

ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS

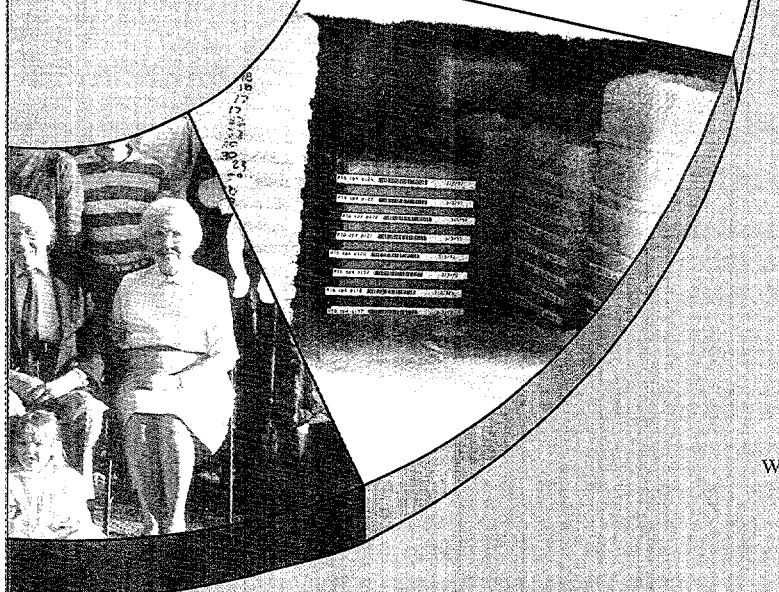
ELSI

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Sex Chromosome



The Human Genome Project is providing a flood of scientifically valuable genetic information. That information promises advances in diagnosis, in prevention, and later in therapy. At the same time, the new knowledge also promises to intensify current health-care problems and bring up perplexing new ethical issues. History demonstrates that genetic information can be misused; in the United States, the most infamous examples were the compulsory-sterilization programs in the early part of the twentieth century. A current, less extreme example is the denial of insurance coverage to a family simply because one member has a genetic disorder—even when the disorder can be inexpensively treated.

Preparing for Changes

The National Institutes of Health (NIH) and the Department of Energy (DOE) have recognized the need to prepare for the social impacts of the Human Genome Project. They have created, as an integral part of the project, a program for studying its ethical, legal, and social implications (ELSI). In fiscal year 1992 \$2 million from the DOE (3 percent of its genome budget) and \$5 million from the NIH's National Center for Human Genome Research (5 percent of the center's budget) were set aside for the ELSI program.

The research funded by ELSI grants is intended to be useful for policymaking related to genetics. ELSI grants also fund education in the science and the social implications of the genome project. A joint NIH-DOE working group has been established to help pursue those goals and advise the sponsoring agencies. Members of the ELSI Working Group have offered advice to the Equal Employment Opportunity Commission (EEOC) and to Congress.

The ELSI program is a first for federally supported scientific research. Traditionally, researchers in the natural sciences concentrated on their investigations and allowed society to interpret and use the results as it chose. Now for the first time a research effort includes a structure in which "hard" scientists, social scientists, health-care workers, legal experts, and philosophers discuss the implications of present and potential scientific results.

The ELSI Working Group has identified four high-priority issues for study: fairness, privacy, delivery of health care, and education. In the context of genetics, fairness means freedom from discrimination on the basis of genotype. Privacy means an individual's control of the generation and disclosure of genetic information about himself or herself. Delivery concerns practices of the physicians, counselors, and laboratories that generate and provide genetic information. Education means helping policymakers, health-care professionals, biologists, and social scientists as well as the general public become aware of the new knowledge and of the problems and opportunities that it creates. In practice, many specific issues fall into more than one of those categories.

Nancy Wexler, president of the Hereditary Disease Foundation and a leading participant in the search for the Huntington's-disease gene, has chaired the ELSI Working Group since its inception. Recently she summarized the situation and the group's mission.

I've heard people say—including people in Congress and even some scientists—that the public can be hurt by genetic information. It's true that in the past that information has been used against people. But genetic information itself is not going to hurt the public; what could hurt the public is existing social structures, policies, and prejudices against which information can ricochet. We need genetic information right now in order to make better choices so we can live better lives. We need the improved treatments that will eventually be developed using genetic information. So I think the answer is certainly not to slow down the advancing science, but to try, somehow, to make the social system more accommodating to the new knowledge.

Fairness and Discrimination

Employment or insurance coverage have reportedly been denied to people identified as having a genetic disorder or as being at risk for genetic disease. Sue Levi-Pearl, the scientific liaison for the Tourette Syndrome Association (TSA) and a member of the ELSI task force on insurance, recently described discriminatory practices that she has encountered.

I've had many opportunities to share the concerns, triumphs, and heartaches of those people with Tourette syndrome and other inherited disorders. While many affected families view recent and imminent scientific breakthroughs with hope, they also view the possibility of new genetic tests with despair. People with inherited disorders know firsthand the ways in which genetic-test results can be misused.

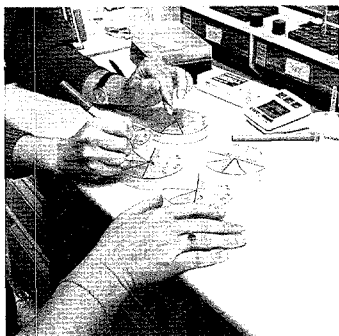
Tourette syndrome is an involuntary-movement disorder. The life spans of affected individuals, unlike the lifespans of people with cystic fibrosis or Tay-Sachs disease, are the same as those of the general population. The disorder has a wide range of expression—from mild tics that disappear in childhood to more severe motor and vocal tics that last a lifetime. Recent data suggest that the vast majority of those affected have mild cases that *never* require medical attention. Yet the typical profile of someone with a confirmed diagnosis is an employed, healthy person in his mid-twenties who takes an inexpensive generic medication—and still cannot obtain health insurance. The two-word explanation for denial of coverage is “Tourette syndrome,” and that's it. I can testify that our organization, TSA, receives scores of such reports every day.

Do insurers understand the variable expression of Tourette syndrome? Absolutely not. People with poorly understood genetic conditions are often rendered uninsurable because an insurer *suspects* the possibility of significant medical expenses.

One recent case concerns a successful, self-employed architect who called TSA in desperation. After his child was diagnosed with a mild case of Tourette syndrome, the architect and his family lost their medical insurance. The insurance company had determined that the child's inherited, and therefore pre-existing, condition would inevitably lead to a brain tumor and require costly medical reimbursement. That medical misinformation was then entered into a large database consulted by the insurance industry, thereby guaranteeing the architect could not obtain insurance at any price. Gone are the days when only you and your physician “knew.” Laws protecting the confidentiality of genetic information must be enacted now. These sorts of problems will be exacerbated in the future because our country's health-care system is already in crisis. If some program of national insurance is not federally mandated, we will soon face a national disaster in health care.

What choices remain for the uninsured families afflicted with genetic diseases? A representative from the National Organization for World





Diseases recently suggested two desperate options: (1) move to Canada, or (2) get a divorce, claim desertion, and become eligible for Medicaid.

The issues are equally complex and worrisome in the area of employment discrimination. Due to the unusual nature of the symptoms, many talented, qualified people with Tourette syndrome have a hard time obtaining employment. The recently confirmed genetic basis of the disease has only compounded the problem. Even a job candidate with mild symptoms could possibly have children with Tourette syndrome and eventually cause high medical expenses for an employer. The employer may say, "Why bother? This person is carrying the wrong genes."

Fairness issues also arise because of differences in culture and societal power between ethnic groups. Recently Troy Duster, director of the Institute for the Study of Social Change at the University of California at Berkeley, talked about some of his concerns at an ELSI Working Group meeting.

I've been asked to comment on the topic of genetics and racial discrimination. Let me begin with a caricature: On one side are Human Genome Project scientists, busily uncovering and disclosing genetic markers and sequencing the genome; on the other side is a society, which is completely homogeneous with respect to ethnicity, race, and class, neutrally receiving the information. I paint this picture because it seems implicit in the funding allocations of the Human Genome Project—97 percent to the uncovering, mapping, and sequencing of the genes and 3 percent to the ethical, legal, and social implications. Thus the assumption behind the project is that scientific discovery is 97 percent of the problem while dissemination and consumption is only a very small issue. But since every society is complex and stratified, the rosy picture of people receiving and responding to genetic information without regard to their strong social differences is untenable.

Indeed, we know from social research over the last two decades how important these social differences can be in populations at greatest risk for a genetic disorder. Certain ethnic groups have seized ownership of information about a genetic disease, controlling the information flow and screening process. Other groups have either rejected the information outright, or received an incomplete, fragmented picture of the disease. For example, screening for Tay-Sachs disease in the United States was controlled and influenced by people of Ashkenazic Jewish descent. The result was an effective, voluntary screening program. At the other extreme were the sickle-cell anemia tests that occurred in Greece in the 1970s: there was no shared notion of sickle-cell anemia being a societal problem; rather, the disease was perceived as the problem of a few individuals and family members. Differing from those two examples was the testing for sickle-cell anemia in America, which was politicized as the disease of blacks. In this case, African-Americans did not control the mandatory screening programs that were put into place. Test results were then used as pretexts for discriminatory employment policies. As with the screening programs in Greece, the genetic information ended up being rejected, but for different reasons.

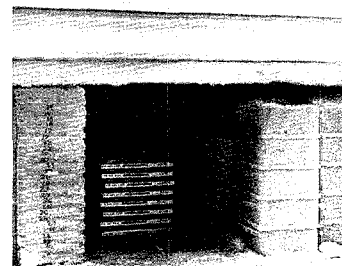
Ethnic perceptions of medical information are crucial. In the early 1960s Irving Zola studied the way different groups describe their disease symptoms to physicians. Some ethnic groups tend to be stoical, almost nonverbal; other ethnic groups tend to express themselves forcefully, even exaggeratedly. In another study the anthropologist Debra Woo examined the ways different groups react to mental-health problems. She observed the Chinese have low rates of contact with the mental-health system, not because they have few mental-health problems, but because of a cultural concept called *pao tin*—taking care of one's own—that makes people less likely to seek help from outside establishments.

Thus, we see different groups responding to health problems in starkly different ways. It is clear genetic information shouldn't simply be dropped into the social realm without a delicate understanding of these dynamics. To do so—especially if the affected group is at the bottom of the social order, with few resources for understanding the information and its implications—is irresponsible.

Few states have laws governing the use of genetic information by employers and insurers. The most important Federal law that implicitly forbids some kinds of genetic discrimination is the Americans with Disabilities Act (ADA) of 1990. That act provides employment protections for people who have disabilities but are nevertheless qualified to do a job. Specifically, the ADA prohibits employers from discriminatory practices in hiring, firing, and promoting people who are disabled for any reason, including genetic illness; people who have a history of illness that does not affect their present ability to work; and people who are perceived as if they were disabled—for example, a severely burned person who is shunned in the workplace. The ADA took effect in July 1992 for all companies with twenty-five or more employees, and will take effect in July 1994 for all companies with fifteen or more employees.

Although the ADA clearly protects people disabled by an expressed genetic disorder, it may not cover a carrier of a genetic disorder. A carrier of an autosomal (not sex-linked) disorder, such as sickle-cell anemia or cystic fibrosis, has one defective gene and one normal gene; such a person does not have the disease caused by the defective gene. If two such carriers have children, on average one-fourth of their children will inherit a defective gene from each parent and therefore have the disease. From an employer's point of view, hiring a carrier means risking higher medical-benefits costs because the carrier has a chance of having children who will need expensive medical treatment. Although the risk is small, an employer might refuse to hire such a person even though he or she is capable of doing the job. There is no evidence that employers are not hiring carriers, but the economic incentives to do so will increase as genetic screening becomes more widespread and less expensive.

Other areas not addressed by the ADA are discrimination against people with late-onset genetic disorders such as Huntington's disease and adult polycystic kidney disease, and against people whose genotypes indicate increased risk of later illnesses. The EEOC has not yet provided regulatory guidance on the applicability of the ADA to people with genes for late-onset disorders. It has stated that additional legislation may be necessary to extend the act to cover genetic predispositions. In 1991, members



of the ELSI Working Group sent a recommendation to the EEOC and testified before Congress on the need to strengthen legal protection against workplace discrimination based on a person's genotype.

In addition to its activities in the employment area, the ELSI Working Group has created an Insurance Task Force to explore potential uses of genetics by the insurance industry and possible means of protecting against unfair discrimination. The task force is chaired by two members of the working group and includes representatives of the insurance industry, corporate benefit plans, academia, and voluntary health organizations.

A commonly expressed fear is that insurers will require genetic tests or will obtain test results. Then they could either deny coverage or charge high premiums to those with genetic diseases or propensities to disease. Insurance carriers have the opposite worry: "adverse selection" by insurance applicants based on information about themselves that is not shared with insurers. For example, a person may receive a battery of genetic tests, discover that he or she has a gene that causes a late-onset disease, and then buy increased health insurance on anticipation of greater health-care costs. Another person may discover that his or her risks are comparatively low and buy less health insurance. Such practices could increase the demand for reimbursement of health-care expenses while reducing insurers' ability to spread the cost across the population. Both problems will get worse as the effects of more genes are discovered. Insurers insist that they should have all the information known to the policyholder. Such an arrangement might discourage people from having themselves tested, since policy-holders may want to avoid knowing about risks that they would be forced to disclose. Eventually, the ELSI Insurance Task Force hopes to recommend health-insurance reforms that balance the interests of insurance companies and consumers.

Privacy

Many people believe that their medical records, including genetic data, should be between them and their physicians. However, medical data are often obtained by third parties—employers, insurers, even the Medical Information Bureau, an information resource for the entire insurance industry. Likewise many people assume that personal data about them will not be generated without their consent. However, with genetic testing that assumption is not always correct—for instance, information about a person's genes can be deduced from information about his or her relatives, sometimes with great certainty. Thus there are many unresolved issues relating to the generation and disclosure of genetic information.



Some privacy questions raised by genetic testing arise from many people's desire not to know genetic information about themselves, especially when tests are subject to error and therapies are not available. For example, when people at risk for Huntington's disease were informed of a free predictive test, only about 10 percent took advantage of the opportunity to take the test. The desire not to know can lead to privacy conflicts in families. For instance, as Huntington's disease usually has a late onset, a young adult might want to be tested although his or her at-risk parent does not have symptoms and does not want to know. If the person tested has the disease gene, the parent must have it as well, so the child's test could provide the parent with unwanted information. Another conflict occurs when parents want their child tested, since the child might later prefer not to know the result. At present, testing

centers only test adults who can provide informed consent, feeling that parents should not know the genetic status of their minor children without the children's informed consent.

Under the aegis of the ELSI Working Group, a Genetic Privacy Collaboration of ELSI grantees and contractors is analyzing privacy issues from several perspectives. In addition, the DOE's ELSI program will concentrate its research funds on studies of privacy issues. One area to be covered is the development of guidelines for genetic databanks. Some state forensic laboratories store genetic "fingerprints" from convicted felons by which they may be identified later (for instance from genetic fingerprints determined from blood or semen found at a crime scene). The Defense Department has announced that it will maintain a bank of tissue samples from every member of the armed forces for use in identifying the remains of people killed in combat. Scientific laboratories maintain pedigree data on research subjects. At present there are no general standards for the protection of information in those databanks.

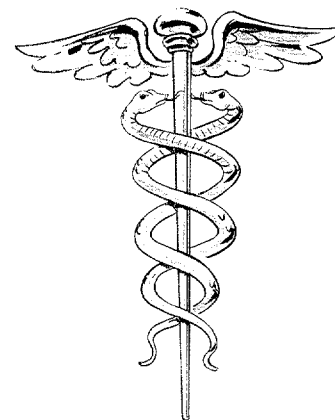
Another research topic is distinguishing genetic information that should be kept confidential or even not generated except at the request of the person involved from genetic information that must be disclosed for valid public-health reasons. The conflicts between privacy and public health related to genetics have some resemblances to the conflicts related to AIDS.

The Genetic Privacy Collaboration will also determine attitudes and expectations of the public and of various subgroups regarding the privacy of genetic information. Investigators will analyze the social-science literature, study public opinion by surveys and other methods, and compare genetic-screening programs in different states and involving different ethnic groups.

ELSI-supported research will also include legal and philosophical studies of the right to privacy in the context of genetic information. The studies will be of use to the states that are currently considering laws to protect genetic data and to Congress if it takes up such legislation. Foreign approaches to safeguarding genetic privacy will be analyzed as well. The European Community and several individual European countries have adopted measures that may serve as models for action in the United States.

Our society is only now beginning to address the topic of genetic privacy. As the ELSI privacy task force and other national privacy study groups analyze and discuss these issues, the limits of genetic privacy and possible ways to protect it should become clearer.

Currently, our society faces a challenge in bringing genetic knowledge into the medical mainstream so that the greatest number of people will reap the benefits. A common decision based on genetic information is whether to abort an embryo that has a genotype associated with a disease. A pregnant woman facing that decision and thus confronting the moral and personal issues of abortion may need accurate information—for instance, the error rate of the test. The symptoms of some genetic diseases, such as fragile-X syndrome, range from severe to practically



Delivery of Genetic Services

unnoticeable. Therapies are available for some diseases; for others therapies seem imminent. Genetic knowledge will be of such magnitude and such medical import that professional genetic counselors—people trained in special master’s-degree or clinical-nursing programs—wonder if they will be able to meet the demand for information. Dianne Bartels, the administrative director of the Center for Biomedical Ethics at the University of Minnesota, outlined some of the concerns raised at an NIH/ELSI conference on genetic counseling in the United States.

Counselor education will become more challenging as information flows in from the Human Genome Project. The massive amounts of information may be beyond the capacities of a single person to assimilate, creating the need for various subspecialties. How will genetic counselors be taught in the future? Who will teach them? Are the current two-year master’s-degree programs adequate? These are just a few of the questions that are being raised about counselor education.

There are also urgent questions about how much information a counselor should impart to a client. Genetic counselors believe it is in the client’s interest to have *all* of the available facts. This leads to a kind of Joe Fridayism—just the facts, Ma’am—that is potentially devastating for the client. Someone may discover, for example, that his father is not really his father during a routine screen for Huntington’s disease. Clearly, there are limits to the factual model for counseling.

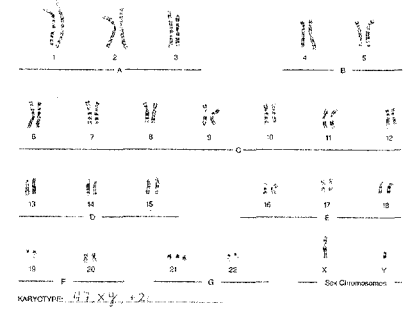
Another issue that stretches this model is finding the XYY karyotype, an abnormal chromosome combination that was once considered to be positively linked to violent, criminal behavior in adult males. The basis for the now-discredited link was a series of studies on a highly select population of XYY males—namely those imprisoned for various crimes. As far as I know, no studies of XYY among the general population have convincingly linked it to violent behavior. But some genetic counselors are telling clients, “It may not be good science, but XYY has been linked to criminal or sociopathic behavior. Genetics textbooks say that XYY males are tall, have acne, and may have learning disabilities. Most people with XYY have no symptoms.” How is a client supposed to make a reproductive decision given that information? I would challenge geneticists and genetic counselors to address what is *relevant* genetic information for clients.



The current standard for the profession is to present information in a “non-directive, value-neutral way” and in a manner that “preserves client autonomy.” Essentially this means the counselor shouldn’t project his or her values onto the patient. But does this standard work in a practical sense? A patient with a high cholesterol level isn’t told by his doctor, “Your cholesterol is 350. It could kill you, so gather some information on cholesterol and make whatever decision you want.” The doctor’s advice will be much more directive; it is likely to include recommendations about treatments or lifestyle changes that can ameliorate the illness. Those in the genetic counseling profession, however, still cling to the “nondirective counselor and autonomous patient” model—I believe this model is increasingly untenable.

We are swiftly reaching the ethical limits of client autonomy. Some clinics and laboratories refuse to give out information about the gender of unborn children. Nevertheless, a recent study shows that 60 percent of genetic counselors will either do, or refer, screening for sex selection. Some clients are saying, "People get abortions for no reason at all—why can't I have an abortion because I want a girl?" Many clinics and genetic counselors respond that gender is not a medical problem to be addressed by genetic testing. Decisions need to be made on who formulates policy: individual labs and clinics, legislatures, or the clients themselves.

We need to conduct more research on what genetic counselors are taught and how they actually respond in clinical situations. Pilot programs on counseling norms—with their societal and ethical implications—could yield important insights as to how counselors ought to be educated. Also, we need to address the information-surfeit problem and what the counselor's role will be in the future. Will counselors specialize to address specific diseases? Will they continue to work in academic centers, in private practices, or in primary practice offices?



Demand for counselors may increase as more tests for genetic diseases are found in the course of the Human Genome Project. At present there are only about 1500 trained genetic counselors in the United States. A multitude of known genetic disorders may require the training of many more professionals who can interpret tests, answer questions, provide counseling, and direct people to treatment services.

To address ways of effectively delivering genetic information to the public, the DOE and NIH are funding a National Academy of Sciences/National Institute of Medicine study on "Assessing Genetic Risks." A second major initiative is a pilot project on cystic-fibrosis testing. Cystic fibrosis is a potentially severe disorder that, until recently, usually resulted in death in early adulthood. About 1 in 2500 North American white children has the disease, implying that about 1 in 25 people in that group carries a defective gene. Although the gene has been isolated and a test has been developed, testing for carriers on a large scale would bring up difficulties. One problem arises from the existence of many disease-causing mutations of the gene, each of which must be tested for individually. Current tests detect only certain mutations that together account for 85 to 90 percent of the total number of cystic-fibrosis carriers. Thus a negative result does not guarantee that the person tested does not carry a defective gene. Also, the frequencies of the disease and of the various mutations differ according to ethnic group. Furthermore, although any doctor could send a blood sample to a laboratory and receive a result, some might be unable to effectively explain that result to patients or to prevent potential psychological trauma. Faced with so many uncertainties, physicians are not routinely testing for cystic fibrosis. Instead, the National Center for Human Genome Research, the National Institute of Child Health and Human Development, and the National Center for Nursing Research are jointly supporting pilot programs to determine whether, under what circumstances, and how such tests should be administered.

Eric Juengst, director of the NIH ELSI program, stated in a press release of October 1991,

Whether clinical testing for cystic fibrosis carrier status should become more routine is still very much an open question. . . . The underlying goal of these studies is to help determine whether testing services should remain focused on members of families already at risk, or whether it is feasible to offer the test more widely in an ethically acceptable manner.

The cystic-fibrosis pilot project aims at supplying health-care professionals with much-needed information about how to maximize a patient's understanding of the test results and to protect privacy. Seven research teams are conducting three-year studies intended to define the best methods for educating and counseling individuals who want to be tested for cystic fibrosis. Several of the studies will survey attitudes toward and understanding of testing among physicians and various populations in the lay public. Others will try out and evaluate strategies for pre-test education and post-test counseling. Such research is a first step toward building a flexible health infrastructure able to take advantage of genetic breakthroughs in the future and to respond to the needs of patients and members of their families who have concerns about genetic information.

Education

The public needs information on both the social issues and the underlying science of the genome project in order to decide the questions that are arising. Providing information to people whose work requires an understanding of genetics is even more important. Many instances of the problems described earlier—unfair insurance practices, discriminatory hiring policies, and inadequate delivery of genetic information—are driven by ignorance. For example, advances in genetics are showing that certain former diagnoses actually labeled two or more diseases. Thus a physician trained in the old school to diagnose neurofibromatosis by certain symptoms, for example, may not realize that what was once considered a single disease is two diseases, each with its own genetic signature, its own symptoms (slightly different from the other's), and its own treatment. Therefore the ELSI program is supporting projects that study ways of bringing information to medical professionals as well as to life-science and social-science researchers and to government officials.

Another aspect of education is the training of scholars studying issues arising from the genome project. Accordingly, the ELSI program includes postdoctoral fellowships for research-oriented training. The fellowships are open to biomedical scientists working on such topics as sociology, ethics, and law and to doctors in the humanities working on science relevant to the genome project. Also, to support research on ELSI topics, the DOE maintains at Los Alamos National Laboratory a library of relevant books and articles and a database indexing the library. Database services—for example, listings of publications selected according to author, key words, and source, or sorted chronologically—are available on request. A bibliography of those materials, containing more than 2600 entries, was published by the DOE in May 1992, and is also available.*

* Requests for the bibliography or for database searches should be sent to Michael R. Roth or Michael S. Yesley, MS A187, Los Alamos National Laboratory, Los Alamos, NM 87545. Telephone: (505) 667-3766. Fax: (505) 665-4424. Electronic mail: ROTH_MICHAEL_R@OFVAX.LANL.GOV or YESLEY_MICHAEL_S@OFVAX.LANL.GOV.

Finally, the ELSI program is intended to help the public understand the issues that have been outlined in this article. Therefore the program has commissioned surveys of public knowledge and attitudes. It has also initiated several public-education efforts. For example, the Colorado Biological Sciences Curriculum Study has prepared a genetics module that can be included in a typical high-school biology course. The module is five to six days long and includes exercises in both hands-on science and ethical analysis. All fifty-five thousand high-school science teachers in the United States will be given the opportunity to include this module in their biology classes. Since many students take biology as their high-school science requirement, the module should be highly effective in getting genetics and related ethical issues into the mainstream. In addition, the ELSI program provided a grant to the New York television station WNET to prepare a television documentary called "The Future of Medicine." The ten-part series dramatizes the impact of genetics on medicine.

Leaders of the ELSI project regard education as a field of paramount importance. Nancy Wexler has discussed both immediate concerns in the education of health-care workers, and the long-term goal of public education and public involvement in decision-making.

Genetics just has not been well taught in many universities. It has been chopped up into pieces and added to lots of different disciplines as an afterthought. We need to think more creatively about improving the curriculum as a whole. We also need to think about helping helping people already working in health care who want more genetic education. I think it's unlikely that every single doctor is going to go out and buy a genetics book. I must say that having patients who ask questions is definitely the best motivation to learn, because doctors want to be able to answer their patients responsibly and intelligently. Nobody wants to have to say, "I haven't a clue, and furthermore I don't feel like finding out." A public that develops a hunger for answers will goad all of us in medical research and practice to try to do a better job.

If you compare society's handling of genetic knowledge to making a movie, then what we in ELSI can do is help write the script. If the movie is going to be made, the public must act as the producers. They have to help raise the money and hire the cast and get it going. If you don't have a script then you don't have a movie—but if you don't have a producer your movie will never be made. The public must be partners every step of the way. ■

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