

GUIDELINES FOR PHYSICIANS
CONCERNING DECISIONS ABOUT GENETIC TESTING

**Joint Committee on Biomedical Ethics
of the
Los Angeles County Medical Association
and
Los Angeles County Bar Association**

Approved by the Los Angeles County Medical Association December 3, 2008
Approved by the Los Angeles County Bar Association January 28, 2009

GUIDELINES FOR PHYSICIANS

CONCERNING DECISIONS ABOUT GENETIC TESTING

I. INTRODUCTION

The ever-increasing quantity of information about genetic testing that is available to the public has become overwhelming, and is often misleading. In addition, vendors of genetic testing services are aggressively engaging in direct-to-consumer marketing, bypassing physicians. These guidelines are intended to answer some of the ethical, medical, legal and cultural concerns associated with a decision to undergo genetic testing. For example: Will the test results be useful in the patient's care? Will the test results be reliable, and dependably predictive? Will they have adverse psychological effects? Will they be worth the risks involved? Will they be kept confidential? If not, what might be the consequences? Is the test cost-effective? Should the results be disclosed to family members? These guidelines also are meant to assist physicians in preparing themselves to discuss these important issues with their patients. In addition, a list of on-line resources for further information is included at the end of these guidelines.

II. PURPOSES OF GENETIC TESTING

Genetic testing provides information -- with varying degrees of certainty -- about whether a person has, is likely to develop, or has the potential to pass on a genetic disease or condition. Discussed below are the four most common uses of genetic testing.

- A. Diagnosis: Diagnostic tests for genetic diseases or conditions include direct genetic testing and protein marker testing, which may be useful when a patient shows evidence of a genetic disease. Note, however, that the absence of protein markers does not necessarily rule out the presence of the disease.
- B. Treatment: Genetic testing can assist in making treatment decisions. Pharmacogenetic testing may indicate how a patient will respond to a particular drug, or whether a patient with a particular genetic profile (such as G6PD deficiency) will have an adverse reaction to a specific type of medication regimen. Gene replacement therapy, although currently available only on a limited basis, may offer other

treatment options.

C. Prediction: Predictive tests are useful in patients who are asymptomatic, but have a family history of an inherited disorder. The presence of a gene may determine the probability that a patient will develop a disease. For example, the presence of the Huntington's Chorea gene would indicate that a person is certain to develop the disease eventually, while the presence of other genes or mutations like BRCA 1 or 2 may indicate only that a patient has an increased potential for developing the disease. In some cases, a person may be able to make choices that would reduce the probability of developing the disease. For instance, genetic testing might identify women who could benefit from immunization against cervical-cancer-causing viruses.

D. Assistance with Reproduction:

1. **Pre-Marital** or **pre-conception testing** for carrier status can inform prospective parents of deleterious genes that potentially could be passed on to their children. Genetic testing also may provide an answer for patients with otherwise unexplained infertility.
2. For patients using assisted reproductive technologies, **pre-implantation testing** may be used to determine which embryos should be implanted.
3. Once a patient is pregnant, **fetal testing** for mutations that cause conditions such as Cystic Fibrosis can assist in deciding whether to continue the pregnancy. Such information also may help prepare parents for the birth, care and treatment of a child with significant medical and/or developmental problems.

III. INDICATIONS FOR GENETIC TESTING

Many diseases may be caused by the presence or interaction of genes, viruses and/or environmental factors. The following topics of inquiry may help a physician identify potential genetic disorders and decide whether or not to recommend genetic testing.

- A. Ethnicity: Certain populations are statistically more likely to carry or suffer from certain genetic disorders. For example, Tay Sachs or Gaucher's are more likely to be found in people of Ashkenazi Jewish descent, and certain types of sickle cell anemia are more likely to be found in people with African ancestry. A detailed family history may be necessary to identify a person's ethnic background.
- B. Family History: Families may carry and pass down particular genetic mutations through several generations. An individual could inherit a mutation that may or may not have been expressed in the individual's parents, but can be found among other relatives. For example, close relatives with breast or colon cancer may indicate that a patient is at risk. Huntington's Chorea in a patient's parent would alert a patient to a similar risk.
- C. Personal Experiences: Even without a positive family history, some conditions may arise spontaneously in an individual. A previously unsuspected genetic defect may be unmasked by particular events or exposures. For example, the autosomal dominant gene for malignant hyperthermia may be unmasked or triggered by certain anesthetic agents. A thorough patient history should be taken and reviewed to discover the types of issues that may be indications for genetic testing. In addition, exposure to environmental triggers, as seen with teratogens, carcinogens or viruses, may alter somatic or germ cells. Examples include Agent Orange, agricultural pesticides or chemotherapies. Many of these triggers currently are subject to ongoing research and have not been confirmed as causing the expression of dormant genes.
- D. Symptoms: A patient may present with symptoms that could indicate a genetic disease. For example, if a child has a high-pitched, yowling cat-like cry, this may indicate Cri du Chat, a chromosomal deletion. Progressive muscle weakness, particularly proximal weakness, may indicate Muscular Dystrophy in a child or adult.
- E. Advanced Parental Age: Even in the absence of the above indicia, testing of the

fetus for genetic anomalies such as Down Syndrome or neural tube defects should be considered if the mother is of advanced age (for pregnancy).

IV. **FACTORS TO WEIGH WHEN CONSIDERING GENETIC TESTING**

The physician and patient together should weigh the value of the information to be gained from genetic testing versus the potential drawbacks. Each of the questions below should be discussed when making a testing decision. No one single factor is likely to be determinative:

- A. Would the test results be useful in the care of the patient? Are treatments or preventive measures available? There is no effective treatment for genetic diseases for which tests are available, such as Huntington's Chorea. Nevertheless, a person may wish to make lifestyle choices based on test results. For example, a person may (1) choose to avoid pregnancy if there is a high likelihood of passing on a disease; (2) seek to avoid environmental triggers that could bring on a disease or condition; or (3) undertake medical interventions that may reduce the probability of developing a disease. As a more specific example of (1), a patient with the BRCA 1 or 2 mutation may choose to adopt or use a gamete donor rather than risk passing on the mutation.
- B. Would test results adversely affect a patient psychologically? For example, a patient with a history of breast cancer in his or her family may want to be tested for BRCA 1 or 2, believing that the test results may alleviate the fear of developing the disease. However, a negative result may lead to a false sense of security, which in turn could cause a failure of appropriate vigilance.
- C. Are test results dependably predictive? While all tests have a false positive or false negative rate, reliability of the test should be taken into consideration. Also, many diseases have varying levels of penetrance or expression. Thus, while the test may be reliable, the disease itself is so highly variable in its expression that it is difficult to determine what a positive result means for the patient. For example, the Cystic Fibrosis mutations are notoriously variable in the degree of their expression even within a single family. Additionally, Cystic Fibrosis has over one thousand

identified mutations. Some of those are unlikely to be picked up by a general test, because they are family-specific or specific only to particular ethnic groups.

- D. Is the testing provider trustworthy? The physician should attempt to ascertain the proposed testing provider's reputation for competence and accuracy before any samples are submitted for testing. If the physician is not familiar with the testing provider, the physician should caution the patient accordingly. Notably, in June 2008, the California Department of Public Health sent letters to thirteen direct-to-consumer genetic testing providers ordering them to stop selling tests until they could prove to the state that they meet its quality and reliability standards, and also that any test for a California resident was ordered by a physician. The New York State Department of Health issued similar letters to nearly two dozen genetic testing providers there in April 2008.¹
- E. Is the test worth the risk? The probability and severity of adverse risks should be weighed against the benefits of testing. For example, the test itself may involve specific physical risks, such as those associated with amniocentesis, which could cause miscarriage, infection or damage to a fetus. Additionally, receipt of test results, whether positive or negative, may cause physical and emotional distress or depression in a patient, and also could have adverse practical consequences.
- F. Can test results be kept confidential? Even the most stringent confidentiality policies are subject to exceptions and errors. A physician and patient should consider the risks of disclosure to the patient's employer (or prospective employer) or payor, or to the government.² On May 21, 2008, President Bush signed into law the federal

¹ *California challenges DNA test start-ups*, L.A. Times, June 17, 2008, at C4 ("The Department of Public Health sent the cease-and-desist letters . . . after an investigation spurred by consumer complaints about the tests' accuracy and costs . . .").

² For example, The California Newborn Screening Program ("NSP"), mandates that all newborns be screened for phenylketonuria (PKU), fatty acid oxidation, amino acid disorders, organic acid disorders, and congenital adrenal hyperplasia (as well as other disorders which may be listed in the footnote continued)

“Genetic Information Nondiscrimination Act of 2008” (“GINA”),³ which prohibits employers, labor unions, and employment agencies from using genetic information when making decisions about hiring, classification, compensation, termination, etc. GINA also prohibits health insurers and plans from using genetic information for underwriting, enrollment or premium-setting purposes. Nevertheless, there remains some risk that genetic testing information might be used in a manner that is detrimental to the patient. For example, despite GINA and state laws (including California law) that disallow or limit the practice,⁴ it is possible that a health insurer might cancel the coverage of a patient who tests positive for a genetic disease with high health care costs, and the patient would have to take legal action to regain coverage. In the past, the government determined that individuals with the sickle cell

future). Cal. Health & Safety Code §§ 124975(j), 124980(f), 125001(b); Cal Code Regs. tit. 17 § 6501. Specimens and information obtained during testing become state property and may be used by the California Department of Public Health (“DPH”) or DPH-approved researchers in a manner that does not identify the patient (unless specifically prohibited in writing). Cal Code Regs. tit. 17 §§ 6502.1, 6505(j). In addition, the California Birth Defects Monitoring Program requires all health facilities to make the following available to authorized DPH staff: records of children suspected or diagnosed as having birth defects (including their mothers’ records), medical records of mothers suspected or diagnosed with stillbirths or miscarriages, and “other records of persons who may serve as controls for interview studies about the causes of birth defects.” Cal. Health & Safety Code § 103830. Further, mandatory testing for sickle cell anemia *may* be conducted by DPH at the following times: (a) upon first enrollment of a child at an elementary school; (b) for any child not tested in elementary school, upon first enrollment at a junior high or senior high school; (c) upon application for a marriage license, and (d) at any other times that the department may designate. Cal. Health & Safety Code § 125030. Also, cases of Parkinson’s Disease are required to be reported to DPH under certain circumstances by health care facilities and health care practitioners pursuant to their required participation in the state’s Parkinson’s Disease Registry (effective throughout the state July 1, 2007). Cal. Health & Safety Code § 103865. This is not an exhaustive list.

³ H.R. 493 (2008).

⁴ See Cal. Ins. Code § 10148, which prohibits insurers from requiring genetic tests for the purpose of determining eligibility for coverage, and from limiting benefits otherwise payable if the loss is caused by the presence or absence of genetic characteristics – unless the insurer limits eligibility or coverage in the same way for other medical conditions. See also, Cal. Gov’t Code § 12926, which prohibits employers from discriminating against applicants or employees based upon genetic conditions, actual or perceived.

trait were unfit to serve in the Air Force, even though oxygen deprivation would not cause sickling crises in such individuals.⁵

G. Is the test cost-effective? While we would like to believe that all medical decisions can be made without regard to financial considerations, this is simply not the reality of our health care system. If a test will not be covered by insurance, the patient and physician must weigh the patient's ability to bear the cost when deciding whether or not the patient should undergo a genetic test. However, keep in mind that high cost does not excuse a physician from failing to recommend an appropriate test. There may be other ways to obtain the desired information if the patient cannot afford the test. For example, it is recommended that gamete donors be systematically screened for various genetic conditions as part of the selection process, and this testing is usually paid for by the recipient.

H. Should test results be disclosed to family members? An individual's genetic data can provide information about the patient's family members as well. A physician has an ethical obligation to persuade a patient to disclose results to family members who might also discover a genetic predisposition if they were to undergo testing, and could act on that information.

V. **THE ROLE OF GENETIC COUNSELORS**

A. Genetic counselors are health care professionals who are trained to provide information and support regarding the nature, inheritance and implications of genetic disorders, and to assist individuals and their families to make informed medical and personal decisions. As part of a health care team, they can work with individuals or families who have genetic disorders or may be at risk for inherited conditions, by providing services such as the following:

⁵ In addition to being aware of these issues, some patients also may want to seek legal advice, to determine how they might be affected by genetic test results.

1. assessing the risk of a genetic disorder by researching a family's history and evaluating medical records;
 2. weighing the medical, social and ethical decisions surrounding genetic testing;
 3. providing support and information to help a person make a decision about testing;
 4. interpreting the results of genetic tests and medical data;
 5. providing counseling or referring individuals and families to support services;
 6. serving as patient advocates;
 7. explaining possible treatments or preventive measures; and
 8. discussing reproductive options.
- B. There are many reasons why a physician may want to refer a patient to a genetic counselor. For example, a physician may not feel confident or have sufficient knowledge to counsel the patient effectively. A patient may insist on testing against the physician's advice. A physician may fear that a patient may not fully appreciate the potential negative psychological consequences of certain test results and, therefore, may wish to engage a genetic counselor to assist in preparing the patient. Physicians also may desire reinforcement of communications or instructions given to their patients. Physicians should recognize that they may be biased, and unable or unwilling to present all available alternatives. At the very least, physicians should disclose any personal beliefs that might impact their recommendations about genetic testing. Physicians may not be sufficiently aware of the tests and treatments currently available, including ongoing studies that may be open for enrollment. There may be other reasons to utilize a genetic counselor; it is not possible for these guidelines to anticipate all possible scenarios.
- C. If there is no available genetic counselor in your area, there are still resources

available by telephone or on the internet. Although not optimal, it is better to consult electronically when in unfamiliar territory than not at all.

VI. CONCLUSION

As information regarding genetic testing, and tests themselves, become more available, physicians should expect to see more patients with questions, concerns and possibly even test results obtained from mail-order laboratories and direct-to-consumer marketers. Physicians should become familiar with the available resources and develop the knowledge to identify and address the various ethical, medical, legal and cultural issues raised by genetic testing. When necessary, physicians should be prepared to refer their patients to genetic professionals. Any decision regarding genetic testing should be undertaken carefully after consideration of each of these issues.

VII. USEFUL WEBSITES

- A. Accredited genetic counseling programs: www.kumc.edu/gec/prof/gcprogs.html
- B. American Board of Genetic Counseling: www.abgc.net/english/view.asp?x=1
- C. Centers for Disease Control and Prevention's National Office of Public Health Genomics: www.cdc.gov/genomics
- D. Genetics & Public Policy Center (at Johns Hopkins): www.dnapolicy.org
- E. March of Dimes: www.marchofdimes.com/pnhec/4439_1120.asp
- F. Mayo Clinic: www.mayoclinic.com/health/genetic-testing/FL00076
- G. National Cancer Institute: www.cancer.gov/search/genetics_services
- H. National Human Genome Research Project: www.genome.gov
- I. National Society of Genetic Counselors: www.nsgc.org
- J. U.S. National Library of Medicine and National Institutes of Health informational web site called Medline Plus: www.nlm.nih.gov/medlineplus/geneticTesting.html