection of the specific cytogenetic monitoring test.

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Appendix D
Federal Research in Genetic Monitoring and Screening

Both the public (State and Federal) and private research funding sectors place a high priority on projects related to human genetics. Part of these efforts include basic research applicable to genetic monitoring and screening in the workplace. Assessing State programs that could involve applications was beyond the scope of this report. However, State spending in biotechnology, including some applications to human genetics was documented recently in New *Developments in Biotechnology: U.S. Investment in Biotechnology (2).* Similarly, surveying private funding efforts in basic research on genetic monitoring and screening was not possible, although the Office of Technology Assessment (OTA) identified that chief among private resources in this area is the Howard Hughes Medical Institute (HHMI). In fiscal year 1989, HHMI funded over 100 studies related to human genetics—many of which could be important to future applications of genetic monitoring and screening (l).

Several Federal agencies fund research applicable to genetic monitoring and screening. This appendix describes federally funded projects underway as of early 1990. Because of the wide variation in both accounting and definitions used by agencies that fund research related to genetics (2), OTA did not attempt to determine the funding levels for genetic research with potential use in the workplace (2). Rather, OTA contacted Federal agencies and asked them to describe areas of basic research they conducted intramurally, or funded extramurally, that could have implications for genetic monitoring and screening in the workplace (all of the data available from the agencies by April 1990 is included here).

Department of Energy

Although the U.S. Department of Energy (DOE) does not directly support a program in occupational safety and genetics, DOE does conduct research into the effects of energy-related agents on human health. DOE, through the Office of Health and Environmental Research, supports approximately 150 projects investigating the effects of radiation and chemicals on living systems, including human health effects. In addition, much of the $27 million DOE is investing in the human genome project in fiscal year 1990 will result in improved ability to carry out genetic monitoring and screening.

As in the past, much of DOE's current genetic research focuses on the development of genetic monitoring tests. A new test, the glycophorin assay, which measures mutations in red blood cell surface proteins, is being applied in the Hiroshima and Nagasaki studies, as well as in studies related to the Chernobyl accident. Cytogenetic **tests** comprise an important part of many DOE projects. Research in genetic monitoring tests is still in early stages, but includes **assays** for DNA repair, sister chromatid exchange, and DNA adduct formation. DOE is also working on a number of models for cellular response to genetic damage in an attempt to elucidate the role of genetic change *per se* and subsequent disease. A noteworthy feature of DOE-funded research is a focus on health effects of radiation, including ultraviolet radiation. A number of DOE projects are also investigating the carcinogenic effects of different chemicals and different radiation exposure levels.

Department of Health and Human Services

The U.S. Department of Health and Human Services (DHHS) is the principal government department responsible for research funding in genetic monitoring and screening. Through several different agencies, DHHS funds three broad categories of basic research that could be important to genetic monitoring and screening in the workplace:

- pursuing new genetic screening tests for specific diseases;
- . developing general DNA assays for monitoring genetic damage; and
- identifying substances that damage DNA.

DHHS agencies involved in genetic monitoring and screening research include the Agency for Toxic Substances and Disease Registry (ATSDR), the Center for Environmental Health and Injury Control (CEHIC), the National Center for Toxicological Research (NCTR), the National Institute for Occupational Safety and Health (NIOSH), and the National Institutes of Health (NIH).

Agency for Toxic Substances and Disease Registry

Established in 1983 within the U.S. Public Health Service (PHS), ATSDR funds several activities designed to protect public health and worker safety. Empowered with health-related mandates under the Superfund Act, ATSDR is charged with determining the health effects associated with exposure to hazardous substances. Where necessary, ATSDR is to develop scientific methods to measure the linkages between human exposure to hazardous substances, with particular concern about substances stored in sites covered by Superfund, and adverse health effects. ATSDR funds several projects related to genetic monitoring and screening in cooperation with both CEHIC and the National Toxicology Program (NTP).

Genetic monitoring tests are a component of work funded by ATSDR. In supporting research through CEHIC, ATSDR is investigating different DNA assays as markers of genetic damage. In particular, one project hopes to develop an assay of human leukocyte cells as an indicator of potentially harmful effects of environmental agents. ATSDR also is cooperating with NTP to test the toxicological effects of chemicals and substances relevant to the Superfund legislation. These studies occasionally employ cytogenetic tests to evaluate DNA damage by hazardous substances. Finally, studies underway also include direct evaluation of chemically altered DNA.

Center for Environmental Health and Injury Control

As the focal group for nonoccupational injury control within the Centers for Disease Control (CDC), CEHIC conducts research in several fields of environmental health. Among CEHIC responsibilities are the prevention of chronic diseases and their morbidity and mortality. CEHIC research includes all aspects of chronic disease, including diagnosis and treatment. Many of these diseases, such as cardiovascular disease, neoplasia, and diabetes have distinct genetic components to be tested and identified.

A second responsibility of CEHIC is cancer treatment and control, including the genetic aspects of carcinogenesis. For example, for coronary heart disease (CHD), CEHIC is developing methods of measuring blood-cholesterol and investigating genetic factors in CHD. In addition to general research in chronic diseases, three particular projects could have important implications for genetic monitoring and screening in the workplace: the role of genetic and oncogenic factors in leukemia and other cancers; the identification of biological and genetic markers associated with chemical effects; and the development of fluorescent assays to detect DNA adduct formation or sister chromatid exchanges. CEHIC also funds studies of radiation effects on human health and chemical toxicology, both areas that could lead to advances in genetic monitoring and screening in the workplace.

National Center for Toxicological Research

Operated within the U.S. Food and Drug Administration, NCTR investigates the biological effects of potentially harmful chemical substances. As applied to genetic monitoring and screening, much of NCTR's efforts emphasize genetic monitoring, e.g., the health effects of prolonged, low-level exposure to and the biochemical effects of chemical toxicants. Like the National Institute of Environmental Health Sciences (NIEHS), NCTR also participates in cooperative research with NTP.

Genetic monitoring research conducted by NCTR falls into two different categories: studies to detector elucidate the mechanism of genetic damage; and studies of specific, chemical-caused damage. Projects cover DNA repair, general effects of chemicals on replication-repair mechanisms, nuclear matrix markers of toxicology, sister chromatid exchanges in mice, and the DNA repair system as a test for genetic damage. NCTR also is measuring the effects of known carcinogens on chromosomal damage, and hopes to extrapolate the data to chemicals with unknown genetic effects. NCTR investigations addressing specific chemicals focus on environmentally pervasive chemicals. During fiscal year 1988, NCTR projects investigated over 25 different chemicals, as well as studies on others supported through NTP.

National Institute for Occupational Safety and Health

NIOSH is a research agency that is part of CDC. It is the lead Federal agency for research into occupational safety and health problems. NIOSH supports intramural and extramural research in a variety of areas related to genetic monitoring and screening. NIOSH participates in cooperative projects with NTP, National Cancer Institute (NCI), and the U.S. Environmental Protection Agency (EPA).

Many of NIOSH's projects investigate exposure and disease surveillance of occupational cancers. Such projects include studies of environmental monitoring, biological monitoring methods, and medical screening (3). Test mechanisms under review include the methodologies to assess DNA adducts, assays as screening tests to determine the carcinogenic potential of chemicals, monitoring methods for various chemicals, sister chromatid exchanges, and chromosomal micronuclei. In addition, extensive epidemiological research is conducted to assess the association between work-related exposure to toxic and hazardous substances and the risk of developing disease (primarily cancer). An example is a study of workers exposed to ethylene oxide and their risk of developing leukemia.

National Institutes of Health

Under its general mission to promote the health of the American people, NIH conducts intramural and supports extramural biomedical research in many fields, including disease prevention. Apart of PHS, NIH is composed of 20 major institutes and centers for public health research. Research into the genetic basis of human disease is conducted by many of the member institutes of NIH, including NCI; the National Heart, Lung, and Blood Institute; the National Institute of Diabetes and Digestive and Kidney Diseases; and NIEHS.

For fiscal year 1990, NIH has awarded over $104 million in grants to support 627 projects that both directly and indirectly relate to genetic monitoring and screening. The majority of NIH research funds are directed to

independent and university-sponsored research groups. Current projects include investigations of: the possible genetic predisposition to alcoholism; cellular DNA repair processes; hazardous occupational and environmental exposures; and chemical toxicity.

National Institute of Environmental Health Sciences—NIEHS supports research on the effects of chemical, biological, and physical factors on human health. A particular research focus of NIEHS is the interaction between these factors and human genetic material as applied to genetic monitoring (e.g., adduct formation). NIEHS conducts intramural research and contributes to private and public projects, including work with NTP.

Intramural and extramural research supported by NIEHS includes a wide array of genetic toxicology experiments that provide new insight to the mechanisms of genetic damage. One area of intensive NIEHS investigation is cancer risk from environmental exposure. Researchers currently are studying human bladder cancer, carcinogen-induced DNA damage, breast cancer, liver tumors, and the role of mutation in cancerous cells. NIEHS-funded projects are pursuing test procedures for detecting genetic damage. Test mechanisms under review at NIEHS include lymphocyte markers, DNA adduct detection, and sister chromatid exchange. Other NIEHS investigations include projects to elucidate the general mechanisms of replication, DNA synthesis, and DNA repair in order to gain an understanding of the role of mutations and DNA repair in genetic disease.

National Toxicology Program

Primarily through contract funding, NTP conducts experimental investigations into the toxicity of environmental substances. As a cooperative program within PHS, NTP research projects are funded by several agencies, including NIEHS, ATSDR, and NCTR. An important part of NTP research involves its efforts in development, standardization, validation, and field application of toxicology tests, including genetic toxicology. NTP projects applicable to genetic monitoring and screening fall within several programs, including cytogenetic testing, genetic toxicology, and germ cell mutation. NTP's cytogenetic testing program includes efforts to develop highly reliable assays with respect to certain mutagens and involving sister chromatid exchange or other chromosomal aberrations.

Department of Veterans Affairs

The U.S. Department of Veterans Affairs (VA) does not support work that directly applies to genetic monitoring and screening in the workplace. As with many Federal research programs, the projects supported by VA include several areas that could become applicable to both genetic monitoring and screening. Cancer morbidity and mortality is a major area of concern in the VA patient population. In particular, several VA facilities are involved in investigating the role of genetics, if any, in carcinogenesis. Cancers of the bowel, bladder, and liver are of particular concern. In the area of genetic monitoring, some basic research to identify specific damage caused by certain chemicals is being conducted by VA. Most chemicals under review are those that veterans could have been exposed to in the course of duty, including ethanol, dioxin, and other Agent Orange components. VA also funds some projects in radiation effects, especially effects of low-level exposures. Finally, VA research includes genotoxic effects of drug therapies for long-term treatment of certain physiological and psychological disorders.

Environmental Protection Agency

Since its establishment in 1970, EPA's research efforts have included, to some extent, research to assess the effects of toxic substances on human populations. A recent EPA report recommended expansion of its research efforts to include investigation of the effects of chemicals on the environment and on humans (4).

In the face of accelerating demands, extramural collaboration and coordination are becoming increasingly important tools in advancing EPA's research agenda. EPA supports several research projects in the area of genetic monitoring. Current EPA-sponsored studies are addressing two main issues: associations between exposure, biological effects, and disease (e.g. the relationship between chemical damage to DNA and chromosomal damage); and the determination of the predictive value of chemical, gene mutation, or chromosomal damage measured inhuman tissues and the risk of cancer in the affected individual.

EPA projects applicable to genetic monitoring fall within two divisions, the Genetic Toxicology Division and the Health Effects Research Laboratory (HERL), located in Research Triangle Park North Carolina. Much of their research focuses on evaluating methods of assessing human exposure to genotoxins. Related efforts include research in DNA adduct formation, genetic bioassays, biomonitoring, and biochemical epidemiology. Research at HERL should help define which biological mechanisms identified in experimental studies are relevant in the assessment of health effects from specific exposures in humans.

National Science Foundation

The National Science Foundation (NSF) promotes the progress of science through the funding of research and education projects in many fields, including genetics. While NSF does not sponsor research of a clinical nature, it does support extramural basic research projects that indirectly apply to genetic monitoring and screening.

Programs supported in fiscal year 1989 include research on the spontaneous and mutagen-induced DNA deletions responsible for many disease-related genetic events. NSF is also currently investigating the potential use of a bacterial virus as an efficient, and rapid identification of the mutational products of different types of DNA lesions.

Appendix D References

1. Howard Hughes Medical Institute, *Research in Progress, 1988* (Bethesda, MD: 1989).
2. U.S. Congress, Office of Technology Assessment, New *Developments in Biotechnology: U.S. Investment in Biotechnology*, OTA-BA-360 (Washington, DC: U.S. Government Printing Office, July 1988).
3. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, *National Institute for Occupational Safety and Health: Projects for FY 1989*, DHHS (NIOSH) Pub. No. 89-112, May 1989.
4. U.S. Environmental Protection Agency, *Future Risk: Research Strategies for the 1990's* (Washington, DC: September 1988).

Appendix E

Survey Instrument: Corporate Health Officers

SURVEY OF WORKPLACE HEALTH AND GENETIC SCREENING AND MONITORING

CORPORATE HEALTH OFFICER VERSION

The Congressional Office of Technology Assessment is conducting a national survey of the opinions and experiences of employers related to the usc of genetic screening and monitoring in the workplace. This questionnaire has been directed to you as the person in your organization whose responsibilities include employee health. We need your assistance in answering, as best you can, some questions about workplace testing and employee health in your company.

For the purposes of this survey and the subsequent report, OTA has adopted the following definitions. By genetic monitoring we mean periodically examining employees to evaluate modifications of their genetic material via tests such as cytogenetic or direct-DNA tests. By **genetic** screening we mean screening job applicants or employees for certain inherited characteristics. Screening tests may be biochemical tests or direct-DNA tests. They can be used to indicate a predisposition to an occupational illness if exposed to a specific environmental agent, or they could be used to detect any inherited **characteristic** such as Huntington's disease. In contrast to periodic monitoring screening tests are generally performed only one time per characteristic

This is an important study, which has been requested by the Congress of the United States, designed to represent the opinion and experience of the employer. We need to know how employers view the technologies of genetic screening and monitoring in terms of their current and future applications to the workplace. We also want to know how these technologies are seen in the broader context of more common forms of employee health screening and monitoring in the workplace.

Your responses are very important, regardless of whether you have had any experience with genetic screening or monitoring. If your company has never explored the technology, the questionnaire will only take ten minutes. If you have some experience with the technology, it may take **a little** longer to complete the questionnaire. In either case, your experiences and opinions will help to inform congressional, opinion about this area.

Please read each question and mark the box(es) that most nearly corresponds to your answer. After each answer continue with the next question unless there is an instruction to skip to a particular question. Please feel free to qualify your answers, if you feel it is necessary. Space has been provided at the end for comments and opinions that you feel arc not adequately represented by the survey questions.

You arc free to decline to answer any questions that you consider inappropriate. The questionnaire and any identifying information will be destroyed after data entry, so that all responses will be anonymous as well as confidential.

1. **In your company, are pre-employment health examinations required of all, most, some, few, or** no job **applicants?**

❑ All ❑ Host ❑ Some ❑ Few

❑ None ——→ *SKIP to* **Q.6**

2. Would your company consider It acceptable or unacceptable to conduct a pre-employment health examination in order to:

	ACCEPTABLE	UNACCEPTABLE
Identify Job applicants who are physically unfit for employment	☐	
Identify job applicants who are emotionally or psychologically unstable	☐	
identify Job applicants who are currently using drugs	☐	☐
Identify job applicants who are at increased risk to workplace hazards	☐	☐
Identify job applicants with genetic susceptibility to workplace exposures	☐	☐
Identify job applicants who represent high insurance risks	☐	

3. Which of the following are normally part of the pre-employment examination in your company for non-administrative positions? *(MARK ALL THAT APPLY)*

Personal medical history	☐	Chest X-ray	☐
Family medical history	☐	Pulmonary function test	☐
Simple physical examinations	☐	Eye and hearing exam	☐
Standard blood chemistry tests	☐	Urinalyses for drug use	☐
EKG	☐	Lower back X-ray	☐

4. Which of the following types of results of pre-employment examinations would normally be released to job applicants?

- Normal results (negative findings) ☐
- Positive findings already indicated in medical history ☐
- Positive findings not reflected in medical history ☐
- Positive findings which disqualify them for employment ☐
- Positive findings which affect position/site eligibility ☐
- All of the above ☐
- None ☐ → *SKIP TO Q.6*

5. How would that information normally be released to job applicants?

Letter	Consultation with medical staff	Both	Other
		☐	☐

6. *Are there* **any specific medical criteria, other than those** mandated by regulation, that would **exclude individuals from eligibility for certain positions, jobs or sites in your company (e.g., hypersensitivity to dust *or* platinum, pregnancy)?**

☐ Yes No ⟶ ***SKIP TO*** Q.7

6a. Which **medical criteria would exclude employment in which jobs?**

Medical Criteria	Excluded Position/Job/Site
1. _____	_____
2. _____	_____
3. _____	_____

7. Are any employees **in your company exposed to chemicals or ionizing radiation in the workplace setting?**

☐ Yes ☐ No ⟶ ***SKIP TO Q.8***

7a. Arc those employees **who are exposed to chemicals or ionizing radiation routinely rotated to avoid prolonged exposure?**

☐ Yes ☐ No

7b. Does your company conduct any form of medical surveillance of employees whose job may expose them to environmental health risks, other than testing required by OSHA?

☐ Yes ☐ No

8. Are any employees in **your company exposed to any known workplace condition where there is a greater risk of negative health outcome, depending upon individual susceptibilities?**

☐ Yes ☐ No ⟶ ***SKIP TO Q.9***

8a. Do you conduct any form of screening to identify employees or job applicants at increased risk *for* these jobs?

☐ Yes ☐ No ⟶ ***SKIP TO*** **(?.9**

8b. Which, if **any, of** the following types ***of*** screening are conducted to identify increased individual susceptibility to workplace risk?

☐ Medical **History** ☐ Non-genetic screening (e.g., lower back X-ray, allergy testing) ☐ Genetic screening ☐ **None**

9a. As part of ongoing worker **health evaluation does the company require, as a condition of continued employment, all employees, only those in certain plants or jobs, only employees with certain medical conditions or histories, or no employees to have:**

9b. Which of these tests (in Q.9a-g), if any, do you offer to employees on a voluntary basis as part of a corporate wellness program?

	Q. 9a REQUIRE — ML PLANTS/ JOBS	CONDITIONS/ HISTORIES	NONE	Q. 9b — OFFER YES	VOLUNTARY NO
a. Routine physical examination	☐	☐		☐	☐
b. Test for hypersensitivity	☐	☐		☐	☐
c. Hearing tests	☐	☐		☐	☐
d. Pulmonary function tests	☐		☐	☐	☐
e. Vision tests	☐	☐	☐	☐	☐
f. Chest X-rays	☐		☐	☐	☐
g. Blood chemistry tests	☐			☐	☐

10. Would your company consider the use *of* genetic screening or monitoring *of* employees or job applicants as generally acceptable or generally unacceptable to:

	GENERALLY ACCEPTABLE	GENERALLY UNACCEPTABLE
Make a clinical diagnosis of a sick employee	☐	
Establish links between genetic predisposition and workplace hazards	☐	☐
Inform employees of their increased susceptibility to workplace hazards	☐	
Exclude employees with increased susceptibility from risk situations	☐	
Monitor chromosomal changes associated with workplace exposures	☐	☐
Establish evidence of pre-employment health status for liability purposes	☐	

11. Does your company have a formal policy related to the use of genetic tests in the screening of job applicants or employees?

☐ Yes ☐ No

12. Does your company have a formal policy related to the use of genetic tests in the monitoring of employee health?

☐ Yes ☐ No

The following questions concern biochemical genetic screening and/or cytogenetic monitoring that may have been conducted by your company on one or more employees or job applicants. By conduct we mean perform, contract for, or arrange for the test as part of a routine or ongoing program.

13. Is your company currently conducting biochemical genetic screening of **any** employees or job applicants, ***for research*** **or any other reason?**

Yes ☐ No ☐ **Not Sure**

14. Has your company conducted any biochemical genetic screening of any employees or job applicants, for research or any other reason in the past 19 yearn?

☐ **Yes** ☐ **No** ☐ **Not Sure**

15. Is your company currently conducting cytogenetic monitoring of any employees or job applicants, for research or any other reason?

☐ **Yes** ☐ **No** ☐ **Not** Sure

16. Has your company conducted any cytogenetic monitoring of any employees or job applicants, for research **or any other reason in the** past **19 years?**

☐ **Yes** ☐ **No** ☐ **Not Sure**

17. Is your company currently conducting direct-DNA screening of any employees or job applicants, for research or any other reason?

☐ Yes 1 ☐ Ho ☐ **Not Sure**

18. Is your company currently conducting direct-DNA monitoring of any employees or job applicants, for research or any other reason?

u ☐ Yes ☐ **Ho** **Not Sure**

19. Has your company conducted any of the following tests, either currently or in the past, as part of a voluntary wellness program, at the **request of an employee, or for diagnosis? *(MARK* ALL *THAT APPLY)***

		BIOCHEMICAL **GENETIC SCREENING**	**CYTOGENETIC** MONITORING	**DIRECT-DNA SCREENING**	**DIRECT-DNA MONITORING**
a. As part of a voluntary wellness program	**Currently..**	☐	☐	☐	☐
	In past 19 years	1		☐	
	No.	☐	☐	☐	
	Not sure.	☐	☐	☐	
b. At the request of the employee:	Currently..	1	☐	☐	☐
	In past 19 years	☐	☐		☐
	No.	☐	☐	☐	☐
	Not SUre.	☐	☐		
c. For diagnosis:	**Currently..**	1	a	☐	
	In past 19 years	☐	☐	☐	
	No.	☐	☐		
	Not sure.	☐	☐	☐	☐

IF YOUR COMPANY HAS NEVER DONE BIOCHEMICAL GENETIC SCREENING, CYTOGENETIC MONITORING, DIRECT-DNA SCREENING, OR DIRECT-DNA MONITORING, SKIP TO QUESTION 28 ***ON PAGE*** 8

IF YOUR COMPANY HAS DONE CYTOGENETIC MONITORING, DIRECT-DNA SCREENING, OR DIRECT-DNA MONITORING OF EMPLOYEES, FOR ANY PURPOSE, BUT NOT BIOCHEMICAL GENETIC SCREENING, SKIP TO QUESTION *21* ***ON PAGE 7***

IF YOUR COMPANY HAS EVER DONE BIOCHEMICAL GENETIC SCREENING OF ANY EMPLOYEE, FOR ANY PURPOSE, PLEASE CONTINUE WITH QUESTION 20

20. **Which of the following types of biochemical screening tests are being conducted by your company of any employees or job applicants?** ***(MARK ALL THAT APPLY)***

FOR EACH TEST CONDUCTED, MARK WHETHER **THE TESTING IS BEING DONE ON A ROUTINE BASIS FOR HEALTH SURVEILLANCE. AS PART OF A VOLUNTARY RESEARCH PROGRAM. AS** PART OF FOLLOW-UP DIAGNOSIS. OR AS PART OF A VOLUNTARY WELLNESS PROGRAm,OR ONLY AT THE REQUEST OF An EMPLOYEE

	NOT DONE	ROUTINE HEALTH SURVEILLANCE	VOLUNTARY RESEARCH PROGRAM	FOLLOW-UP DIAGNOSIS	VOLUNTARY AT WELLNESS PROGRAM	VOLUNTARY AT EMPLOYEE REQUEST
Sickle cell trait	❑	❑		❑		❑
Glucose-6-phosphate dehydrogenase deficiency (G-6-PO)	• 1	❑	❑			
Methemaglobin reductase deficiency	• 1		❑			❑
Serum alpha-1-antitrypsin deficiency	• 1		❑			
Alpha and beta thalassemias	• 1	❑		❑		❑
Aryl **hydrocarbon hydroxylase inducibility (AHH)**	❑			❑	El	❑
Slow vs. fast acetylatlon	• 1		❑			❑
Allergic respiratory disease	❑					
Contact dermatitis	❑	❑				❑
Histocompatibility **markers (HLA)**	❑	❑			❑	❑
Other immune system markers	• 1	El		❑		
Bloom syndrome	❑		❑			n
Fanconi syndrome	❑	❑		❑	❑	❑
Ataxia-telangiectasia	• 1	❑			❑	❑
Xeroderma pigmentosum	❑		❑		❑	❑
Other heterozygous chromosome? **instabilities**	❑	❑	❑	n		❑

21. Which of the following types of cytogenetic monitoring are being conducted by your company of any employees? ***(MARK ALL THAT APPLY)***

FOR EACH TEST CONDUCTED, MARK WHETHER THE TESTING IS BEING DONE ON A ROUTINE BASIS FOR HEALTH SURVEILLANCE, AS PART OF A VOLUNTARY RESEARCH PROGRAM, AS PART OF FOLLOW-UP DIAGNOSIS, AS PART OF A VOLUNTARY WELLNESS PROGRAM, OR ONLY AT THE REQUEST OF AN EMPLOYEE

	NOT DONE	ROUTINE HEALTH SURVEILLANCE	VOLUNTARY RESEARCH PROGRAM	FOLLOW-UP DIAGNOSIS	VOLUNTARY WELLNESS PROGRAM	AT EMPLOYEE REQUEST
Chromosomal aberrations	☐	☐	☐	☐	☐	☐
Sister chromatid exchanges	☐	☐	☐	☐	☐	
Mutations by assaying the DNA	☐	☐	☐	☐	☐	
Mutations by assaying the enzyme/protein	☐	☐	☐	☐	☐	☐
HPRT mutation rate	☐	☐	☐	☐	☐	
DNA adduct formation	☐	☐	☐	☐		
Other (SPECIFY) _____	☐	☐		☐		

22. Has genetic screening or monitoring ever been done in your company based on:

	YES	NO
Family history	☐	☐
Gander	☐	☐
Ethnic or racial background	1	☐
Co-factors (e.g., smoking)	☐	1
Job exposures	1	1

23. **Are all employees routinely informed of abnormal (positive) findings, normal (negative) findings, both or neither from genetic screening and monitoring tests?**

- Abnormal (positive) ☐
- Normal (negative) ☐
- Both ☐
- Neither ☐

24. **Is counseling offered to all employees with abnormal (positive) genetic test results by the company or are they referred to their own physicians?**

- Company counseling ☐
- Referred to own physicians ☐

25. Does your company employ or contract with a genetic counselor?

❑ Employ ❑ Contract with ❑ Neither

26. Has an employee ever been referred for genetic counseling by your company% medical staff as a result of any medical or genetic testing?

❑ Yes ❑ No

27. As **a result of a genetic screening or monitoring program has your company ever..-?**

	YES	NO
Suggested an emloyee seek job elsewhere	❑	❑
Placed an employee or transferred an employee to a different job in the company	❑	❑
Implemented engineering control	❑	❑
Recommended personal protection devices	❑ 1	❑
Implemented a research program	❑ 1	
Discontinued a product or changed materials in **a** product	❑	❑

28. Has your company ever instituted or changed a workplace practice or exposure level due to the results of:

	YES	NO
Genetic monitoring in your own establishment(s)	❑	❑
Other non-genetic medical monitoring in your own establishment(s)	❑	
Genetic monitoring in another company's establishments	❑	❑
Other non-genetic medical monitoring in another company's establishments	❑	
Information published by federal agencies, including NIOSH and OSHA	❑	

29. **In the past 10 years has your company chosen not to use genetic screening or monitoring due to the results of:**

	YES	NO
Genetic monitoring in your own establishment(s)	❑	❑
Genetic monitoring in another company's establishments	❑	❑
Genetic screening in your own establishment(s)	❑	❑
Genetic screening in another company's establishments	❑	❑

30a. Which office determines whether or not a specific test will be conducted as part of pre-employment screening?

30b. Which office determines whether or not a specific test will be conducted as part of employee health surveillance?

	PRE-EMPLOYMENT SCREENING	EMPLOYEE HEALTH SURVEILLANCE
Corporate personnel.....	☐	☐
Corporate health.....	☐	☐
Location personnel.....	☐	☐
Location health.....	☐	☐
Other (SPECIFY) _____.....	☐	1

31. Is your company currently considering conducting direct-DNA screening of employees or job applicants for any reason?

☐ Yes ☐ No ☐ Not sure

32. Is your company currently considering conducting direct-DNA monitoring of employees or job applicants for any reason?

☐ Yes ☐ No ☐ Not Sure

33. Does your company anticipate conducting any biochemical genetic screening, for any reason, in the next five years?

☐ Yes ☐ No ☐ Not Sure

34. Does your company anticipate conducting any cytogenetic monitoring, for any reason, in the next five years?

☐ Yes ☐ No ☐ Not Sure

35. Does your company anticipate conducting any direct-DNA screening, for any reason, in the next five years?

☐ Yes ☐ No ☐ Not Sure

36. Does your company anticipate conducting any direct-DNA monitoring for any reason, in the next five years?

Yes ❑ No Not Sure

37. Which office/division within the company is/will be responsible **for administering genetic tests?**

_____

38. Which position/ofl'ice within the company Mill be responsible for interpreting genetic test results?

_____

39. *Which office* in your company is responsible for employee health records?

tkdfcal/Occupational **health**. . . . . ❑ 1
Personnel . - . . . . . ❑
Other (SPECIFY)

_____

40. Does **your company permit access to employee medical records -- at company discretion, with employee permission, or both, to:**

	AT COMPANY DISCRETION	EMPLOYEE PERMISSION	BOTH
Personnel department	❑	❑	❑
Health Insurance carriers	❑	❑	
Life insurance carriers	❑ 1	❑	❑
Disability insurance carriers	❑	❑	❑
Unions	❑ 1	❑	❑
Other companies	❑ 1	❑	
Employee	❑	❑	❑
Employee's spouse	❑		❑
Other family	❑	❑	❑

GENERAL ATTITUDES

41. How do you feel about the following general statements concerning genetic screening and monitoring in the workplace? For each statement, please indicate whether you agree strongly, agree somewhat, disagree somewhat, or disagree strongly.

	AGREE STRONGLY	AGREE SOMEWHAT	DISAGREE SOMEWHAT	DISAGEE STRONGLY
It's fair for employers to use genetic screening to identify individuals whose increased **risk of occupational disease poses the potential for greater costs to the employer**	❑	un		
The employer should have the option of deciding how to use the information obtained through genetic screening **and** monitoring	❑	00		❑
The decision **to perform genetic screening of job applicants and em-**ployees should be the employer's	❑	00		
The decision to **perform genetic monitoring of employees should be** the employer's	❑	ncl		❑
Government agencies **should** provide guidelines **for genetic screening of job applicants and employees.**	❑	00		❑
Government agencies should provide guidelines for genetic monitoring of employees	❑	00		❑
Genetic screening in the workplace represents a potential threat to the rights of employees	❑	00		❑

DEMOGRAPHICS

D1. What is the major industrial classification of your company (sue.haschemicals,fo@textil~etcJ ?

_____

D2. Approximately how many persons are employed in the Unlted States by your company?

❑ **Less than 1,000** 1 **1,000-4,999** 1 **5,000-9,999** 1 **10,000 or more**

D3. What proportion of the establishments in your company have occupational health care professionals on premises?

All ❑ **Host** **Some** ❑ **Few** ❑ **None**

D4. Which of the following types of health professionals are employed, either full or part time, as part of the occupational health staff of this company?

Physicians (MD/Do) **Physician assistants** ❑ **Nurse practitioners** ❑ **Registered** nurses **Industrial** hygienists **Other health** professionals

D5 What is your job title?

_____

D6. What are your main job responsibilities?

_____

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us any other opinions, concerns or suggestions related to genetic testing in the workplace that you feel our questions did not address. These comments may be "incorporated in our report to Congress. We would also appreciate your comments on any survey questions that you found confusing or difficult to answer, to help us analyze the results. 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 completely anonymous. No linkage between companies and questionnaires will be retained. The label from the completed questionnaire will allow us to eliminate your company from those that we have to recontact.

However, if you feel that you cannot complete the questionnaire if there is even temporary identification, then peel off the label before returning the questionnaire. We appreciate your help and we want you to be Comfortable with doing the survey.

_____

PEEL OFF LABEL WITH SAMPLE IDENTIFICATION NUMBER HERE

_____

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

Schulman, Ronca and Bucuvalas, Inc.
444 Park Avenue South
New **York New York 10016**

(212) 4814$200 Attn: Dr. **Mark Schulman**

Appendix F
Survey Instrument: Corporate Personnel Officers

SURVEY OF WORKPLACE HEALTH AND GENETIC SCREENING AND MONITORING

CORPORATE PERSONNEL OFFICER VERSION

The Congressional Office of Technology Assessment is conducting a national survey of the opinions and experiences of employers related to the usc of genetic screening and monitoring in the workplace. This questionnaire has been directed to you as the person in your organization whose responsibilities include personnel issues. We need your assistance in answering, as best you can, some questions about workplace **testing** and employee health in your company.

For the purposes of this survey and the subsequent report, OTA has adopted the following definitions. By genetic monitoring we mean periodically examining employees to evaluate modifications of their genetic material via tests such as cytogenetic or direct-DNA tests. By genetic screening wc mean screening job applicants or employees for certain inherited characteristics. Screening tests may be biochemical tests or direct-DNA tests. They can be used to indicate a predisposition to an occupational illness if exposed to a specific environmental agent, or they could be used to detect any inherited characteristic such as Huntington's disease. In contrast to periodic monitoring screening tests arc generally performed only one time per characteristic.

This is an important study, which has been requested by the Congress of the United States, designed to represent the opinion and experience of the employer. We need to know how employers view the technologies of genetic screening and monitoring in terms of their current and future applications to the workplace. We also want to know how these technologies are seen in the broader context of more common forms of employee health screening and monitoring in the workplace.

Your responses arc very important, regardless ***of*** whether you have had any experience with genetic screening or monitoring. If your company has never explored the technology, the questionnaire will only take ten minutes. If you have some experience with the technology, it may take a little longer to complete the questionnaire. In either case, your experiences and opinions will help to inform congressional opinion about this area.

Please read each question and mark the box(es) that most nearly corresponds to your answer. **After each** answer continue with the next question unless there is an instruction to skip to a particular question. Please feel free to qualify your answers, if you feel it is necessary. You arc free to decline to answer any questions that you consider inappropriate. The questionnaire and any identifying information will be destroyed after data entry, so that all responses will be anonymous as well as confidential. Space has been provided at the end for comments and opinions that you feel arc not adequately represented by the survey questions.

We would like to begin with a few questions about your views on the appropriateness of employee testing in certain workplace situations.

1. Do **you think that it is generally appropriate or generally inappropriate for a company to require pre-employment health examinations of job applicants in workplace settings where there are no known health risks?**

Appropriate ..... 1 Inappropriate ..... ❑

2. Do **you think that it is generally appropriate or generally inappropriate for a company to require pre-employment health examinations of job applicants in workplace settings where there are known health risks?**

Appropriate .,..... ❑ Inappropriate ..... ❑

IF 'INAPPROPRIATE IN BOTH Q. 1 AND Q. 2, SKIP To Q. 4.

3. **Would your company consider it acceptable or unacceptable to conduct a pm-employment health examination in order to:**

	ACCEPTABLE	Unacceptable
Identify job applicants who are physically unfit for employment	❑	❑
Identify job applicants who are emotionally or psychologically unstable	1	1
Identify job applicants who are currently using drugs	❑	❑
Identify job applicants who are at increased risk to workplace hazards	❑	❑
Identify job applicants with genetic susceptibility to workplace exposures	❑	❑
Identify job applicants who represent high insurance risks	❑	1

4. Do you think that it is generally appropriate or generally inappropriate for a company to require periodic medical testing of employees in workplace settings where there are no known health risks?

Appropriate ❑ Inappropriate 1

5. Do you think that it is generally appropriate or generally inappropriate for a company to require periodic medical testing of employees in workplace settings where there are known health risks?

Appropriate ❑ Inappropriate 1

IF "INAPPROPRIATE" IN BOTH Q.4 AND Q.5, SKIP TO Q.7.

6. Do you think that it is generally cost effective or not cost-effective for a company to conduct periodic medical testing of employees foR:

	COST EFFECTIVE	NOT COST EFFECTIVE
High blood pressure	c1	❑
Respiratory function	❑	❑
Malignancies	❑	❑
Hearing function	1	1
Vision	❑	1
Chromosome abnormalities	❑	1
Drug abuse	❑	❑

7. Do you think it is currently cost-effective or not cost-effective for a company like yours to:

	COST EFFECTIVE	NOT COST EFFECTIVE	NOT SURE
conduct biochemical genetic tests as part of pre-employment screening	❑		DO
Conduct direct-DNA tests as part of pre-employment screening	❑		on
Conduct genetic monitoring of all workers exposed to workplace hazards	❑		on
Conduct genetic screening of workers to detect genetic susceptibilities to workplace hazards	❑		00

8. **Would your company consider the use of genetic tests for employees or job applicants generally acceptable or generally unacceptable to:**

	ACCEPTABLE	UNACCEPTABLE
Make a clinical diagnosis of a sick employee	❑	
Establish links between genetic pre disposition and workplace hazards	❑	❑
Inform employees of their increased susceptibility to workplace hazards	1	
Exclude employees with increased susceptibility from risk situations	1	❑
Monitor chromosomal changes associated with workplace exposures	1	❑
Establish evidence of pre-employment health status for Inability purposes	❑	

9. If an employer becomes aware that an employee has a genetic susceptibility to serious illness if he or she is exposed to substances in the workplace, do you think the employer should exclude that employee from those jobs for which he/she is at increased risk, or do you think the employer should allow the employee to take those jobs, if he/she waives corporate liability?

Should be excluded ❑ Allowed to take ❑

10. As part of your pre-employment hiring practices, do youcurrently require each of the following as a condition of employment for all applicants, only applicants for certain plants or job classifications, only applicants with certain medical conditions or histories, or for no applicants?

	ALL	PLANTS/ JOBs	CONDITIONS/ HISTORIES	HONE
Routine physical "examination	❑	❑	❑	❑
Biochemical genetic screening tests	❑	❑		
Cytogenetic monitoring tests	❑	❑		❑
Other medical criteria, e.g., lower back X-ray, allergy testing	1	❑		❑
PersonalitY/psychological testing	❑	❑		❑
Drug testing	J	❑		❑

IF "NONE" TO ALL IN Q. IO, SKIP To Q.12

11. Is it company policy to inform applicants of positive test results?

Yes. 1 No. 1

ha. Is it company policy to refer applicants to appropriate health care providers if positive test results are obtained?

Yes. ❑ No. 1

12a. Does your company have a policy concerning hiring-

FOR EACH "YES" IN Q. *12a*

12b. Generally speaking, would you say it is against company policy to hire...

	Q.12a HAVE POLICY NO	Q.12a HAVE POLICY YES	Q. i2b AGAINST POLICY YES	Q. i2b TO HIRE NO	Q. i2b TO HIRE DEPENDS
Cigarette sinkers	❑	❑	❑	a	n
Persons with criminal records	❑	0	❑	o	n
Persons with pre-existing medical conditions	❑	cl	❑	❑	❑
Persons with *increased* genetic susceptibility to substances or conditions in the workplace	❑	0	❑	**0**	**0**

IF YOUR COMPANY HAS NEVER DONE ANY BIOCHEMICAL GENETIC SCREENING, CYTOGENETIC MONITORING, DIRECT-DNA SCREENING, OR DIRECT-DNA MONITORING, SKIP TO QUESTION 19.

1.3. To the **best of your knowledge, which of the following were important factors in the decision to conduct genetic screening or monitoring of employees in your company?**

	IMPORTANT	NOT IMPORTANT
Cost **benefit analysis**	❑	❑
Evidence of a possible association between chemical exposure and illness in animal studies	1	1
Evidence of a possible association between chemical exposure and illness in epidemiological studies	❑	1
Legal consequence of failure to test	❑	❑
Union/employee initiative	❑	❑
Something else (Please Specify) _____	❑	❑

14. To the best of **your knowledge, has your company ever rejected a job applicant, primarily or partly, based on the results of genetic screening tests?**

Yes ❑ No ❑ → ***SKIP TO Q. 15***

14a. When was the most recent time that occurred?

- Within past month ❑
- Within past year ❑
- 1-2 years ago 1
- 3 or more years ago ❑

14b. What was the condition(s)?

_____

14c. Was the applicant informed of the reason for the rejection?

yes ❑ No ❑

14& Was alternative employment within your **company offered?**

Yes..... ❑ **No.....** ❑

15. Have any medical or physical criteria been specified that would disqualify individuals from:

work in the company	YES ❑ ;
Work in specified plants or locations	❑ o
Work in specified jobs	❑ **0**

16. Does your company maintain statistical data on job applications, outcomes, and reasons for rejection?

Yes..... • **1** **Ho.....** ❑ —> ***SKIP TO Q. 18***

17. Are biochemical or cytogenetic tests used as rejection categories in these data?

Yes..... ❑ **NOEJ**

18. Has your company ever transferred or terminated an employee, primarilyor partly, based on the results of genetic screening or monitoring?

Yes..... ❑ **INO** ..... ❑ —> ***SKIP TO Q. 19***

18a. When was the most recent **time that occurred?**

Within past month.	❑
Within past year.	• 1
1-2 years ago..	• 1
3 or more years ago.	❑

18b. what was the condition?

_____

l8c. Was the employee informed of the reason for the action?

Yes..... ❑ **l)iocl.....**

19. Is it your company's policy to conduct periodic medical testing of persons in any risk categories?

Yes..... ❑ **No.....** ❑ —> ***SKIP TO Q. 20***

19a. Is it company policy to inform employees of positive test results?

Yes..... • **1** **No.....** ❑

19b. Is it company policy to refer employees to appropriate health care providers if positive test results are obtained?

Yes..... • **1** **No.....** ❑

19c. Is it company policy to release positive test results to anyone outside of the company, other than the employee?

Yes..... ❑ **No.....** ❑ —wsKIP TO **Q. 20**

19d. Under what circumstances?

_____

19e. Was alternative employment within your company offered?

Yes. . . . . ❑ . . . . 0 . . . .

19f. Does your company have a set of guidelines for this type of situation or is it left to the discretion of the particular establishment?

Yes. . . . . • ❑ . . . . . No

20. Does your company maintain statistical data on the masons for job terminations?

Yes. . . . . ❑ No. . . . . ❑ → SKIP TO Q. 21

20a. Are biochemical or cytogenetic tests used as rejection categories in these data?

Yes. . . . . ❑ "o . . . . . ❑ . . . . . .

20b. Are other medical criteria used as rejection categories in these data?

Yes. . . . . • No 1 . . . . . ❑

21. Within the next five years, do you anticipate that your company will conduct:

	YES	NO
Mandatory biochemical genetic screening.	❑	
Voluntary biochemical genetic screening	❑	❑
Mandatory cytogenetic monitoring	• 1	❑
Voluntary cytogenetic monitoring.	❑	❑
Mandatory DNA-based genetic screening	❑	
Voluntary MA-based genetic screening,.	• 1	❑
Mandatory DNA-based genetic monitoring.	❑	
Voluntary DNA-based genetic monitoring.	• 1	

22. If you were asked, would you recommend to your company that genetic screening be done as part of pre-employment screening?

Yes. . . . . ❑ → Based on what criteria? _____

No. . . . . • 1 _____

23. If you were asked, would you recommend to your company that periodic genetic monitoring of employees be done?

Yes. . . . . • 1 → Based on what criteria? _____

No. . . . . • 1 _____

24. Approximately what proportion of your employees are covered by collective bargaining agreements?

Less than 10%. . . . . • 1

10% to 49%. . . . . • 1

50% to 75%. . . . . • 1

More than 75%. . . . . • 1

25. Have union contract negotiations ever covered the topic of genetic screening and/or genetic monitoring?

Yes. . . . . ❑ h 1

26. What proportion of your company% employees are covered by health insurance offered by the company?

All . . . . . ❑ Host . . . . . ❑ Some . . . . . ☐ Few . . . . . ☐ None . . . . . ☐ → *SKIP TO Q. 27*

26a. Is the company% current health insurance plan(s) purchased from a private carrier, self-insured or both?

Private carrier . . . . . ❑ Self-insured . . . . . ☐ Both . . . . . n

27. **If a job applicant is currently healthy and able to perform the job, but is considered to be a health insurance risk would that consideration reduce the likelihood of his/her being hired by your company - a lot some or not at all?**

A lot. . . . . ❑ Some . . . . . ☐ Not at all . . . ☐

28. Does your company assess the health insurance risk of job applicants on a routine basis, sometimes or never?

Routine. . . . . ❑ Sometimes . . . . ☐ Never . . . . . ☐ → *SKIP TO Q. D1*

28a. Does the health insurance assessment of job applicants also consider the health of dependents?

Yes. . . . . ❑ No . . . . . ☐

DEMOGRAPHIC CHARACTERISTICS

D1. What& the major industrial classification of your company (such as chemicals, food, textiles, etc.) ?

_____

D2. Approximately how many persons are employed in the United States by your company?

Less than 1,000 . . . . . ❑
1,000 - 4,999 . . . . . ❑
5,900- 9,999 . . . . . • 1
10,000 or more. . . . . • 1

D3. What is your job title?

_____

D4. What are your main job responsibilities?

_____

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us any other opinions, concerns or suggestions related to genetic testing in the workplace that you feel our questions did not address. These comments maybe incorporated in our report to Congress. We would also appreciate your comments on any survey questions that you found confusing or difficult to answer, to help us analyze the results. 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 completely anonymous. No linkage between companies and questionaires will be retained. The label from the completed questionnaire will allow us to eliminate your company from those that wc have to recontact.

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PEEL OFF LABEL WITH SAMPLE IDENTIFICATION NUMBER HERE

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Schulman, Ronca and Bucuvalas, Inc
444 *Park* **Avenue South**
New York **New York 10016**

(212) 481-6200 Attn: Dr. **Mark Schulman**

Appendix G
Survey Instrument: Union Presidents

SURVEY OF WORKPLACE HEALTH AND GENETIC SCREENING AND MONITORING

LABOR UNION VERSION

The Congressional Office of Technology Assessment is conducting a national survey of the opinions and experiences of unions related to the use of genetic screening and monitoring in the workplace. We need your assistance in answering as best you can, some questions about workplace testing and member health in your union.

For the purposes of this survey and the subsequent report, OTA has adopted the following definitions. By genetic monitoring wc mean periodically examining members to evaluate modifications of their genetic material via tests such as cytogenetic or direct-DNA tests. **By genetic screening, wc mean screening members or potential members for** certain **inherited characteristics. Screening tests may be biochemical tests or direct-DNA** tests. They can be used to indicate a predisposition to an occupational illness if exposed to a specific environmental agent, or they could be used to detect any inherited characteristic such as Huntington's disease. In contrast to periodic monitoring screening tests arc generally performed only one time per Characteristic

This is an important study, which has been requested by the Congress of the United States, designed to represent the opinion and experience of leading unions. We need to know how unions view the new technology of genetic screening and monitoring in terms of its current and future applications to the workplace. We also want to know how these technologies arc seen in the broader context of more common forms of employee health screening and monitoring in the workplace.

Your responses arc very important, regardless of whether your union has had any experience with genetic screening or monitoring. If your union has never explored the technology, the questionnaire will only take ten rminutes. If you have some experience with the technology, it may take a little longer to complete the questionnaire. In either case, your experiences and opinions will help to inform congressional opinion about this area.

Please read each question and mark the box(es) that most nearly corresponds to your answer. After each answer continue with the next question unless there is an instruction to skip to a particular question. Please feel free to qualify your answers, if you feel it is necessary. Space has been provided at the end for comments and opinions that you feel are not adequately represented by the survey questions.

You arc free to decline to answer any questions that you consider inappropriate. The questionnaire and any identifying information will be destroyed after data entry, so that all responses will be anonymous as well as confidential.

1. Are health examinations required by companies that employ members of your union of all, most, some, few or no members?

a All ❑ Host ❑ Some ❑ Fen

❑ None ——→ SKIP to Q.3

2. Which of the following are normally part of the examination that is given by companies for your union members? (MARK AU THAT APPLY)

Personal medical history	❑	Chest X-ray	• 1
family medical history	• 1	Pulmonary function test	❑
Simple physical examinations	• 1	Eye and hearing exam	❑
Standard blood chemistry tests	• 1	Urinalysis for drug use	❑
EKG	❑	Lower back X-ray	• 1

3. **Are any members of your union exposed to chemicals or ionizing radiation in the workplace setting?**

❑ Yes ❑ No → SKIP TO Q.4

3a. Are those members who are exposed to chemicals or ionizing radiation routinely rotated to avoid prolonged exposure?

• 1 Yes 1 no

3b. Does your union conduct any form of medical surveillance of employees whose job may expose them to environmental health risks?

Yes ❑ No

4. Are any members of your union exposed to any known workplace condition where there is a greater risk of negative health outcome, depending upon individual susceptibilities?

❑ Yes ❑ No → SKIP TO Q.5

4a. Is any form of screening conducted to identify members of your union at increased risk for these jobs?

Yes, by union | Yes, by company | ❑ Yes, by union and company | ❑ No → SKIP TO Q.5

4b. Which, if any, of the following types of screening are conducted to identify increased individual susceptibility to workplace risk?

	CHECK ALL THAT APPLY CONDUCTED BY UNION	CONDUCTED BY COMPANY
Medical History.....	1	❑
Non-genetic screening (e.g.. lower back X-ray, allergy testing)....	❑	❑
Genetic screening	❑	
Genetic Monitorlng.....	❑	❑
None.	1	❑

S. Does **your union have a formal policy related to the use of genetic tests in the screening of employees or job applicants?**

❑ Yes ❑ No

6. Does your union have a formal policy related to the use of genetic tests in the monitoring of employee health?

❑ Yes Ho

7. Has your union ever recommended to a company that it change a workplace practice or exposure level due to the results of:

	YES	NO
Genetic monitoring in establishment(s) where your members work.	❑	1
Other non-genetic medical monitoring in establishment(s) where your members work	❑	❑
Genetic monitoring in establishments where your union is not represented	❑	1
Other non-genetic medical monitoring In establishments where your union is not represented	❑	❑
Information published by federal agencies, including NIOSH and OSHA.	❑	❑

8. **Have union contract negotiations ever covered the topic of genetic screening and/or genetic monitoring?**

❑ Yes ❑ No

9. **Has your union ever filed an employee grievance related to genetic screening or monitoring?**

❑ Yes ❑ No ——→ **SKIP TO Q.1O**

9a. Did that grievance involve employee firing, transfer or something else?

❑ Firing ❑ Transfer ❑ Other

10. To the best of your knowledge, has a member of your union applying for a job been rejected, primarily or partly, based on the results **of genetic screening tests?**

❑ Yes ❑ No → SKIP TOQ.11

10a. When was the most recent time that occurred?

Within past month. . . . . • 1
Within past year. . . . . ❑
1-2 years ago. . . . . ❑
3 or more years ago. . . . . ❑

10b. What was the condition(s)?

_____

10c. Was alternative employment within **the company offered?**

❑ Yes ❑ No

11. To the best of your knowledge, has any member of your union been transferred or terminated by a company based on the results of genetic screening or monitoring?

❑ Yes ❑ No → SKIP TO Q.12

ha. When was the most recent time that occurred?

Within past month. . . . . ❑
Within past year. . . . . ❑
1-2 years ago. . . . . ❑
3 or more years ago. . . . . ❑

11b. What was the condition?

_____

12. **Does your union maintain statistical data on the reasons for job terminations?**

❑ Yes ❑ No ——→ **SKIP TO Q.13**

12a. Are biochemical and cytogenetic tests used as rejection categories in these data?

❑ Yes ❑ No

12b. Are other **medical criteria used as rejection categories in these data?**

❑ Yes ❑ Ho

13. Would your union consider It acceptable or unacceptable for an employer to conduct a health examination of job applicants In order to:

	ACCEPTABLE	UNACCEPTABLE
Identify job applicants who are physically unfit for employment	❑	❑
Identify job applicants who are emotionally or psychologically unstable	: 1	❑
Identify job applicants who are currently using drugs	: 1	❑
Identify job appl icants who are at increased risk to workplace hazards	❑	❑
Identify Job appl icants with genetic susceptibility to workplace exposures....	1	c 1
Identify job appl icants who represent high insurance risks.	: 1	❑

14. How do you feel about the following general statements concerning genetic screening and monitoring in the workplace? For each statement, please indicate whether you agree strongly, agree somewhat, disagree somewhat, or disagree strongly.

	AGREE STRONGLY	AGREE SOMEWHAT	DISAGREE SOMEWHAT	DISAGREE STRONGLY
It's fair for employers to use genetic screening to identify individuals whose increased risk of occupational disease poses a threat for greater costs to the employer	❑	❑	❑	❑
The employer should have the option of deciding how to use the information obtained through genetic screening and monitoring	❑			❑
The decision to perform genetic screening of Job applicants and employees should be the employer's	• 1	❑	❑	❑
The decision to perform genetic monitoring of employees should be the employer's	❑			❑
Government agencies should provide guidelines for genetic screening of job applicants and employees	❑		❑	❑
Government agencies should provide guidelines for genetic monitoring of employees	❑	❑		
Genetic screening in the workplace represents a potential threat to the rights of employees	❑		❑	

15. Would your union consider the use of <u>genetic screening</u> or <u>monitoring</u> of employees or job applicants by employers as generally acceptable or generally unacceptable to:

	GENERALLY ACCEPTABLE	GENERALLY UNACCEPTABLE
Make a clinical diagnosis of a sick member	❑	
Establish links between genetic predisposition and workplace hazards	❑	❑
Inform members of their increased susceptibility to workplace hazards	❑	
Exclude members with increased susceptibility from risk situations	❑	❑
Monitor chromosomal changes associated with workplace exposures	❑	
Establish evidence of pre-employment health status for liability purposes	❑	❑

16. If an employer becomes aware that an employee has a genetic susceptibility to serious illness if he or she is exposed to substances In the workplace, do you think the employer should exclude that employee from those jobs for which he/she is at increased risk, or do you think the employer should allow the employee to take those jobs, if he/she waives corporate liability?

Should be excluded . . . . . ❑ Allowed to take 0

The following questions concern biochemical genetic screening and/or cytogenetic monitoring that may have been conducted by your union on one or more members or potential members. By conduct we mean perform, contract for, or arrange for the test as part of a routine or ongoing program.

17. Is your union currently conducting biochemical genetic screening of any members or potential members, for research or any other reason?

❑ Yes No • 1 Not Sure

18. Has your union conducted any biochemical genetic screening of any members or potential members, for research or any other reason In the past 19 years?

❑ Yes No ❑ Not sure

19. Is **your** union currently conducting cytogenetic monitoring of **any members or potential members, for research or any other reason?**

1

❑ Yes No ❑ Not Sure

20. Has **your union conducted any cytogenetic monitoring of any members or potential members, for research or any other** reason in the past **19 years?**

❑ Yes Ho Not Sure

21. Is your union currently conducting direct-DNA screening of any members or potential members, for research or any other reason?

❑ Yes No ❑ Not Sure

22. Is your union currently conducting direct-DNA monitoring of any members or potential members, for research or any other reason?

❑ Yes No ❑ Not Sure

23. Has your **union conducted any of the following tests, either currently or in the past, as part of a voluntary wellness program, at the request of a member, or for diagnosis? (MARK ALL THAT APPLY)**

		BIOCHEMICAL. GENETIC SCREENING	CYTOGENETIC MONITORING	DIRECT-DNA SCREENING	DIRECT-DNA MONITORING
a. As part of a voluntary wellness program	Current ly..	❑	❑		
	In past 19 years	❑	❑		
	No.	1	❑	❑	❑
	Not sure.	❑	❑		
b. At the request of the member:	Currently..	1	❑		
	In past 19 years	1		❑	
	No	1	❑	❑	❑
	Not sure.	1	❑		❑
c. For diagnosis:	Currently	❑	❑		❑
	In past 19 years	❑	1		❑
	No.	❑	❑	❑	❑
	Not sure.	1	❑	❑	❑

IF YOUR UNION HAS NEVER DONE BIOCHEMICAL GENETIC SCREENING, CYTOGENETIC MONiTORING, DIRECT-DNA SCREENING, OR DIRECT-DNA MONITORING, SKIP TO QUESTION 32 0N PAGE 12

IF YOUR UNION HAS DONE CYTOGENETIC MONITORING, DIRECT-DNA SCREENING, OR DIRECT-DNA MONITORING OF MEMBERS, FOR ANY PURPOSE, BUT NOT BIOCHEMICAL GENETIC SCREENING, SKIP TO QUESTiON 25 0N PAGE 10

IF YOUR UNION HAS EVER DONE BIOCHEMICAL GENETIC SCREENING OF ANY MEMBER, FOR ANY PURPOSE, PLEASE CONTINUE WITH QUESTiON 24

24. **Which of the following types of biochemical screening tests are being conducted by your union of any members or potential members? (MARK AU THAT APPLY)**

FOR EACH TEST CONDUCTED, MARK WHETHER THE TESTING IS BEING DONE ON A ROUTINE BASIS FOR HEALTH SURVEILLANCE, AS PART OF A VOLUNTARY RESEARCH PROGRAM, AS PART OF FOLLOW-UP DIAGNOSIS, OR AS PART OF A VOLUNTARY WELLNESS PROGRAM, OR ONLY AT THE REQUEST OF A MEMBER

	NOT DONE	ROUTINE HEALTH SURVEILLANCE	VOLUNTARY RESEARCH PROGRAM	FOLLOW-UP DIAGNOSIS	VOLUNTARY WELLNESS PROGRAM	AT MEMBER REQUEST
Sickle cell trait	1	❑	❑	❑		
Glucose-6-phosphate dehydrogenase deficiency (G-6-PO)	❑	❑		❑	❑	
deficiency	❑	❑	❑			❑
alpha-1 def	❑	❑	0	❑		❑
Alpha and beta thalassemias	1	❑	u		❑	❑
Aryl hydrocarbon	❑				❑	❑
vs. fast o	❑		❑			❑
Allergic respiratory disease	❑	❑			❑	❑
Contact	❑		❑	❑		❑
(HIA)	1	❑		❑	❑	❑
Other	❑	❑	❑			❑
Bloom	❑	❑		❑	❑	❑
	1		❑	❑	❑	❑
	❑			❑		
	❑		❑	❑		❑
Other	1			❑		

25. Which of the following types of cytogenetic monitoring are being conducted by your union of any members? (MARK ALL THAT APPLY)

FOR EACH TEST CONDUCTED, MARK WHETHER THE TESTING IS BEING DONE ON A ROUTINE BASIS FOR HEALTH SURVEILLANCE, AS PART OF A VOLUNTARY RESEARCH PROGRAM, AS PART OF FOLLOW-UP DIAGNOSIS, AS PART OF A VOLUNTARY WELLNESS PROGRAM, OR ONLY AT THE REQUEST OF A MEMBER

	NOT DONE	ROUTINE HEALTH SURVEILLANCE	VOLUNTARY RESEARCH PROGRAM	FOLLOW-UP DIAGNOSIS	VOLUNTARY AT WELLNESS PROGRAM	MEMBER REQUEST
Chromosome aberrations	1			❑	n	❑
Sister chromatid exchanges	1	❑	❑	❑	n	❑
Mutations by assaying the DNA	1	❑		❑	❑	
Mutatlons by assaying the enzyme/protein	❑	❑	❑	❑	n	❑
HPRT mutation rate	❑		❑	❑	n	❑
DNA adduct formation	1	❑	❑	❑	❑	❑
Other (SPECIFY) _____	❑	❑	1	❑	o	❑

26. To the best of your knowledge, which of the following were important factors in the decision to conduct genetic screening of your members?

	IMPORTANT	NOT IMPORTANT
Cost benefit analysis	❑	❑
Evidence of a possible association between chemical exposure and illness In animal studies	❑	❑
Evidence of a possible assocciation between chemical exposure and Illness in epidemiological studies	❑	❑
Legal consequence of failure to test	❑	❑
Union/employee initiative	1	❑
Something else. (PLEASE SPECIFY) _____	❑	1

27. Are all members routinely informed of abnormal (positive) findings, normal (negative) findings, both or neither from genetic screening and monitoring tests?

- Abnormal (positive) ❑
- Normal (negative) ❑
- Both ❑
- Neither ❑

28. Is counseling offered to all members with abnormal (positive) genetic test results by the union or are they referred to *their own* physicians?

Union counseling. . . . . ❑

Referred to own physicians... . . : 1

29. Does your union employ or contract with a genetic counselor?

❑	❑	❑
Employ	Contract with	Neither

30. Has a member ever been referred for genetic counseling by your union's medical staff as a result of any medical or genetic testing?

	❑
Yes	No

31. As a result of a genetic screening or monitoring program has your union ever—?

	YES	NO
Suggested a member seek a job in another company....	❑	
Suggested a member seek a transfer to a different job in the same company	❑	
Recommended company implement engineering control	❑	
Recommended company provide personal protection devices . . .	❑	❑
Recommended company implement a research program	❑	❑
Recommended company discontinue a product or change materials in a product	❑	❑
Some other action (PLEASE SPECIFY)	❑	❑

_____

32. Is **your union currently considering conducting direct-DNA screening of members or potential members for any reason?**

❑ Yes ❑ No ❑ Not Sure

33. Is your union currently considering conducting direct-DNA monitoring of members or potential members for any reason?

❑ Yes ❑ No ❑ Not Sure

34. Does your union anticipate conducting any biochemical genetic screening, for any reason, in the next five years?

1 Yes 1 No 1 Not Sure

35. Does your union anticipate conducting any cytogenetic monitoring, for any reason, in the next five years?

❑ Yes ❑ No ❑ Not sure

36. Does your union anticipate conducting any direct-DNA screening, for any reason, in the next five years?

❑ Yes ❑ No 1 Not Sure

37. Does **your union anticipate conducting any direct-DNA monitoring for any reason, in the next the years?**

❑ Yes ❑ no Not sure

38. Which office/division within the union is/will be responsible for administering genetic tests?

_____

39. Has genetic screening or monitoring ever been done of your union members based on:

	CHECK ALL THAT APPLY CONDUCTED BY UNION	CONDUCTED BY COMPANY
Family History	❑	❑
Gender	❑	❑
Ethnic/racial background	❑	❑
Co-factors (e.g. smoking)	❑	❑
Job exposures	❑	❑
NO TEST CONDUCTED	❑	❑

DEMOGRAPHICS

D1. What are the major industrial classifications (such as chemicals, **food, textiles, etc.) of those** companies in companies in which your members **work?**

_____

D2. Approximately how many members does your union have?

_____

D3. What is your job title?

_____

D4. What are your main job responsibilities?

_____

Thank you very much for your cooperation in answering our questions. We would also like to give you an opportunity to give us any other opinions, concerns or suggestions related to genetic testing in the workplace that you feel our questions did not address. These comments may be incorporated in our report to Congress. We would also appreciate your comments on any survey questions that you found confusing or difficult to answer, to help us analyze the results. Please write these comments below.

We have attached a peel-off identification number on the questionnaire. This is the only link between the unions 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 completely anonymous. No linkage between unions and questionnaires will be retained. The label from the completed questionnaire will allow us to eliminate your union from those that wc have to recontact.

However, if you feel that you cannot complete the questionnaire if there is even temporary identification, then peel off the label before returning the questionnaire. We appreciate your help and we want you to be comfortable with doing the survey.

PEEL ***OFF LABEL WITH SAMPLE IDENTIFICATION NUMBER HERE***

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

Schulman, Ronca and Bucuvalas, Inc.
444 Park Avenue South
New York New York 10016

(212) 481-6200 Attn: Dr. Mark Schulman

Appendix H
Acknowledgments

OTA would like to thank the members of the advisory panel who commented on drafts of this report and the many individuals and organizations that supplied information for the study. In addition, OTA acknowledges the following individuals who reviewed drafts of this report:

Ronald T. Acton
University of Alabama
Birmingham, AL

Lori B. Andrews
American Bar Foundation
Chicago, IL

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Eastman Kodak Co.
Rochester, NY

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Tenneco, Inc.
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Human Services
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Appendix I
List of Contractor Documents

For this report, OTA commissioned papers on various topics concerning genetic monitoring and screening in the workplace. The manuscripts are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161, telephone (703) 487-4650.

"Confidentiality of Genetic Information in the Workplace," Lori B. Andrews, American Bar Foundation, Chicago, IL.

"The Ethics of Genetic Testing in the Workplace," Baruch A. Brody, Baylor College of Medicine, Houston, TX.

"Genetic Predisposition to Occupationally Related Diseases: Current Status and Future Directions," Edward J. Calabrese, University of Massachusetts, Amherst, MA.

"Genetic Testing in the Workplace: The NLRA, NLRB, and Collective Bargaining," Hastings S. Trigg, Jr., E.I. du Pent de Nemours & Co., Wilmington, DE.

"Human Rights and Genetic Testing in the Workplace," Alan Gewirth, University of Chicago, Chicago, IL.

"Selected Legal Issues Surrounding Genetic Testing in the Workplace," Robert I. Field, Dilworth, Paxson, Kalish & Kauffman, Philadelphia, PA.

Appendix J

Acronyms and Glossary of Terms

Acronyms

A — adenine
ADA — Americans with Disabilities Act
AHH — aryl hydrocarbon hydroxylase
AIDS — acquired immunodeficiency syndrome
ALA — aminolevulinic acid
AMA — American Medical Association
ANFI — absolute nuclear flourescence intensity
AOMA — American Occupational Medical Association
APKD — adult polycystic kidney disease
AS — ankylosing spondylitis
ASO — allele-specific oglionucleotide
AT — ataxia telangiectasia
ATSDR — Agency for Toxic Substances and Disease Registry (PHS, DHHS)
BC/BS — Blue Cross/Blue Shield
BLS — Bureau of Labor Statistics (DOL)
C — cytosine
CA — chromosomal aberration
CAD — coronary artery disease
CDC — Centers for Disease Control (PHS, DHHS)
CEHIC — Center for Environmental Health and Injury Control (CDC, DHHS)
CEO — Chief Executive Officer
CHD — coronary heart disease
CML — chronic myelogenous leukemia
COPD — chronic obstructive pulmonary disease
DHHS — U.S. Department of Health and Human Services
DNA — deoxyribonucleic acid
DOD — U.S. Department of Defense
DOE — U.S. Department of Energy
DOL —U.S. Department of Labor
EPA — U.S. Environmental Protection Agency
FA — Fanconi's anemia/syndrome
FPP — fetal protection policy
G — guanine
G-6-PD — glucose-6-phosphate dehydrogenase
GM — General Motors
GSH — reduced glutathione
HCS — hereditary cancer syndrome
HD — Huntington's disease
HDL — high-density lipoprotein
HERL —Health Effects Research Laboratory (EPA)
HHMI — Howard Hughes Medical Institute
HIV — human immunodeficiency virus
HLA — human leukocyte antigen
HPRT — hypoxanthine-guanine phosphoribosyltransferase
IDDM — insulin-dependent diabetes mellitus
IgA — immunoglobulin A
IOH — Institute of Occupational Health (Finland)
LDL — low-density lipoprotein
MRP — medical removal protection
NADH — nicotinamide adenine dinucleotide, reduced form
NAS — National Academy of Sciences
NCI —National Cancer Institute (NIH, DHHS)
NCTR — National Center for Toxicological Research (FDA, DHHS)
NIEHS — National Institute of Environmental Health Sciences (NIH, DHHS)
NIH —National Institutes of Health (DHHS)
NIOSH — National Institute for Occupational Safety and Health (CDC, DHHS)
NLRA — National Labor Relations Act
NLRB — National Labor Relations Board
NOES — National Occupational Exposure Survey (NIOSH)
NRC —National Research Council (NAS)
NSF — National Science Foundation
NTP — National Toxicology Program (PHS, DHHS)
OCT — ornithine carbamoyl transferase
OSH Act — Occupational Safety and Health Act
OSHA — Occupational Safety and Health Administration (DOL)
OSHRC — Occupational Safety and Health Review Commission (DOL)
OTA — Office of Technology Assessment
PCBs — polychlorinated biphenyls
PCR — polymerase chain reaction
PHS —U.S. Public Health Service (DHHS)
PKU — phenylketonuria
PTL — phenylthiourea
Px — peroxidase
Rb — retinoblastoma
RFLP — restriction fragment length polymorphism
RNA — ribonucleic acid
SARA — Superfund Amendments and Reauthorization Act of 1986
SAT — serum alpha-l-antitrypsin
SCE — sister chromatid exchange
SIC — standard industrial code
SOD — superoxide dismutase
SRBI — Schulman, Ronca, & Bucuvalas, Inc.
T — thymine
TSCA —Toxic Substances Control Act
TSD — Tay-Sachs disease
VA — U.S. Department of Veterans Affairs
XP — xeroderma pigmentosum

Glossary of Terms

Acetylation: The introduction of one or more acetyl groups into an organic compound.

Acquired immunodeficiency syndrome (AIDS): The most severe clinical manifestation of immune dysfunction caused by the human immunodeficiency virus (HIV).

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.

Amino acid: Any of a group of 20 molecules that combine to form proteins in living things. The sequence of amino acids in a protein is determined by the genetic code.

Autosome: Chromosome not involved in sex determination. In a complete set of human chromosomes, there are 44 autosomes (22 pairs).

Base pair: Two complementary nucleotides (adenosine and thymidine or guanosine and cytidine) held together by weak bonds. Two strands of DNA are held together in the shape of a double helix by the bonds between base pairs.

Biochemical genetics: The analysis of mutant genes on the basis of altered proteins or metabolizes.

Carcinogen/carcinogenesis: A chemical or physical agent that causes cancer.

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

Cell: The smallest component of life capable of independent reproduction.

Cell culture: Growth in the laboratory of cells isolated from multicellular organisms. Each culture is usually of one cell type (e.g., lymphocytes, fibroblasts, etc.).

Chromosomal aberrations: An abnormal chromosomal complement resulting from the loss, duplication, or rearrangement of genetic material.

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.

Clastogens: Chromosome-damaging agent.

cloning: The process of asexually producing a group of cells (clones), all genetically identical to the original ancestor. In recombinant DNA technology, the process of using a variety of DNA manipulation procedures to produce multiple copies of a single gene or segment of DNA.

Cytogenetics: The study of the relationship of the microscopic appearance of the chromosomes and their behavior to the genotype and phenotype of the individual.

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.*

DNA adducts: The binding of exogenous and xenobiotic materials to DNA to form additional products. They can be viewed as markers of exposure to specific toxicants.

DNA probes: Segments of single-strand DNA that are labeled with a radioactive or other chemical marker and used to identify complementary sequences of DNA by hybridizing with them.

DNA sequence: Order of nucleotide bases in DNA.

Dominant: An allele that exerts it phenotypic effect when present either in homozygous or heterozygous form.

Dosimeter: Device or methodology for measuring the dose of a chemical or ionizing radiation to a biological system.

Double helix: The shape in which two linear strands of DNA are bonded together.

Electrophoresis: Technique used to separate molecules such as DNA fragments or proteins. An electric current is passed through a medium containing the mixture, and each kind of molecule travels through the medium at a different rate, depending on its electrical charge and size. Separation is based on these differences.

Enzyme: A protein that acts as a catalyst, speeding the rate at which a biochemical reaction proceeds, without being permanently altered or consumed by the reaction so that it can be used repeatedly.

Epidemiologic studies: Studies concerned with the relationships of various factors determiningg the frequency and distribution of diseases in a human population.

Gamete: Mature male or female reproductive cell with a haploid set of chromosomes (23); that is, a sperm or ovum.

Gel: The semi-solid matrix used in electrophoresis to separate molecules.

Gene: The fundamental unit of heredity; an ordered sequence of nucleotide base pairs to which a specific product or function can be assigned.

Genetic monitoring: Involves periodically examining employees to evaluate modifications of their genetic material+. g., chromosomal damage or evidence of increased occurrence of molecular mutations-that may have evolved in the course of employment. It ascertains whether the genetic material of the group of individuals has altered over time.

Genetic screening: A process to examine the genetic makeup of individuals for certain inherited characteristics. It can be used to detect occupationally and nonoccupationally related traits.

Genetic testing: Technologies that determine a person's genetic makeup or that identify changes (damage) in the genetic material of certain cells. As used in the

workplace, it encompasses both genetic monitoring and screening.

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.

Genotype: The genetic constitution of an organism, as distinguished from physical appearance, or phenotype.

Germ cell: The male and female reproductive cells; egg and sperm.

Hemoglobin: The oxygen-carrying molecule found in red blood cells.

Hemoglobinopathies: A collection of hereditary disorders of hemoglobin structure and/or function. Examples are sickle cell anemia and thalassemia.

Hemolysis: Condition involving the destruction of red blood cells.

Heterozygous: Having two different alleles at a particular locus.

HLA: see *human leukocyte antigen.*

Homozygous: Having the same allele at a particular locus.

Human Genome Project: Research and technology development efforts aimed at mapping and sequencing some or all of the genome of human beings and other organisms.

Human immunodeficiency **virus (HIV): The** retrovirus that is the etiologic agent of AIDS.

Human leukocyte antigen (HLA): Located on the surface of most cells, except blood cells, these protein-sugar structures differ among individuals and are important for acceptance or rejection of tissue or organ grafts and transplants.

Hybridization: The process of joining two complementary strands of DNA, or of DNA and RNA, together to form a double-stranded molecule.

In vitro: Literally, "in glass," pertaining to a biological process or reaction taking place in an artificial environment, usually a laboratory.

In vivo: Literally, "in the living," pertaining to a biological process or reaction taking place in a living cell or organism.

Linkage: The proximity of two or more markers (e.g., genes, RFLP markers) on a chromosome; the closer together the markers are, the lower the probability that they will be separated during meiosis and hence the greater the probability that they will be inherited together.

Locus: A specific, physical position on a chromosome.

Lymphocyte: One of the major groups of white blood cells.

Marker: An identifiable physical location on a chromosome (e.g., restriction enzyme cutting site, gene, RFLP marker) whose inheritance can be monitored. Markers can be expressed regions of DNA (genes) or some segment of DNA with no coding function but whose pattern of inheritance can be determined.

Metaphase: see *mitosis.*

Micronuclei: Result from the exclusion of fragments or whole chromosomes from nuclei formed at mitosis. Their presence can be taken as an indication of the previous existence of chromosomal aberrations.

Mitosis: The process of division involving DNA replication that results in two daughter cells with the same number of chromosomes and cytoplasmic material as the parent cell.

Mutagen/mutagenicity: A substance capable of inducing a heritable change in the genetic material of cells.

Mutation: Changes in the composition of DNA.

Neoplasm: A localized population of proliferating cells in an animal which are not governed by the usual limitations of normal growth. The neoplasm is said to be benign if it does not undergo metastasis and malignant if it undergoes metastasis.

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.)

Oncogene: A gene, one or more forms of which is associated with cancer. Many oncogenes are involved, directly or indirectly, in controlling the rate of cell growth.

Phenotype: The appearance of an individual or the observable properties of an organism that result from the interaction of genes and the environment.

Polymerase chain reaction (PCR): An in vitro process, through which repeated cycling of the reaction reproduces a specific region of DNA, yielding millions of copies from the original.

Polymorphism: The existence of more than one form of a genetic trait.

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 phenotype effect only when present in homozygous form, otherwise being masked by the dominant allele.

Recombinant DNA technology: Processes used to form a DNA molecule through the union of different DNA molecules, but now commonly used to refer to any techniques that directly examine DNA.

Reliability: The ability of a test to accurately detect that which it was designed to detect and to do so in a consistent fashion.

Replication: The synthesis of new DNA from existing DNA. PCR is an in vitro technology based on the principles of replication.

Restriction endonuclease: An enzyme that has the ability to recognize a specific DNA sequence and cut

it at that sequence.

Restriction enzyme: See *restriction endonuclease.*

Restriction fragment length polymorphism (RFLP): Variations in the size of DNA fragments produced by a restriction endonuclease at a polymorphic locus.

RFLP analysis: DNA techniques using single-locus or multilocus probes to detect variation in the DNA sequence by revealing size differences in DNA fragments produced by the action of a restriction enzyme. See *restriction fragment length polymorphism.*

Sensitivity: The ability of a test to identify correctly those who have a disease.

Single gene disorders: Hereditary disorders caused by a single gene (e.g., Duchenne muscular dystrophy, retinoblastoma, sickle cell disease).

Sister chromatid exchange: Crossing over between the sister chromatics (two daughter strands of a duplicated chromosome) during cell division (mitosis).

Somatic cells: Any cells in the body except reproductive cells and their precursors.

Southern blot: The nylon membrane to which DNA has adhered after the process of Southern blotting.

Specificity: The ability of a test to identify correctly those who do not have the trait or disease which is being tested.

Teratogen/teratogenesis: A physical or chemical agent (e.g., radiation, alcohol) that can cause congenital abnormalities as a result of exposure in utero.

Trait: A distinguishing feature; a characteristic or property of an individual.

Validity: The extent to which a test will correctly classify true susceptible and true nonsusceptible individuals; sensitivity and specificity are components of validity.

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