Two circumstances have served to focus the attention of life insurers on genetic testing issues. The first is the pace of technological advances. It is only a matter of time until researchers identify a genetic component to most, if not all, common diseases. These discoveries will be accompanied by screening, diagnostic and prognostic tests that rely heavily on genetic principles. When that time arrives, insurers will find that most information concerning an applicant’s mortality risk is either directly or indirectly genetic in nature.

The second circumstance regards legislative activity. A number of state legislatures have introduced bills that would have prohibited life insurers from using genetic information to classify risks. Whatever the intent of this legislation, the consequence would have been the prohibition of medical underwriting by all life insurance companies and premium increases that might have made life insurance unaffordable for almost everyone.

In Part II of this paper, I would like to address the developments of particular concern to insurers. The intent will be twofold: first, to demonstrate that genetics will become such an integral part of medical care that it will be impossible to draw meaningful distinctions between genetic and non-genetic information; second, to voice the concern that an inability to access genetic information could force a fundamental restructuring of the entire life insurance industry and a significant decrease in the number of people who were able to afford life insurance coverage.

GENETICS: THE FUTURE STANDARD OF CARE

Case Study

A recent analysis of voided urine specimens, collected in 1967 from the late Hubert H Humphrey confirmed the presence of a p53 mutation suggestive of bladder cancer. The test was based on a probe developed for a codon 227 mutation found in an invasive bladder carcinoma resected in 1976. The p53 mutation was found in a urine sample collected nine years before Humphrey underwent cystectomy, six years before he received any therapy for bladder disease, two years before a diagnosis of in situ carcinoma was established by biopsy, and at a time when cancer could not be identified grossly in his bladder.

With further refinements in this technology, will testing for p53 mutations in urine specimens become a routine procedure and the standard of care in patients with signs or symptoms suspicious for cancer of the urinary tract? Would detection of a p53 mutation in a urine sample be considered a genetic test, regardless of whether the mutation was inherited or somatic (i.e., a mutation acquired later in life due to exposure to environmental carcinogens or errors in DNA replication or repair)? Finally, if a patient with this type of p53 mutation applied for life insurance, should this information be shared with the company that is being asked to assume the risk? From the perspective of a physician working for a life insurance company, the answer to this final question would be an unqualified “Yes.”

Screening

The practice of medicine will soon be dominated by genetic technology. As the Human Genome Project continues, tens if not hundreds of new genetic tests will compete for introduction into routine clinical practice. Fost observed that “Potential new genetic tests roll off the conveyor belt of the Human Genome Project almost once a week.” Riccardi and Rotter suggested in an editorial column that “Now is the time to begin thinking about how we make the ‘new genetics’ an integral, even mundane element of the ‘new medicine’.” The need for a “generic” consent form to facilitate use of a screening panel of genetic tests has already been discussed.

The Institute of Medicine Committee on Assessing Genetic Risks predicts that multiplex genetic testing will become the “standard of care” for routine use, with numerous genetic tests being performed on a single blood or other tissue sample. The committee envisions the time when the public will be offered genetic screening via “walk-in testing (e.g., at shopping malls), mail-order kits, and home test kits...” Such futuristic projections are given credence by reports from the lay press of biotechnology firms that are wedding semiconductor and genetic techniques in an effort to develop rapid, inexpensive screening genetic tests. One such company has developed a methodology that involves affixing a million DNA fragments to a disposable silicon microchip, adding a sample of the patient’s blood, and reading the result with a laser scanner. Developers suggest that “doctors with DNA chips and chip scanners in their offices may one day provide while-you-wait patient diagnoses.” The company has been awarded a $31.5 million grant (one of the largest advanced-
technology grants ever given) by the commerce department to pursue this line of research.

**Monitoring genetic status as disease evolves**

A research team has developed a flow cytometry test to detect the cellular abnormalities that foreshadow adenocarcinoma in patients with Barrett’s esophagus. Over several years, large numbers of abnormal – but not yet cancerous – esophageal cells appeared in some patients. In those with aneuploidy (defined in this reference as “huge masses of extra DNA”), cancer of the esophagus developed in approximately 50 percent of cases in 18 months to seven years (average three years). Those without aneuploidy remained cancer free for at least three years.

This report exemplifies the extent to which our knowledge of pathophysiology will change in the future. It will be possible to monitor the genetic evolution from health to disease. For certain disorders, this knowledge will eradicate traditional pathologic distinctions between metaplasia, varying degrees of dysplasia, and cancer, and molecular biological tests will replace standard histologic techniques. For a life insurance medical director, it makes no difference if an applicant has a pathologic diagnosis of moderate-to-severe dysplasia, or the genetic counterpart. In either case, there is a definite risk of cancer in the near future.

**Presymptomatic testing**

Polymerase chain reaction (PCR) techniques have been used to detect exfoliated neoplastic cells in the stool of patients with colorectal neoplasms, in the sputum of patients with lung and head and neck cancer, in the blood, bile, and stool of patients with pancreatic cancer, and in the urine of patients with bladder cancer. Unlike the previous example concerning patients with Barrett’s esophagus, these patients already have cancer. When it becomes technologically feasible to screen asymptomatic patients for cancer, would these results be shared with life insurers? PCR tests are clearly genetic since the technology involves amplification of a specific DNA sequence. Would it make a difference if the mutation was inherited or somatic? What about PCR tests performed in patients with infectious diseases such as hepatitis, or any of a host of other disease processes?

Distinctions between genetic and non-genetic tests will completely unravel when dealing with presymptomatic tests that measure gene products, since many of these tests are genetic in nature. Included within this group are tumor markers such as prostate-specific antigen (PSA) and many common blood chemistry and hematologic tests.

**Treatment**

Many new forms of therapy will be based on genetic principles. In oncology, major pharmaceutical companies are racing to develop innovative cancer drugs that target abnormal genes and the proteins they produce. The goal will be to repair the protein mutations and restore their normal function. Other researchers predict exponential growth in the use of antisense drugs to treat conditions as diverse as heart disease, cancer, neurologic disorders, and infectious diseases.

From the field of cardiovascular research, success has been reported in attempts to use gene therapy to stop smooth muscle cell proliferation following balloon angioplasty. In a related article from The New York Times, Hathaway (director of the Krannert Institute of Cardiology, Indiana University) has suggested that this type of therapy was “definitely the wave of the future” and Swain (chief of cardiovascular medicine, University of Pennsylvania School of Medicine) observed that the difficulties that remain are “engineering problems, not conceptual problems.” The latter comment is particularly germane to this discussion. Conceptually, there is little doubt that genetic therapy will be possible for many different diseases; the engineering problems will be solved in future years and decades.

The ultimate impact of genetic forms of treatment is perhaps best summarized by a viewpoint article written by Henry Miller of the Institute for International Studies: “Somatic-cell human gene therapy applied to genetic defects, cancer, and cardiovascular disease may approximate in the first half of the next century what antibiotics have been in the second half of this century.”

**Prognosis**

This is an area where genetic testing will become important in the near future. The studies cited in the following paragraphs deal with localized and metastatic cancer.

A recent report discussed the prognostic value of allelic loss of chromosome 18q in patients with TNM stage II or III colorectal carcinoma. Among patients with stage II disease, the five-year survival rate was 95 percent in those whose tumor had no evidence of allelic loss of chromosome 18q, and 54 percent in those with allelic loss. For those with stage III disease, survival was 52 percent and 38 percent, respectively. The authors concluded that the prognosis in patients with stage II cancer and chromosome 18q allelic loss was similar to that in stage III cancer. In contrast, patients with stage I disease who did not have chromosome 18q allelic loss in their tumor had a survival rate similar to that of patients with stage I disease.

A reverse transcriptase-PCR assay identified what were probably metastatic prostate cancer cells in the blood of men with known prostate cancer. Given that the assay was an accurate predictor of cure rate in patients undergoing radical cancer surgery, and far superior to conventional staging modalities, future use of this test is certain. Another group of researchers used genetic technology to detect circulating melanoma cells in peripheral blood. They suggested that someday physicians may be able to detect primary cancers in this way, thereby eliminating the need for more invasive diagnostic methods.

In each of these cases, would insurers be asked to ignore the results of these prognostic tests because they were genetic in nature?
Or would they be instructed to ignore only unfavorable genetic test results, a position advocated in some jurisdictions that have attempted to enact legislation dealing with use of genetic information by life insurers?

**Genetics as the final common pathway**

This brief review was intended to illustrate that it is already impossible to distinguish between genetic and non-genetic tests, diseases, and information. A listing of common diseases with a genetic component includes virtually all of the conditions encountered in an average medical practice. The Institute of Medicine Committee on Assessing Genetic Risks has stated that information regarding family history, physical examinations, and past treatment may be genetic. Many current screening and diagnostic laboratory tests provide genetic information, and a number of new imaging procedures will be considered genetic because the technology is based on incorporation of radioisotopes into the DNA of target tissues.

The interrelationships between genetic and non-genetic information have been acknowledged by the National Center for Human Genome Research. A report published in 1993 stated that “For policy purposes, it will become increasingly difficult to distinguish genetic from non-genetic diseases, and genetic information from non-genetic information.” They further observed that “Recognizing that our genes affect many common diseases not previously thought of as genetic will transform the scope and meaning of terms such as genetic information, genetic test, asymptomatic condition, presymptomatic condition, and genetic predisposition to disease.”

Since most medical information will be directly or indirectly genetic, and it will be used by applicants to guide their insurance purchases, life insurers are understandably concerned by legislative attempts to restrict their access to this information.

**RISK CLASSIFICATION: THE CENTRAL ISSUE**

Earlier I stated my goal would be to clarify what is and what is not possible within a private life insurance system, and explain the reasons why. Risk classification is the central issue in this discussion. In the future, applicants will use genetic information to guide their insurance purchases. When that time arrives, life insurers will need access to this same information. Without it, they would be unable to classify applicants into any group: standard, substandard, or declined. This could lead to the demise of the private life insurance industry as it exists today.

A private insurance system must retain the ability to identify the risks it is asked to insure – genetic or non-genetic – classify them into groups with similar expectations of loss, and charge a price that reflects the level of risk posed by the group. This conclusion is supported by theories of private life insurance that have evolved over the century, historical experience of assessment societies that collapsed because of failure to coordinate risk and premium, and basic economic principles discussed later in this article.

Suggesting that genetic information not be used to classify risks is tantamount to advocating a fundamental restructuring of the life insurance industry. The economic scope of such an undertaking would be immense. Large-scale cross-subsidies would be required between healthy and unhealthy policyholders. Premiums would become intolerably high for most people. To retain some semblance of the current private life insurance mechanism, mandatory participation by all consumers would be required, and the government would need to subsidize the life insurance purchases of those who could not afford the higher premiums.

The United States public has chosen a free-market life insurance mechanism, a system that has made Americans one of the best insured populations in the world. The reason is, in large part, due to the perceived value for the money spent. Statistics reveal that life insurance is one of the few consumer products to have experienced a steady drop in cost, even through the inflationary 1970s. As an example, the percentage of income needed to purchase adequate life insurance coverage (i.e., an amount equal to five times income) for the average 25-year-old worker has declined to half what it was in 1960. Even with this degree of cost control, the insurance buying public continues to insist that premiums be further lowered.

**COMMUNITY RATINGS**

A number of individuals from outside the insurance industry have suggested that life insurers could compensate for a lack of genetic information during the application process by changing to a system where premiums were based on modified community rates. Under such a system, age would continue to be the primary factor used to calculate premiums, but expected mortality rates would be based on a community average for a given age rather than on the much lower mortality rates that have historically been used by life insurers for the standard class. Other elements of this proposal would include premium increases for most new policyholders, a broadening of the standard group to include almost all applicants (including most of those currently classified within the substandard group), and a marked narrowing of the declined category.

This arrangement would be doomed to failure. Insurance mechanisms that base premiums on community rates rather than the risks posed by individual applicants cannot survive in a private, competitive environment. The reason for this relates to a basic economic principle: people at low risk have no economic incentive to voluntarily pay higher premiums to subsidize those at higher risk. This principle was convincingly demonstrated by the failure of numerous assessment societies that based their life insurance premiums on community rates, and is further illustrated by the following two case studies.

Starting in April 1993, all companies selling medical expense insurance to individuals and employee groups of fewer than 50 in New York state were required to accept applicants using premiums based on a community-wide average, with adjustments only for geographic location. Rates immediately shot up for younger,
healthier people and fell for older, sicker groups. About 30 percent of subscribers faced hikes of 20 percent to 59 percent. Premiums for 30-year-old men rose the most, 170 percent. In contrast, 60-year-old men enjoyed a 45 percent rate cut. What followed was a drop in the number of New Yorkers with medical expense insurance. State figures showed a net decline of three percent, or about 44,000 people, in the individual and small group markets through March 1994. The biggest drop, 12 percent, occurred in the individual market. Due to the exodus of younger and healthier subscribers, premium increases were planned for the remaining subscribers since relatively more claims were expected from older and sicker people who kept their coverage. This situation is reminiscent of the experience of assessment societies of the late 19th century.

Repeal of the Medicare Catastrophic Coverage Act was a highly publicized example of the backlash against forced subsidization. This act provided expanded hospital and nursing home benefits for Medicare recipients. It was repealed after having been passed with great fanfare only 16 months earlier. A major reason for its demise was “that it unfairly required middle- and upper-income seniors to subsidize care for the indigent.” A vivid illustration of the vehement political opposition to the bill was provided by reports of Representative Dan Rostenkowski “being chased down a Chicago street by seniors angry over the surtax” engendered by the bill.

This latter example highlights an inevitable consequence of basing life insurance premiums on average community mortality rates for a given age: the greatest premium increases would occur for people aged 55 years and older, one of the fastest growing segments of both society and the insurance buying public. The reason is that community mortality rates for older individuals are much higher than the mortality rates currently used by life insurers for standard risks (e.g., an insured lives table lists the expected mortality rate for a 60-year-old male in the first policy year as .00323, as compared to the much higher value of .01846 in United States Decennial Life Tables). Proponents of a community-rated life insurance system have acknowledged the dangers of antiselection and suggested that the deleterious effects could be limited by imposing a “minimum life expectancy” between insurance purchases and death (e.g., life expectancy must be at least five to 10 years to purchase life insurance at community rates). This proposal would be of little use to the elderly and (4) policyholders would have less money to spend on other needs, reflecting the fact that all economic costs are eventually paid for by individuals.

It is worth restating an important principle mentioned earlier, namely, the company would not expect all the above mentioned 30-year-old males with a life expectancy of only five to 10 years to experience the same mortality rates as 70- or 80-year-old men. In fact, it is certain this will not be the case. Rather, what is expected is that the average mortality rate for individuals in the 30-year-old group will be similar to that of men aged 70 or 80 years.

ELASTICITY OF DEMAND

It is a basic tenet of economics that people demand less of a product as it becomes more expensive. This tendency can be quantitated by calculating the price elasticity of demand, a measurement of the relative sensitivity of demand for a good to changes in the price of that good. An analysis of the price elasticity of demand for whole life insurance policies sold in the United States from 1953 to 1979 reported a strong negative price elasticity of demand. In other words, people were less willing to buy life insurance when prices increased. Significant price increases would be inevitable if insurers were unable to obtain and use the type of information needed to correlate risks and benefits. Because life insurance purchases conform to established economic principles, it is important to consider the potential impact from a consumer perspective.

Some consumers would decide to buy less life insurance than they would have purchased if prices had remained at current levels, a reflection of the fact that insurance is a normal good, in an economic sense. Others would choose not to buy any coverage because the protection had become too expensive. It is likely that lower income families would be most adversely affected since life insurance is viewed as one of the few available investment options for low-asset households.

Some people might buy the same amount of life insurance but have less money available for financial investments, mortgage payments, or the purchase of medical expense, disability income, or long term care insurance. One final group, those with the highest risk of death, would definitely buy life insurance in spite of price increases, and probably in amounts much greater than previously. The reason relates to the remarkable economic incentive: a high claim expectation and a low premium rate. It would be impossible to predict the overall effects of these cost-induced shifts in purchasing patterns. It seems safe to say, however, that (1) the percentage of people who could buy life insurance would not surpass the current level of 96 percent, (2) lower income and older aged applicants would be disproportionately affected, (3) the total amount of life insurance purchased would decrease, and (4) policyholders would have less money to spend on other needs, reflecting the fact that all economic costs are eventually paid for by individuals.
PRIVACY AND CONFIDENTIALITY

Over the years, the insurance industry has built an unparalleled track record for safeguarding the confidentiality of personal information relating to AIDS, cancer, alcoholism and other sensitive diseases and conditions. Nonetheless, the industry’s proven ability to protect sensitive medical information will probably do little to muffle warnings that insurers cannot be trusted with information as personal as genetic test results.

To study the issues of confidentiality and privacy in greater depth, particularly concerning genetic testing, a task force of chief executive officers of member companies of the American Council of Life Insurance (ACLI) and the Health Insurance Association of America (HIAA) reviewed a report on company practices, current laws and regulations, and special concerns that may be warranted for genetic information. This task force concluded that special protections for genetic testing information may be necessary to meet public expectations. To achieve this goal, four confidentiality principles were developed, and it was recommended that insurers embark upon a voluntary program to implement these principles. Although it is true that most insurance companies already adhere to the substance of these principles, it was thought that having companies formally adopt a “code of confidentiality” would serve as a strong reminder that the industry is committed to safeguarding privacy and confidentiality.

The confidentiality principles can be summarized as follows:

Principle 1: A commitment should be made to applicants and insureds alike that, with the exception of several defined specific circumstances, the re-disclosure of genetic test information will be made to third parties only with the written consent or authorization of the individual or a representative.

Principle 2: All permissible re-disclosures should contain only such information reasonably necessary for the recipient to perform its function, and the recipient, in turn, should generally be prohibited from making further re-disclosures without the specific consent of the individual.

Principle 3: Internal operating policies and procedures should restrict access to all genetic testing information to those who are aware of internal confidentiality policies and who also have a legitimate reason to have access to such information.

Principle 4: Insurers should publicize their policies about confidentiality and the restrictions they impose on the re-disclosure of genetic test information.

DISCRIMINATION

Life insurance is inherently a “discriminatory” product since premiums must be based on differences in expected mortality rates of applicants. The differences recognized by the risk classification system are not intended to jeopardize fundamental rights. They are necessary so that actuaries will know how much premium to collect in order to pay future claims. As noted earlier, the result of this process is that 91 percent of applicants are offered insurance at standard rates, five percent are offered coverage at substandard rates, and four percent of applications are declined.

There is consensus in most countries that life insurers should not use race, ethnic background or religious preference during the risk classification process. Insurers have been fully supportive of this position.

Within the context of discrimination, genetic information is much different from race, ethnicity and religious preference for the following reasons. First, it is likely that many and perhaps most genetic defects that cause disease in later life will not be inherited but will be acquired as somatic mutations. When reviewing medical information from these applicants, there would be nothing unique about charging a higher insurance premium if cancer developed because of genetic injury caused by cigarette smoke, ultraviolet light or some other environmental toxin. The same could be said for presymptomatic cancer tests of urine, stool or blood specimens, since most cancer-causing mutations are somatic.

Second, in the average patient (or insurance applicant), it will usually be impossible to determine if genetics or the environment played the predominant role in the disease process. Finally, unresolvable risk classification dilemmas would occur if genetic information were treated in a manner similar to race, ethnic background or religious preference.

If genetic tests were used to monitor the evolution of cancer (as in the example of Barrett's esophagus), would applicants be treated differently if the cancer-causing gene was inherited rather than somatic? When genetic factors are identified that correlate with increased longevity or a lower risk of disease, will applicants with these favorable traits be told this information cannot be used by insurers?

Would a 30-year-old man with a life expectancy of only 10 years be treated differently if genetic rather than environmental factors were responsible?

CONTROL AND FAULT

Life insurers are interested in an applicant’s mortality risk compared to other individuals the same age. Fault or control is not a consideration. For example, many companies use cardiovascular risk factors to estimate likelihood of premature coronary heart disease. If there were a number of unfavorable risk factors, a company medical director would never consider whether the applicant was or was not at fault or in control because of failure to exercise, maintain a normal weight, or follow a recommended diet.

From a practical viewpoint, distinctions between fault and control will lose much of their meaning as more genes are discovered. Genes are known to influence cardiovascular risk factors such as obesity, hypertension, hyperlipidemia, diabetes.
Throughout the last century, life insurers have adapted to tremendous changes in the epidemiology of disease, the standards of medical care, and consumer needs. It is now routine to be able to obtain life insurance within six months after a myocardial infarction, and within two to three years following successful treatment for most cancers. Applicants with a history of malignant arrhythmias due to an atrioventricular accessory pathway are finding that insurance at standard rates is the rule after successful radiofrequency catheter ablation of the accessory pathway. Insurance at standard rates is even available to recovering alcoholics and applicants with a history of marked obesity or cocaine. These latter examples are indications of the beneficial effects of a competitive, free-market insurance mechanism.

Life insurers feel confident they will be able to assimilate genetic information and still maintain the level of insurability at current levels. This confidence reflects experience in dealing with the uncertainty of risk and an understanding that probabilities (as with genetic information) are not the same as certainties. In this regard, insurers would agree with a philosophy espoused by the Institute of Medicine Committee on Assessing Genetic Risks: "In counseling for non-Mendelian disorders, it is unlikely that individuals will be grouped easily into two distinct categories — those at no (or very low) risk and those at high risk. The proper model for counseling may include a very large number of categories, with the risk ranging from low to high depending on the particular constellation of genes at many loci."

To date, the insurance industry has been very deliberate in addressing genetic testing issues. Under the auspices of the American Council of Life Insurance (a national trade association with 614 member companies that account for approximately 90 percent of the life insurance in force in the United States), a Genetic Issues Committee comprised of insurance medical directors was formed in 1988. A task force on genetic testing, consisting of company chief executive officers, was formed in 1990. These and other initiatives led to the release of reports that addressed confidentiality and other important genetic testing issues.

A two-day conference was held in 1993 to discuss recent technical developments and issues of concern to insurers, geneticists and consumers. In attendance were more than 110 medical directors and other insurance professionals, as well as representatives from the genetics community. Sponsoring organizations included the American Society of Human Genetics, the American Council of Life Insurance, the Health Insurance Association of America, and the American Academy of Insurance Medicine (formerly the Association of Life Insurance Medical Directors of America). This last organization was founded in 1889 and is among the oldest medical specialty organizations in the United States. It also holds delegate status in the American Medical Association.

Most recently, a number of life insurance companies have initiated contacts with geneticists at major medical centers. The purpose is to discuss issues of concern to insurers, geneticists and consumers, and seek assistance with technically complex genetic testing questions.

**CONCLUSION**

From the perspective of a consumer, a physician, and an insurance medical director, I recognize that the risk classification sys-
tem is not perfect. Yet, it allows 96 percent of people who apply for life insurance to buy coverage, a percentage that has remained at approximately the same level during the remarkable medical and social changes of the last century. I believe this percentage can be maintained when genetic testing becomes the standard of care in routine medical practice.

It is time for life insurers to pursue a more active dialogue with the medical community for the purposes of mutual education and the identification of areas where problems can be anticipated. Physicians working for life insurance companies are genuinely interested in finding ways to integrate genetic information into the risk classification process without jeopardizing the ability of future policyholders to obtain life insurance protection to satisfy their personal, business, and estate planning needs.

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