Chapter 2

Introduction: Occupational Illness and Genetic Testing

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chapter 2

Introduction: Occupational Illness and Genetic Testing

The problem of occupational illness

Occupational illness is a major problem in this country. In a 1981 private sector work force of approximately 75.6 million people, there were an estimated 126,000 cases of work-related acute illness, which resulted in more than 850,000 lost workdays, according to the Bureau of Labor Statistics (2). * Moreover, an estimated 5 percent of all cancers are believed to be associated with exposure to harmful substances in the workplace (17). * * Litigation over illness claimed to have resulted from one substance alone—asbestos—could result in insurance payments as high as $38 billion over the next 35 years, and one major manufacturer of asbestos, faced with more than 16,500 lawsuits, has filed for reorganization under the Bankruptcy Act (21,22).

The health risks posed by the workplace environment vary with the industry and the type of job but are often associated with exposures to harmful substances or agents. These substances or agents include minerals, chemicals, and ionizing radiation. This report focuses on an emerging technology, genetic testing, that may be useful in reducing occupational illness arising from such exposure, especially to chemicals and ionizing radiation.

*The accuracy of these figures is subject to much debate among the experts The Bureau of Labor Statistics itself acknowledges that the figures understate the amount of occupational illness because they do not adequately reflect chronic diseases and diseases with long latency periods because of problems with detection and recognition (2) They are used here simply to provide the reader with a general notion of the magnitude of the problem.

● "Estimating the amount of cancer associated with occupational exposures is extremely difficult, and experts often disagree. In the past, estimates have ranged from 5 to 38 percent In 1981, OTA suggested that almost all estimates of work-related cancer fit into a range of 10 (±5) percent of all cancer (14). Data presented at an international conference on quantification of occupational cancer suggest that the (ITA estimate may have been too high (17). Five percent now appears to be the figure acceptable to most experts, although some experts still argue for estimates greater than 20 percent(17,19).

Genetic testing, as used in the workplace, encompasses two types of techniques. Genetic screening involves examining individuals for certain inherited genetic traits (9). Genetic monitoring involves examining individuals periodically for environmentally induced changes in their genetic material. The assumption underlying both types of procedures is that the traits or changes may predispose individuals to illness. Although this technology is still in its infancy, genetic testing potentially could play an important role in the prevention of occupational diseases. It is technologically and economically impossible to attain a no-risk workplace by lowering the level of exposure to hazardous substances to zero. However, if individuals or groups predisposed to occupational diseases could be identified, other preventive measures could be specifically directed at those persons. This is the promise of genetic testing. At the same time, however, the technology has potential drawbacks and problems. For example, it could result in workers being unfairly excluded from jobs or in attention being directed away from efforts to "clean up" the workplace.

Because genetic testing is still in its infancy, many of its potential impacts—both positive and negative—at present cannot be precisely defined. Nonetheless, it is not too soon for society to begin to consider how genetic testing may affect us. In industry, genetic testing has been little used to date, but an Office of Technology Assessment (OTA) survey has found several companies interested in using it in the future. Thus, this report, requested by the Committee on Science and Technology of the U.S. House of Representatives as an assessment of genetic testing, can provide a foundation for future debate as this technology continues to develop.

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Health hazards in the workplace

Of the many different kinds of hazardous substances or physical agents in the workplace, chemicals and ionizing radiation are the two categories of hazards for which genetic testing has been used and for which some data exist for evaluating the scientific validity of that testing.

Hazardous chemicals

Many, but not all, chemicals are hazardous. Chemicals may be irritating, toxic, mutagenic, teratogenic, and/or carcinogenic. They may enter the body through the skin, the lungs, and the gastrointestinal tract. Contact with skin can produce irritation and dermatitis. Breathing chemicals can cause irritation or damage to the upper respiratory tract and the lungs. Contact with some chemicals through virtually any route may cause cancer.* Exposure to more than one chemical may result in a synergistic effect--diamage greater than the combined damage of the individual exposures. The degree of risk posed by a hazardous substance depends on the degree to which a person is exposed to it, and risks can be reduced by reducing exposures,

There are more than 55,000 different chemicals in commerce (14). The percentage of these that are hazardous at current exposure levels is unknown. Chemicals are found not only in companies that produce them but throughout the manufacturing sector. The National Occupational Hazard Survey (NOHS), conducted by the National Institute of Occupational Safety and Health, estimated that approximately 8.5 million workers were exposed to chemical hazards in the manufacturing sector during the years 1972 to 1974 (11). Because the manufacturing labor force grew at a 0.7 percent annual rate during the years 1973 to 1979, the number of exposed workers in manufacturing in 1980 may have totaled 8.9 million (11). According to the Occupational Safety and Health Administration, exposure to chemicals is the most important occupational health problem because of the number of workers involved (13).

● The National Institute of Occupational Safety and Health has published a list of approximately 2,400 suspected carcinogens (14).

Photo credit: Occupational Safety and Health Administration

Exposure to chemicals in work-related environments over long periods of time can be hazardous to health

For the individual, the hazard of working with chemicals is compounded by the likelihood of multiple exposures. A worker may be exposed to numerous chemicals at any one time or over a long period of employment. Rubber workers, for example, are exposed to an estimated 3,000 chemicals (18). The NOHS data indicate that more than 280 million chemical exposures* occurred in the manufacturing sector during 1972 to 1974 (18). By 1980, based on growth projections in the number of workers and in the number of chemicals, * * chemical exposures among workers in manufacturing were estimated to be 361 million. * * *

● NOHS defined "exposure" as "employees' actual or potential, direct or indirect, contact with any chemical and biological agent, or physical and safety condition" (1 1).

* *Data indicate that new chemical substances are generated at the rate of about 8 percent annually and 5 percent of existing chemicals are discontinued, resulting in an assumed annual growth rate of 3 percent (3,12).

●* ● 47 Fed, Reg. 12092, 12108 (1982).

Photo credit' Occupational Safety and Health Administration

Special clothing protects worker's skin and respiratory tract from exposure to toxic chemicals

Ionizing radiation

Ionizing radiation is energy in the form of waves or particles that produces certain charged particles known as ions in passing through matter. It may harm exposed individuals or their unborn children. For the exposed individual, the principal risk is that he or she may develop cancer. Radiation-induced cancers include leukemia and most of the commonly occurring solid cancers. Other possible adverse effects of ionizing radiation include eye cataracts, nonmalignant skin damage, blood disorders, and impaired fertility. Unborn children can be harmed in two ways. The first is through radiation-induced adverse changes in the genetic material from their parents, which can be passed on to future generations. The second is by direct in utero exposures which can result in birth defects, growth retardation, or cancer (4).

Occupational exposures to ionizing radiation occur in many fields. In the health professions, for example, exposures result from the use of medical and dental X-rays and radiopharmaceuticals. In industry, exposures result from the use of X-rays and gamma rays for flaw detection and other testing of materials. In the production and use of nuclear energy, exposures occur for miners, fuel processors, material handlers, and others. Radium workers and research laboratory workers often are exposed to ionizing radiation.

Estimates vary on the number of workers potentially exposed to ionizing radiation. The Environmental Protection Agency estimated that 1.1 million workers were potentially exposed in 1975 (4). * The Committee on the Biological Effects of Ionizing Radiation estimated that approximately 750,000 workers each year were potentially exposed, based on exposure data for different groups in different years between 1969 and 1977 (8),

Control of occupational health hazards

To prevent occupational disease, health hazards must be recognized, evaluated, and controlled.

● workem exposed in mining operations were not included in these estimates; there is little information on exposure of such workers with the exception of underground uranium miners.

Environmental and biological monitoring, engineering controls, personal protective measures, and modified work practices are the techniques used to accomplish this goal (1). Genetic testing is just one of many techniques that fall into these general categories, It could complement but probably not replace any of the existing techniques.

Recognition and evaluation of hazardous substances or agents involves identification of potential hazards in the workplace and determination of the degree of exposure. The two major complementary ways to do this are through environmental and biological monitoring (1), Environmental monitoring uses various sampling instruments or personal monitoring devices to identify hazardous substances in the environment and to determine their concentration (l). Biological monitoring uses biochemical and other tests on body fluids, tissues, expired air, or human wastes to estimate the amount of a hazardous substance actually absorbed by a particular worker as well as its health effects (7). Some genetic testing techniques are a type of biological monitoring,

Control of hazardous substances and their effects may be accomplished by engineering techniques designed to lower or eliminate exposure or by measures designed to protect individual workers (I). Engineering controls include the substitution of a less harmful material for a hazardous one, the alteration of a process to lower the degree of exposure, the isolation or enclosure of a process to lower the degree of exposure, the use of exhaust systems, and ventilation with clean air (l). Measures targeted to individuals include personal protection devices such as respirators or special clothing and workplace practices such as job placement in a suitable environment, job rotation to minimize exposure, and job denial (1).

The use of personal protective measures requires the identification of individuals or groups who can benefit from them. Such identification is the goal of medical surveillance, a preventive activity using preemployment or periodic medical examinations both to identify individuals or groups that may be predisposed to some occupational illnesses and to monitor the health experience of workers exposed to presumably safe levels of potentially hazardous substances (7). Genetic testing has potential for use in medical surveillance.

Photo credit: Occupational Safety and Health Admlnistration

Environmental monitoring

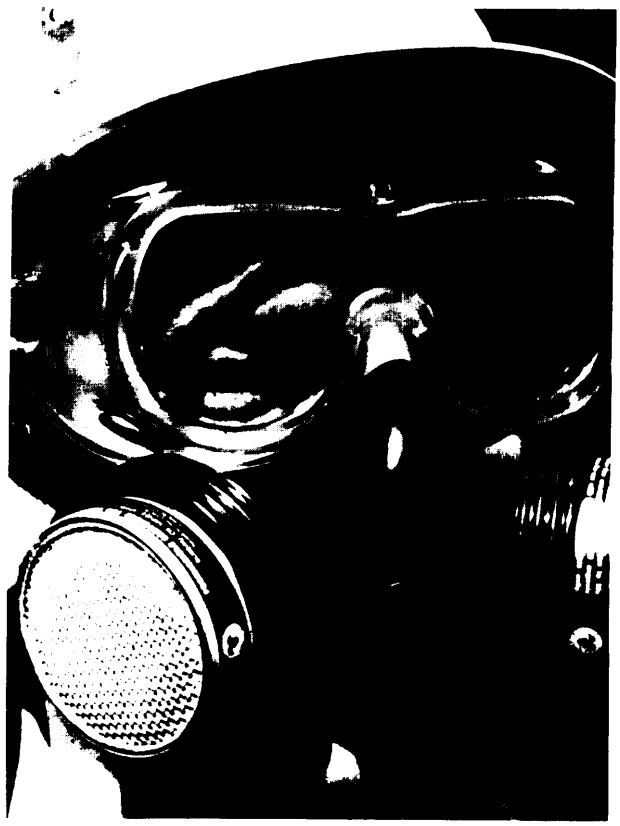


Photo credit.' Occupational Safety and Health Adminlstration

Personal protection mask is utilized to safeguard workers in many occupations where hazardous substances are present

Genetic testing

Theoretical foundations: biological diversity and differential susceptibility

Genetically determined individuality is a fact of life. People differ not only in such obvious physical characteristics as height, facial features, and skin color, but also in ways that can only be determined in a laboratory, such as blood type and types of proteins found in blood plasma. Variations in some characteristics or traits result from the interaction of many genes; variations among other traits result from variations in a single gene that controls that trait. On the basis of a mere two dozen traits that have been extensively studied, some scientists have calculated that the probability of any two people (except identical twins) being exactly alike is roughly 1 in 4 billion **(15). ***

Genetic variability is also a factor in the different reactions of people to environmental factors, including disease-causing agents such as bacteria, viruses, and chemicals. There is evidence that some people are at a higher risk than others of contracting diseases-cancer and heart disease, for example—not only because of environmental factors such as diet or smoking, but because of their genetic makeup (5,6). In fact, there are a few cases where a person's genetic makeup has been proven to predispose him or her to certain illnesses in the presence of some environmental factor. One situation involves a deficiency in the enzyme glucose-6-phosphate dehydrogenase (G-6-PD). The production of this enzyme is controlled by a single gene; some people have a variant form of that gene that results in a deficiency in the enzyme. The deficiency generally causes them no harm. However, if they take certain antimalarial drugs or eat a type of bean known as the fava bean, they may suffer from acute anemia (16). Thus, G-6-PD deficient individuals are at a higher risk of illness than other people when exposed to those environmental stresses.

'Another approach to the question of human variability is to look at the number of nucleotides in the human genome, which is about log on this basis, the chances of two people being exactly alike is 1 in 1 0^{18} (10^9 X 1()').

Many factors besides genetic makeup can cause an individual to be predisposed to illness triggered by environmental factors. Among these are age, sex, nutritional status, lifestyle, and prior exposure to the environmental factors.

Prior exposure is particularly important for the purposes of this report. If the environmental factor is a chemical, it may be in the body at levels where only slight additional amounts could cause illness. In fact, the prior exposure may already have begun the disease process even though the disease itself may not appear for many years.

These considerations lead to the concept in occupational medicine of unequal risk. Individuals or groups that may be predisposed to illness have been called, among other terms, "hypersusceptible," '(high -risk," and "sensitive." These terms often have been used interchangeably but also have been defined by different experts in different ways.

This report uses the terms "increased risk, " "genetically predisposed)" and "susceptible. " When applied to individuals or groups, the terms "increased risk" or "susceptible" refer to a higher probability than average of developing a condition, illness, or other abnormal status. In the context of genetic testing, this increased risk may result from either inherited genetic traits or previous exposure to environmental insult. The term '(genetically predisposed" refers to the situation where one or more of an individual's inherited genetic traits may cause him or her to be at an increased risk of illness when exposed to some environmental stresses.

Detection of individuals or groups at increased risk

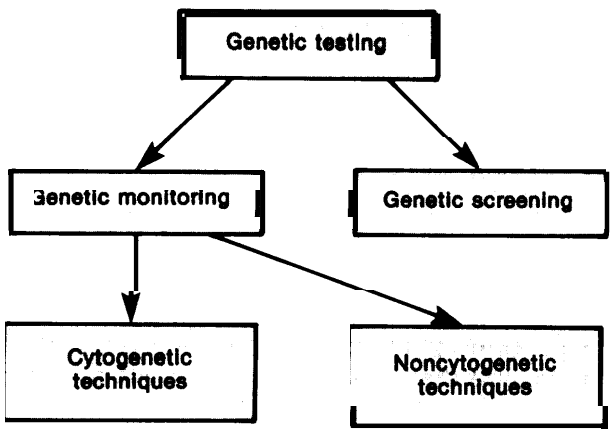
Genetic testing, as used in this report, applies to several techniques used to examine workers for particular inherited genetic traits or environmentally induced changes in their genetic material on the assumption that the traits or changes may predispose them to illness. It has been used by some manufacturing companies and utilities in both medical practice and research. There are

two inherently different kinds of testing, genetic monitoring and genetic screening (fig, 1).

Genetic monitoring is done to assess whether or not genetic damage has occurred in certain cells of an individual as a result of exposure to hazardous chemicals or ionizing radiation. Monitoring can also be done over a period of time to look for responses to variations in exposure. Thus, it can be used to measure genetic changes in certain cells from before exposure through various levels of exposure. Monitoring can be done in one of two ways. Cytogenetic techniques look for damage to the gross structure of chromosomes, the cellular structures that contain the genetic material, deoxyribonucleic acid (DNA). Noncytogenetic techniques look for damage to the actual molecular structure of DNA. For the most part, these latter techniques are still in a developmental stage.

Genetic monitoring involves examining blood and other body fluids for evidence of genetic damage to cells from chemicals or ionizing radiation. This damage may indicate exposure to a hazardous agent and the possibility that the group so exposed will be at an increased risk of developing diseases, particularly cancer. Thus, this procedure has potential as an early warning system, by indicating that exposures to known or suspected carcinogens are too high or that a previously unsuspected chemical should be viewed as a potential carcinogen.

Figure 1.—Components of Genetic Testing



SOURCE: Office of Technology Assessment

In contrast, genetic screening is a one-time testing process to determine the presence of particular genetic traits, regardless of whether the person has been exposed to a hazardous substance (9). Some genetic traits appear to predispose an individual to adverse health effects in the presence of a particular chemical. while normally not harmful, the traits may make the individual susceptible to hemolytic chemicals, pulmonary irritants, oxygen deprivation, or other physical or chemical stresses in the workplace. For example, two scientists proposed in 1963 that workers in the chemical industry be tested for G-6-PD deficiency on the grounds that 37 chemicals or families of chemicals may cause such employees to develop anemia (20). Most screening tests require that blood be drawn for laboratory tests.

In sum, screening is used to determine individual susceptibility, whereas monitoring may be able to assess a chemical's effect on an exposed population in order to determine if that population is at increased risk. Because of this distinction, one use of screening could be to exclude genetically susceptible individuals from jobs where they would be exposed to hazardous substances, whereas monitoring would most likely indicate a need to lower exposure levels for a group identified to be at increased risk.

Genetic monitoring must be subjected to two principal technical questions: Are the techniques used to assess genetic damage reliable and valid? Is there an association between positive test results and an increased risk of disease? Similarly, the reliability and validity of screening tests are important technical questions, but the key question here is whether or not there is an association between the genetically determined trait and any increased susceptibility of that individual to harm from particular chemicals.

When used as described here, screening and monitoring are forms of medical practice. They can also be used in medical research. It is important to distinguish between medical practice and medical research because different legal and ethical principles can govern each, depending on the situation. The term "practice" generally refers to medical interventions that are designed solely to enhance the well-being of an individual and that have a reasonable expectation of success, The

purpose of medical practice is to provide diagnosis, preventive treatment, or therapy to individuals. Research, on the other hand, refers to an activity designed to test a hypothesis so that conclusions may be drawn. Its purpose is to contribute to a general body of knowledge, expressed in the form of theories, principles, and statements of relationships (10). Medical research is often done to determine the value of new techniques for medical practice. It generally does not enhance the well-being of the individual, and, in fact, may have some risks associated with it.

Potential benefits and risks of genetic testing

Advocates of genetic testing believe it might be able to play an important role in the prevention of occupational disease. By identifying workers who may be at increased risk of disease because of past or potential exposure to hazardous substances, additional preventive measures could be taken by the company or the workers themselves. In addition to the obvious and significant benefits of preventing serious illness, there could be indirect benefits, such as a reduction in the costs associated with occupational disease for employers, employees, and society. These costs include medical, insurance, and legal expenses; time lost from work; and disability or unemployment payments,

The use of this emerging technology, however, raises several questions. Are the techniques sufficiently developed so as to predict reliably an association between either genetic damage or a person's genetic makeup and disease? Since many of the genetic traits sought in screening are found disproportionately among some races and ethnic groups, could the use of the tests result in discrimination on the basis of race, sex, or national origin? How will the availability of the tests affect the employer's responsibility for maintaining a safe workplace? How might these procedures affect efforts to reduce the level of hazardous substances in the workplace? If the tests are shown to be effective, to what degree should society protect high-risk individuals or groups, at what cost, and who should bear that cost?

Organization and scope of report

This report attempts to assess the potential risks, benefits, and effects of genetic testing. Part I discusses the extent of testing on the basis of a survey of major companies and unions conducted by OTA. Part H explains the underlying scientific principles. Part III assesses the current state of the technology and expected future developments. It addresses the question of whether the technology in fact could play a role in reducing occupational disease. Part IV analyzes the legal, ethical, and economic issues raised by this technology. It considers whether genetic testing is compatible with law or established ethical principles and how the costs and benefits of the technology could be assessed. Part V integrates the findings of the previous parts into a discussion of issues and policy options for possible congressional action.

The report does not consider certain aspects of genetic testing. Hazards to offspring are not addressed; the report considers only the risk to the workers themselves. The report also does not assess many of the claimed risks of the widespread use of this technology. Because genetic testing is an emerging technology, little evidence exists concerning its potential impacts. Finally, it was not within the scope of this study to assess whether occupational exposures to hazardous substances are at "safe" levels and whether other technologies might be more appropriate for preventing occupational diseases.

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