

# **MODULE 8**

## **Public Health Genetics: Screening Programs and Individual Testing/Counseling**

***Ruth Gaare Bernheim, PhD***  
***Institute for Practical Ethics, University of Virginia***

***Richard Bonnie, LLB***  
***School of Law, University of Virginia***

***Phillip Nieburg, MD, MPH***  
***Center for Biomedical Ethics, University of Virginia***

### **Issue Essay**

Advances in genetic science provide new insight into the complex, interactive roles that genetic and environmental factors play in morbidity and mortality, and they consequently create innumerable opportunities for disease prevention and health promotion. Should genetic information and genetic interventions, however, be used routinely in public health—like other health data and services—or are they different? Answers to this question essentially frame the ethical debates about public health genetics.

While some people argue that the uniquely personal nature of genetic information requires an individual rights approach that limits public health use, others view genetic data as just another type of population data that can be collected, aggregated, and used along with other surveillance and environmental data to produce social utility. Still others focus on the significant power of genetic advancements to improve individual lives and, from a distributive justice perspective, emphasize public health's responsibility to not only ensure access to genetic information throughout the population but more importantly to provide genetic services for the disadvantaged. Public health must address these and other competing ethical claims when developing public health genetics policies.

### **Public Health Ethics**

Public health genetics has been defined as “the application of advances in genetics and molecular biotechnology to improve public health and prevent disease.”<sup>1</sup> As with public health generally, it is teleological (end-oriented) and consequentialist—it draws on a population-wide analysis to identify strategies for improving the health of the entire population, in contrast to the patient-centered focus of clinical genetics.

Several of the major ethical principles or considerations that animate public health include: producing population benefits, preventing and removing harms, and producing the maximal balance of benefits over harms and other costs (utility). These values provide a *prima facie* warrant for public health action.

Newborn genetic screening programs are just one example of public health interventions justified by these values.

Other general moral considerations in public health, however, are recognized as setting limits or constraints on what may be done in pursuit of population health and social utility. These concerns include respecting individuals' autonomous choices and actions, protecting privacy and confidentiality, distributing benefits and burdens fairly, and maintaining trust with the community. Unlike with public health interventions directed at the entire population, such as water fluoridation, genetic interventions are at their core individually focused, requiring the collection of individual-specific data and often targeting individuals and groups at risk for genetic conditions. Thus, public health genetic interventions have the potential to cause or increase social harms, especially when the targeted individuals or groups have been vulnerable in the past to discrimination or social stigmatization because of race or ethnicity. For this reason some critics maintain that few, if any, government-sponsored public health genetics interventions are appropriate. This perspective often is based on a balancing of the potential population benefits of genetic interventions with what these critics consider to be the stronger moral claims against the intervention which arise from the risk of social harms and from individual interests in autonomy, privacy, and confidentiality.

For some genetic interventions, such as newborn screening, ethical considerations such as respect for individual autonomy, privacy, and confidentiality, therefore, may act as ethical constraints on public health action. This perspective is evident in arguments that call for requiring explicit informed consent from parents for all newborn screening programs, even though requiring consent will likely lead to a decrease in both population and individual benefit because some infants will not be screened. Ethical justification for this position is based both on (i) a heightened autonomy interest, because the potential social harm to individuals from the misuse of genetic data is judged to be greater than with other types of medical data, and (ii) a related need to explicitly involve individuals in genetics decisions in order to maintain trust with community members, who are partners with public health officials in defining and achieving population health benefits.

These autonomy-based ethical arguments are countered generally in public health genetics policies by claims that genetic science fundamentally challenges and requires new specifications of the concept of autonomy. After all, by establishing the genetic links among individuals, families, and groups, genetic science generates new questions and insight about moral obligations to those who are genetically related—and to the public in general. Given humans' common genetic heritage and the fact that genetic advancements result from (and often *depend* on) the analysis of population data and the collective efforts of scientists and organizations, this perspective suggests that individual interests cannot easily be separated from population benefits, and that even individual interests are supported in the long run by acknowledging the weight of moral claims to produce population health benefits.

This perspective, based on the view that genetic science heralds a new era of medical and pharmacogenetic treatment, may even lead to ethical claims that human genetic data are a form of common property that should be collected and analyzed for purposes of social utility and population health. With this line of argument, for instance, genetic data from newborn screening programs might be viewed as common property; thus, being screened and providing genetic data for population-based surveillance to allow for analysis of genetic/environmental interactions might be considered an

obligation of citizens for the social good, similar to the obligation to submit to compulsory immunizations or to pay taxes.

It is common in public health practice for conflicts to arise among important moral considerations such as, in newborn screening programs, between producing population benefits and respecting individual liberty (by requiring parental consent). To help determine whether promoting public health with a particular program warrants overriding conflicting values such as individual liberty, Childress, Faden and Gaare, *et al.*, propose five “justificatory conditions” or criteria. These are 1) effectiveness (the public health program will likely realize its goal); 2) proportionality (the probable benefits of the program outweigh the infringed general moral considerations); 3) necessity (the program is essential to achieve the public health goal); 4) least infringement (the program is the least restrictive alternative); and 5) public justification (public justification can be given).<sup>2</sup> An ethical analysis of newborn screening programs using these criteria would be aided by empirical data, as well as public consultation. For example, information about parents’ willingness to give consent if the screening programs were voluntary would provide evidence about whether the mandatory programs satisfy the least infringement condition.

### **The History of Eugenics**

A long shadow is cast on public health genetics by the history of eugenics, a social movement of the early 20<sup>th</sup> century that carried to an extreme the impetus to improve the human population through government interference in reproduction and in the selective transmission of genes to future generations. Although people often remember eugenics as an evil Nazi project to purify Germany’s gene pool, it was in fact widely popular in the U.S., Europe, and other countries as a way to cure social ills such as drunkenness, criminal behavior, and poverty. Groups with divergent political views, including Progressives, reformists, feminists, and successful capitalists, believed that society ought to foster the breeding of those with favorable traits (positive eugenics) and discourage or prevent the breeding of the biologically inferior (negative eugenics).

Although eugenicists varied greatly in their particular beliefs and approaches, class and race prejudices were pervasive. In Northern Europe and the United States, eugenicists generally “favored standards of fitness and social value that were predominantly white, middle-class, Protestant....”<sup>3</sup> Positive eugenics programs rarely went beyond providing encouragements, such as “Fitter Family” competitions or family allowances. Negative eugenic projects, however, led to coercive measures like the eugenic sterilization laws enacted in Northern Europe, including Denmark, Sweden, and Germany, and in more than two dozen American states by the mid-1930s. The constitutionality of these laws was upheld in the 1927 U.S. Supreme Court decision, *Buck v. Bell*. The court’s now-dubious opinion, written by Justice Oliver Wendell Holmes, stated that “(t)he principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes,”<sup>4</sup> and explicitly proposed the worrisome connections between public health and eugenics.

### **Public Values and Accountability**

The integration of genetics into public health practice today must be understood in the context of significant progress made during the last 50 years in scientific and technological knowledge and in the development of national and international norms for medical research, professional ethics, and reproductive rights—all of which provide safeguards against a revival of eugenic policies. For instance, public health ethics increasingly acknowledges the partnership between public health professionals and

the community in jointly defining goals and articulating values. (This is similar to the evolution that occurred in clinical medical ethics during the last half-century, in which the doctrine of informed consent, based on respect for the autonomy of individual patients, increasingly established the patient as a partner in defining his or her treatment plan.)

The public health/community partnership extends not only to defining community health problems, collecting and interpreting data, and designing appropriate interventions but also to jointly developing policies, regulations, and laws to protect individual and group interests that may be adversely affected. When considering public health genetics policies, many public health professionals and researchers explicitly address the history of eugenic abuses. For example, the Association of State and Territorial Health Officers' (ASTHO's) public health genetics policy statement includes a section on eugenics that states:

In the early to mid twentieth century, approximately 30 states enacted eugenics laws to limit the transmission of perceived undesirable characteristics such as mental retardation by restricting the reproduction of affected individuals. There was little scientific evidence by current standards that would have indicated that a person with one of the targeted traits would have offspring with the same condition; however, tens of thousands of women and men were involuntarily sterilized as a result of these laws. A situation like this must never be allowed to occur.<sup>5</sup>

Condit, Parrott, and O'Grady are even more specific, identifying at least three lessons learned from the past: Genetic information can be used to stigmatize; genetic information should be used to benefit individuals; and "genetically based decisions must be made by individuals, based on their own values and preferences, not on externally imposed criteria, whether or not these criteria are perceived to be true and just by socially sanctioned experts."<sup>6</sup> They question public health choices that favor financial concerns about efficiency over individual rights, and suggest, for instance, that voluntary newborn screening programs may be superior to nonvoluntary approaches, in part because research suggests that parents who voluntarily involve their families may be "more likely to follow through on treatment regimens because they understand and are committed to their value."<sup>7</sup>

An ethical analysis of a genetic intervention by a public health agency, then, might begin with the following questions: *What is at stake in the situation? What is at stake in alternative courses of action? Who are the critical stakeholders?* A stakeholder is anyone who might be affected by the decision, and part of the analysis would include consideration of the costs and benefits of an action for each stakeholder as well as the nature of the relationships with and among stakeholders. With questions of genetics, for which "stakeholders" can include distant relatives or future generations, a stakeholder approach to understanding and balancing the conflicting moral obligations and principles provides a useful framework for identifying ethically relevant considerations.

This "ethics process," especially when it is public and includes actual stakeholders (when possible) rather than representatives speaking on their behalf, can facilitate real understanding. Ethical deliberation also can illuminate questions that can be addressed by empirical research (e.g., assessing the actual risk of genetic discrimination) and the need for legislative action (e.g., anti-discrimination laws). Public health policy evolves as empirical evidence about the effectiveness and the social effects of interventions accumulates, and as societal responses change.

For *government* public health officials, public health ethics requires a process of public accountability. At a minimum, their accountability involves “transparency in openly seeking information from those affected and in honest disclosure of relevant information to the public.”<sup>8</sup> For genetics and other issues about which there is ethical disagreement, public health ethics also requires a fair process, which—as defined by Norman Daniels in a different context—includes: (1) transparency and publicity about the reasons for a decision; (2) appeals to rationales and evidence that fair-minded parties would agree are relevant; and (3) procedures for appealing and revising decisions in light of challenges by various stakeholders. As Daniels explains, “Since we may not be able to construct principles that yield fair decisions ahead of time, we need a process that allows us to develop those reasons over time as we face real cases.”<sup>9</sup>

## Public Health Genetics

The role of governmental public health agencies in addressing genetic advancements encompasses the three core functions defined for public health practice by the Institute of Medicine:

- Assessment (of data on the population’s health)
- Assurance (of high quality health services)
- Policy development (to serve the public interest by promoting the use of scientific knowledge)

The Centers for Disease Control and Prevention (CDC), in addition to state and local health departments, currently have oversight of large health care databases, including birth and death records, disease registries, and statistics on reportable diseases, and with these data, they determine the need for and benefit of population interventions, such as educational programs on nutrition or screening programs for high blood pressure or cancer. Khoury, Burke, and Thomson call for the collection of additional surveillance data “to determine the population frequency of genetic variants that predispose people to specific diseases, both common and rare; the population frequency of morbidity and mortality associated with such diseases; and the prevalence and effects of environmental factors known to interact with given genotypes in producing diseases.”<sup>10</sup>

Current birth-defects surveillance illustrates the value of such population data—for instance, in understanding the etiology of certain genetic conditions or birth defects clusters, such as those caused by new teratogens in the environment or health services. Botto and Mastroiacovo point out that population monitoring was useful in identifying valproic acid as a cause of spina bifida and the association of a cluster of limb anomalies among infants with their mothers’ chorionic villus sampling (CVS). They suggest that international comparisons of the prevalence of neural-tube defects, for instance, may provide insight about gene-environment interactions, particularly if prevalence data are integrated with population data on genetic variation (e.g., the frequency of polymorphisms of folate-related genes) and dietary intake (e.g., micronutrient consumption).<sup>11</sup>

Identifying the connection between environmental risk factors and inherited susceptibility to cancer also has been called a “new paradigm” for cancer prevention and control, and Coughlin and Burke describe the need for additional population-based molecular epidemiologic research to explore these connections. They hypothesize, for instance, that for women at risk of breast cancer, gene-environment interactions between gene mutations and nongenetic factors, such as ionizing radiation or cigarette smoking, may be identified and lead to new targeted prevention programs.<sup>12</sup>

These examples illustrate the vagueness of the term “genetic condition.” While it often refers to relatively rare conditions in which a single gene is implicated (e.g., Huntington’s Disease), public health genetics has a much broader focus. In fact, because virtually all human disease involves both genetic variants and environmental factors (broadly defined to include infectious, physical, and social factors), viewing any particular condition in public health as “genetic” is as much a matter of public choice and ethics as it is genetic science.

Some scientific distinctions about genetic disorders and causation may not even be helpful in determining the appropriate role for public health. An example is the distinction medical geneticists make between disorders resulting from single-gene variants, such as PKU and hemochromatosis, and other disorders associated with susceptibility genes, such as colon cancer and breast cancer. Khoury, Burke, and Thomson describe the complexity of genetic labels by pointing out that even many of the classic single-gene metabolic disorders are the result of both a deficiency in a nutritional enzyme and a dietary exposure to one or more chemicals (e.g., phenylalanine and phenylalanine hydroxylase deficiency in PKU; iron intake and mutations in the HFE gene in hereditary hemochromatosis).<sup>13</sup> They quote Rothman: “It is easy to show that 100% of any disease is environmentally determined and 100% is genetically determined as well. Any other view is based on a naive understanding of causation.”<sup>14</sup> Given the pervasive role of genetic factors in human disease, then, the more important issue involves not whether some disorder is labeled “genetic” rather than behavioral or environmental but instead, when and how to use genetic information and technology effectively, and ethically, in public health policy and practice.

Tobacco use, commonly viewed as a behavioral or environmental problem, illustrates this point. Even though more than 90% of lung cancers may be caused by smoking, only 10-15% of smokers develop lung cancer, which suggests “the interaction of smoking with other factors including genetic ones.”<sup>15</sup> If a genetic test became available to determine an individual’s susceptibility to cancer from exposure to tobacco smoke, what would be an appropriate public health response? Would including the genetic test be justified as part of the state newborn screening program, so that public health professionals could alert parents to take particular precautions to protect the child from second-hand smoke? Would the state be justified in following up later in childhood and targeting particular anti-smoking interventions to middle-school children with genetic susceptibilities? Would the public health department be justified in requiring genetic analysis of lung cancers in the cancer registry, so that family members could be told of their potential susceptibility—and, if so, should such notification be mandatory or voluntary? Should public health departments provide access to genetic tests for susceptibility? If so, should they collect the data in order to target education and behavior modification interventions to those at special risk, including the family members of those tested?

In answering many of these questions, scientific assessments of the magnitude of genetic susceptibilities may be less important than the ethical considerations. These include concerns about individual rights, such as liberty of action and the risk of discrimination, stigmatization, and social harm, in addition to concerns about ensuring equitable access to services and maintaining public trust. Determining whether to use genetic technology and genetic information about tobacco in a public health program requires examining the social, economic, and political implications of such a decision. There are implications for individuals, such as the potential for discriminatory use of genetic information in insurance and employment, as well as widespread social effects, such as a potential public perception that tobacco use is merely a genetic problem of a subgroup of the population. This in turn may lessen a sense of

collective responsibility for addressing the underlying economic and political issues related to tobacco production and use.

A complex web of individual and group interests, benefits, and costs is involved in these questions, and the public health agency provides a public structure to facilitate transparent ethical reflection, deliberation, and consensus-building. Public health accountability ensures that tradeoffs and balancing of ethical claims will be made openly, with explicit acknowledgement that individuals' fundamental well-being and values are at stake and that reasons, grounded in ethics, will be provided to those potentially affected by the decisions. At the same time, public health ethics with its population perspective focuses attention on the level and distribution of well-being throughout the population and "makes explicit the competition for scarce resources that has proven difficult to address in the patient-centered maze of medical ethics."<sup>16</sup>

### Genetic Testing

Genetic tests are rapidly being developed and marketed for clinical diagnosis, treatment, and prevention, and are now available for hundreds of inherited and chromosomal disorders and genetic predispositions. A genetic test is defined as:

*[T]he analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes. Such purposes include predicting the risk of disease, identifying carriers, and establishing prenatal and clinical diagnosis or prognosis. Prenatal, newborn and carrier screening, as well as testing in high risk families, are included. Tests for metabolites are covered only when they are undertaken with high probability that an excess or deficiency of the metabolite indicates the presence of heritable mutations in single genes. Tests conducted purely for research are excluded from the definition, as are tests for somatic (as opposed to heritable) mutations, and testing for forensic purposes...Some, but not all, predictive genetic testing falls under the rubric 'genetic screening,' a search in a population for persons possessing certain genotypes.*<sup>17</sup>

The 1997 Final Report of the Task Force on Genetic Testing (established by the National Institutes of Health-Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research) provided extensive recommendations on the safety and effectiveness of genetic tests, as well as the overarching principles excerpted below as guides for future policy:<sup>18</sup>

***Informed Consent.*** The Task Force strongly advocates written informed consent [for genetic testing]. The failure of the Task Force to comment on informed consent for other uses does not imply that it should not be obtained.

***Test Development***—Informed consent for any validation study must be obtained whenever the specimen can be linked to the subject from which it came.

***Testing in Clinical Practice***— (I) It is unacceptable to coerce or intimidate individuals or families regarding their decision about predictive genetic testing. Respect for personal autonomy is paramount. People being offered testing must understand that it

is voluntary. Their informed consent should be obtained. Whatever decision they make, their care should not be jeopardized.

(2) Prior to the initiation of predictive testing in clinical practice, health care providers must describe the features of the genetic test, including potential consequences, to potential test recipients.

*Newborn Screening*—(1) If informed consent is waived for a newborn screening test, the analytical and clinical validity and clinical utility of the test must be established and parents must be provided with sufficient information to understand the reasons for screening. By clinical utility, the Task Force means that interventions to improve the outcome of the infant identified by screening have been proven to be safe and effective.

(2) For those disorders for which newborn screening is available but the tests have not been validated or shown to have clinical utility, written parental consent is required prior to testing.

***Prenatal and Carrier Testing.*** Respect for an individual's/couple's beliefs and values concerning tests undertaken for assisting reproductive decisions is of paramount importance and can best be maintained by a nondirective stance. One way of ensuring that a non-directive stance is taken and that parents' decisions are autonomous is through requiring informed consent.

***Testing of Children.*** Genetic testing of children for adult onset diseases should not be undertaken unless direct medical benefit will accrue to the child and this benefit would be lost by waiting until the child has reached adulthood.

***Confidentiality.*** Protecting the confidentiality of information is essential for all uses of genetic tests. (1) Results should be released only to those individuals for whom the test recipient has given consent for information release. Means of transmitting information should be chosen to minimize the likelihood that results will become available to unauthorized persons or organizations. Under no circumstances should results with identifiers be provided to any outside parties, including employers, insurers, or government agencies, without the test recipient's written consent.

(2) Health care providers have an obligation to the person being tested not to inform other family members without the permission of the person tested, except in extreme circumstances.

***Discrimination.*** No individual should be subjected to unfair discrimination by a third party on the basis of having had a genetic test or receiving an abnormal genetic test result. Third parties include insurers, employers, and educational and other institutions that routinely inquire about the health of applicants for services or positions.

***Consumer Involvement in Policy Making.*** Although other stakeholders are concerned about protecting consumers, they cannot always provide the perspective brought by consumers themselves, the end users of genetic testing. Consumers should be involved in policy (but not

necessarily in technical) decisions regarding the adoption, introduction, and use of new, predictive genetic tests.

### **Public Health Genetic Testing**

The formulation of sound public health policy regarding genetic testing and screening programs requires an on-going, systematic, evidence-based analysis of the benefits, risks, and costs of genetic tests and follow-up interventions. Multidisciplinary research and perspectives from history, cultural anthropology, economics, psychology, and other disciplines provide important information. Given that the risks and harms of genetic testing are primarily psychosocial, empirical evidence is necessary in order to assess whether the tests are justified—that is, whether the probable benefits outweigh the probable harms or costs. As Beauchamp and Childress point out, the probable benefits also “vary from genetic condition to condition, depending on whether the screening and testing are for disease, disposing condition, or carrier status, whether preventive or treatment measures are available, whether the information is important for reproductive decisions, and the like.” They summarize: “For any genetic screening or testing, fundamental questions concern who will use the resulting information, how they will use it, and for what purposes.”<sup>19</sup>

As with any public health decision, critical questions involve (1) deciding what factors to include in the calculations of costs and benefits (e.g., whether to include in the cost calculations the future lost productivity of children who die or suffer disability as a result of not being screened as newborns) and (2) determining how to value the costs of social stigma that may result from targeting particular groups at high risk.

The following types of genetic testing are especially relevant to this discussion.

***Newborn Screening Programs for Phenylketonuria (PKU).*** These programs were among the first genetic screening programs developed in the United States and, along with testing for hypothyroidism and hemoglobinopathies, are now conducted in all 50 states and the District of Columbia. Widely touted as a public health success, they identify infants with the hereditary metabolic disorder so that special dietary treatment can prevent life-long mental disabilities. However, commentators have criticized the way the PKU screening programs were initially developed and their legacy of mandatory newborn screening without parental consent.

The PKU programs were established throughout the United States during the 1960s and 1970s, without the initial support of the American Academy of Pediatrics and the medical community in general, without prior controlled clinical trials, without appropriate empirical evidence about the optimal diagnosis and management of PKU, and without adequate treatment programs. Even today, the economic impact on and financial support available for U.S. families affected by the disease are not well documented. The fact that testing for a rare condition affecting fewer than 400 American infants a year attracted such a groundswell of support has been attributed in part to the advocacy of various groups, such as the March of Dimes Birth Defects Foundation and the National Association for Retarded Citizens (now the ARC), which proposed model legislation to create public programs and conducted lobbying campaigns. Other support came from PKU clinicians, parents, and the Kennedy Administration’s Presidential Advisory Commission on Mental Retardation, which hired an advertising group to develop a public campaign advocating mandatory screening.<sup>20</sup>

Given the widespread public acceptance of PKU screening, many states also began screening for sickle cell disease (SCD) in the early 1970s. SCD, an autosomal recessive hemolytic anemia that occurs most frequently in African Americans, causes serious infections, life-threatening splenic sequestration and severe anemia, stroke, and respiratory problems. When SCD screening laws were first introduced, they varied greatly, with some targeting special populations and some including newborns, preschool children, and even individuals seeking marriage licenses. New York's statute, for instance, required screening for urban school children but not rural ones. Most laws did not include confidentiality provisions; the result, in some cases, was stigmatization, charges of racism, and documented discrimination, especially in the military. An Institute of Medicine Report (IOM) states: "Initial supporters of SCD screening were spurred on by the success of PKU screening, but the clear difference between SCD and PKU was not fully appreciated until later. There was no intervention for SCD at this time other than counseling to avoid marriage or pregnancy (prenatal SCD screening was not feasible)."<sup>21</sup>

The National Sickle Cell Anemia Control Act, enacted in 1972, made federal funding for screening contingent on programs being voluntary. However, since a prophylactic regimen of penicillin in infants was shown in the 1980s to significantly reduce the morbidity and mortality of SCD, and a National Institutes of Health consensus panel in 1987 recommended universal (not targeted) newborn screening, about 40 states and the District of Columbia have now adopted universal newborn screening programs for SCD. The IOM report summarizes the lessons learned from the early sickle cell screening programs as follows:

*The experience with SCD screening in the 1970s illustrates the difficulties that can arise when the goals of screening programs are not clearly specified, when there is no treatment that improves health outcomes, and when the intervention is not acceptable to the target population because of stigma and discrimination....The change in approach to SCD screening over time, as new facts and treatment opportunities emerge, illustrates that programs must have the flexibility to change over time, as the situation changes.*<sup>22</sup>

These early experiences led to numerous multidisciplinary policy statements, beginning with a National Academy of Sciences report in 1975, all of which recommend that empirical research on the benefits and risks of a particular genetic test be undertaken before mass screening programs are established. The 1997 Report of the National Institutes of Health-Department of Energy's Task Force on Genetic Testing, for instance, stated the newborn screening tests must have primary benefit for the infant identified and are not justified solely to determine the carrier status of the infant or parents.<sup>23</sup> Others have called for assessing the community's interest in and acceptance of a genetic test, particularly if a particular group will be targeted for screening; assuring laboratory quality; addressing issues of education, informed consent, privacy, and confidentiality; assuring the availability of follow-up services; and assessing the costs and the priority of the particular test, given the limited financial resources.<sup>24</sup>

Newborn screening programs currently vary greatly among the states, so that the 4 million infants born annually in the United States are tested for different conditions depending on where they are born. Mounting pressure from parents, advocacy groups, medical professionals, and test manufacturers is being exerted on state legislatures to increase the number of conditions included in state screening programs, while numerous groups are calling for national standards so that all newborns in this country will have equitable access to appropriate newborn screening and its potential benefits. The 1994 Institute of Medicine Committee on Assessing Genetic Risks recommended that three conditions be met before a newborn screening program is initiated: (1) The identification of the genetic condition provides

a clear benefit to the child; (2) a system must be in place to confirm the diagnosis; and (3) treatment and follow-up must be available for affected newborns.<sup>25</sup> In fact, however, state newborn screening policies are influenced by many other factors, such as community values; political and economic conditions; and the availability of health data, public health personnel, laboratory facilities, and technical capabilities within the state.

A Report from the Newborn Task Force on Newborn Screening in 2000 explicitly recommended that “public health agencies must involve health professionals, families and the general public in the development, operation, and oversight of newborn screening systems.”<sup>26</sup> Current controversies focus on the role of various stakeholders in allocation and financing decisions related to screening programs, particularly given the cost of follow-up programs that must be supported by state health departments and the need to balance resources among competing community health needs, including screening and services for other genetic disorders. Particular attention is focused on the methods and role of cost-effectiveness analysis in determining which tests to include in newborn screening programs and on the appropriateness of informing and seeking consent from parents for newborn screening.

The ethical issue of informed consent for newborn screening was addressed by the American Academy of Pediatrics in its 2001 policy statement, “Ethical Issues with Genetic Testing in Pediatrics.”<sup>27</sup> The report provides the following analysis:

A persistent ethical issue in newborn screening is whether screening should be voluntary or mandatory. Whether programs are voluntary or mandatory has significant implications for informed responses to test results and for the integration of new tests into established programs. A voluntary approach in this context entails an informed decision by parents about newborn screening. Wyoming and Maryland are the only 2 states that require informed consent for newborn screening, although 13 other states require that parents be informed about newborn screening before testing (18). A mandatory approach in this context requires an explicit refusal of screening by parents who object to this intervention. All states except South Dakota permit parental refusal of newborn screening for religious or personal reasons (18).

*The principal ethical justification offered for mandatory screening is the claim that society's obligation to promote child welfare through early detection and treatment of selected conditions supersedes parental prerogatives to refuse this simple medical intervention (19). An opposing argument maintains that parents traditionally have broad discretion for making health care decisions for their children. Although parents do not have the prerogative to forgo effective treatments for life-threatening conditions, they generally have the prerogative to pursue a variety of options in less threatening circumstances, including options that some medical professionals would consider unwise. Furthermore, it is argued that the great majority of parents will continue to be supportive of newborn screening when they are informed adequately of the risks and benefits (20).*

*With continued broad public support, approaches involving informed consent (that is, parental permission) (21) may fulfill the important goals of the programs and enhance program quality while respecting traditional parental prerogatives to be informed participants in health care decisions for their children. In a study of newborn screening in Maryland involving informed consent, the majority of women preferred that permission be asked before screening, and the informed refusal rate was only 5 per 1000 infants (22). In the Maryland study, the consent*

*process typically took 5 minutes or less of staff time. Additional research to develop and evaluate models of parental education and consent will be valuable.*

*Two potential advantages of obtaining informed consent for newborn screening include more prompt and efficient responses to positive results and an ability to incorporate experimental tests into established screening programs. Under current programs, the information provided to parents about newborn screening is often minimal. A significant source of problems in newborn screening programs is slow or uninformed responses to test results by parents and physicians (23). If an informed consent process promotes more thorough understanding of the implications of the tests, slow or inappropriate responses to positive results may decrease. Second, advances in genetic research will offer many additional tests for consideration by newborn screening programs (24). The relative risks and benefits of new tests will be uncertain until adequate clinical research has been conducted. In these circumstances, experimental tests should be offered on a voluntary basis with informed consent. Experimental tests could be integrated more easily in screening programs that routinely sought informed consent for newborn screening tests.<sup>28</sup>*

Additional ethical questions about informed consent arise regarding the storage and later use of newborn blood spots to evaluate the effect of genetic variation on population morbidity and mortality. While informed consent is universally understood to be required for genetic research, no consensus exists regarding informed consent standards for the use of stored samples—especially anonymous ones—to conduct epidemiological studies based on large-scale screening and/or surveillance data. Khoury, Burke, and Thomson describe the “debate about the practicality of re-contacting subjects from population studies (for informed consent); whether or not genetic studies pose more than ‘minimal risks’ to subjects; the definitions and desirability of ‘anonymization’ of existing samples; and whether or not coded but ‘linked’ or linkable’ samples can be used.”<sup>29</sup> Balancing the potential harms to individual interests with the potential benefits to individual and population health requires a systematic assessment of the benefits, risks, and costs to individuals, perhaps through pilot demonstrations; an evaluation of methods for maintaining privacy and confidentiality within public health registries; and an exploration of ways to minimize the potential stigmatization of population subgroups.

***Predictive Genetic Testing to Learn the Risk of Future Disease.*** These tests can reveal the presence of genetic disorders presymptomatically, as in the case of hereditary hemochromatosis, or can reveal susceptibility to certain diseases, such as with BRCA1 breast cancer or colon cancer. Genetic testing or screening is most appropriate when early treatment or other modifiable risk factors allow for behavior change or preventive interventions that can reduce the probability of harm, and when an assessment of the benefits, harms, and costs of testing and population screening programs provides the basis for the public health policy. Ethical issues are often related to the potential psychological harm to individuals, family members, and family interactions and relationships that may result from testing, inaccurate or misunderstood results, and the potential misuse of genetic risk information in insurance and employment discrimination.

Hereditary hemochromatosis (HH), a common adult-onset genetic disorder for which screening tests and treatments are available, illustrates the challenges for public health policy making. The disorder, which is estimated to occur in one out of every 200 to 400 people of European heritage, causes

excessive iron storage and can lead to damage of the liver and other organs, arthritis, and diabetes in many but not all affected adults. Treatment by removing iron from the blood is safe and effective and can lead to a normal life expectancy if initiated before organ damage has occurred. Many in the medical community, as well as patient support groups, advocate population screening. However, universal screening for HH was rejected by a 1997 consensus panel, in part because of inadequate clinical knowledge about the natural history of hemochromatosis, uncertainty about the proportion of people with genetic risk who will develop the complications of iron overload, and concern about possible genetic discrimination.<sup>30</sup> The president of the American Society of Human Genetics challenged the consensus statement and argued that the potential to prevent disease outweighed the various problems. Other commentators also have expressed similar concern: "We are facing the dilemma of waiting until all requisite information about diagnostic process and therapeutic indications is available or cautiously initiating a more vigorous screening program that will detect unsuspected disease with potential morbidity and mortality, realizing that unnecessary therapy and anxiety may occur."<sup>31</sup> One worry in particular about HFE mutation testing for hemochromatosis is the possibility that follow-up treatment will be initiated in individuals who may test positive but who may never develop the iron overload condition. The Centers for Disease Control and Prevention recommends, instead, iron overload testing (not genetic testing) for individuals who have affected blood relatives. CDC experts believe that "strategies are needed to disseminate information to family members about their genetic risk and to aid their efforts to be tested, and that this "must be accomplished in the course of patient care."<sup>32</sup> Public policy regarding HH population screening shows the complexity of initiating population genetic screening programs, given the need to evaluate the predictive value of the test, measure the benefits and harms of testing and not testing, protect against genetic discrimination, and act without complete knowledge.

With the proliferation of genetic tests comes a number of particularly challenging issues regarding the benefits of tests for disorders for which there currently is no clear treatment. These issues include (1) the difficulty of assessing the results of many genetic tests and providing helpful information about genetic risks and (2) the appropriate role for government regulation of commercial tests with uncertain predictive accuracy. Genetic tests available for breast cancer and Alzheimer's disease, for instance, indicate only a propensity or increased probability of developing the diseases, while even tests for other disorders that are completely penetrant (i.e., always result in disease), such as Huntington's Disease, do not provide information about severity or onset of the disease, which can be highly variable.

Consequently, providing genetic information does not always influence individuals to undertake prevention activities. Andrews describes the complex reactions and psychological harms that can result from genetic testing. She writes: "In fact, there is evidence that the stress created by genetic information can actually lessen the likelihood that the individual will engage in surveillance strategies and monitor himself or herself for early signs of the disease."<sup>33</sup> Andrews also points out other potential harms that may arise from the misinterpretation of a negative test result, including a false sense of security. Numerous ethical questions arise regarding the benefits and harms that result from such tests; the appropriateness of commercial marketing of these tests, particularly given the fears associated with certain genetic conditions; and insurance reimbursement or government financial support for the tests and for follow-up prophylactic interventions, such as removal of breasts.

Predictive genetic testing of children and adolescents for late-onset disorders, such as Huntington's Disease and hemochromatosis, raises unique ethical questions because testing in childhood limits the child's freedom of choice later in life to decide not to be tested (many adults choose not to be tested,

so consent cannot be presumed) and subjects the child to the risk of stigma and discrimination. The American Academy of Pediatrics' policy states that, unless there is anticipated benefit to the child or the availability of interventions that can be initiated in childhood to reduce morbidity and mortality, "genetic testing for adult-onset conditions generally should be deferred until adulthood or until an adolescent interested in testing has developed mature decision-making capacities."<sup>34</sup>

***Reproductive Testing and Prenatal Screening.*** These tests raise particular challenges for public health practice and policy, such as ensuring that the reproductive freedom of vulnerable individuals is adequately protected; clearly defining and implementing nondirective goals for genetic counseling programs; and developing assessment tools for cost-effectiveness evaluation of public health prenatal screening programs. Family history has long provided clues about an individual's risk of genetic disease, but hundreds of genetic tests are now available to clearly identify people who are carriers of genetic conditions that may be passed on to their children, including Tay-Sachs disease, muscular dystrophy, cystic fibrosis, and sickle cell anemia. Many people emphasize that carrier testing and genetic counseling can provide significant benefit to individuals by enhancing their capacity to make informed choices about reproduction. The information about genetic risk presents individuals with numerous options: prior to conception they can decide whether to conceive and/or whether to use reproductive technologies to decrease the risk of transmitting a genetic condition, and after conception they can decide whether to abort an affected fetus.

Providing universal access to low-cost public health carrier screening and reproductive genetic counseling would therefore seem to be desirable from an individual rights perspective (because it facilitates informed reproductive choice for more people and would reduce suffering of future generations) and from a public health perspective (because it would tend to reduce the prevalence of disease and disability). However, universal access to genetic counseling has been challenged on the grounds that it could tend to erode the reproductive freedom of vulnerable individuals. Benkendorf, Peshkin, and Lerman raise concerns that vulnerable individuals may not understand that they are free to refuse recommendations provided by public health programs and may also may feel pressure to act on information about abnormal genetic results in ways that are "inconsistent with their values."<sup>35</sup>

Others explicitly challenge the motives for government genetic counseling programs and the presumption that individual and social interests are congruent. Diane B. Paul, for instance, writes: "Today, everyone favors increasing the choices available to women. But fostering reproductive autonomy is rarely if ever the primary goal of governments when they choose to fund genetic services. That states expect to save money is evident in the arguments actually made to legislatures, which are typically framed in cost-benefit terms. Thus it seems that the new consensus on reproductive autonomy rests on the old assumption that families will ordinarily make the 'right' decisions."<sup>36</sup>

In response, some people point out that reproductive freedom can be threatened not just by the state but also by market forces and societal pressures. Underwriting and reimbursement policies of health insurance companies, marketing and pricing by for-profit genetic testing and technology companies, the rhetoric of advocacy groups, and the beliefs held by religious groups are among the many factors that may exert a strong influence on individual reproductive decisions. Calling for expanded clinical genetic services "at public expense if necessary," Buchanan, Brock, Daniels, and Wikler suggest that the state can remove potential pressures to curtail reproductive freedoms—by providing prospective parents with

both adequate information and “alternative means of having children, when the more customary methods threaten genetic harms.”<sup>37</sup>

Because of public funding and the ethical requirements of public accountability, public health initiatives are subject to greater public review and evaluation than private programs. Measuring the benefits of reproductive genetics programs and justifying their costs present yet another challenge, especially using conventional cost-effectiveness evaluation methods. If the goal of these programs is to enhance reproductive decision making, Lin-Fu and Lloyd-Puryear point out the inappropriateness of measuring the costs of the programs against the number of women who undergo amniocentesis or chorionic villus sampling. They question whether public health officials will “deviate from conventional cost-benefit analysis” and consider a sufficient justification for funding a program to be providing the public with “a basis for informed decision making.”<sup>38</sup>

Given their policy development role delineated by the Institute of Medicine, public health professionals increasingly must work with professional organizations and consumer groups to decide when and how to integrate genetic advances into public health. These decisions must be based on at least the following considerations: an epidemiological assessment of the impact or likely impact of a genetic variation on the disease risk; the degree to which the genetic risk or condition is modifiable or treatable; the degree to which the public regards public health action by government as appropriate for the particular condition; and justification that the particular intervention is ethical.

### State of the Debate

Current debates in public health genetics about genetic testing focus generally on defining, measuring, and balancing competing moral values, particularly population benefit, individual interests, and distributive justice. Underlying the discussion about ethical principles and frameworks is the fundamental question of genetic exceptionalism—that is, whether to treat information derived from genetic testing as different from other health-related information by, for example, providing genetic-specific privacy and antidiscrimination laws.

In support of this position, Ronald Green and Mathew Thomas recognize five unique aspects of genetic information: (1) DNA’s informational nature; (2) its longevity; (3) its potential use as a personal identifier; (4) the familial risks indicated by the information; and (5) the effects on communities.<sup>39</sup>

George Annas also argues that genetic information is “uniquely private” and in need of special legislative protection. He suggests that a person’s genetic information can be viewed as a coded “future diary,” which should be considered “as personal and private as a diary about that person’s past.”<sup>40</sup> Annas describes four different ways of thinking about privacy in this country: private information, private relationships (husband-wife), private decisions (such as reproductive), and private places (such as bedrooms). Since genetic information involves three of these four, Annas suggests that genetic information may be “more powerfully private than other types of information.” He goes beyond the usual concerns about the use of genetic information in employment and insurance discrimination because that “discussion assumes that information has already been collected, analyzed, and stored somewhere.” Annas asserts:

*I believe that if you are really interested in genetic privacy, you have to protect people before the information has been collected by giving people a choice to participate or not. To make*

*privacy protection more meaningful, the law should make it clear that each of us owns our DNA.*<sup>41</sup>

Challenging Annas's use of the term "future diary," which "implicitly supports genetic exceptionalism," Douglas Ginsburg argues that our genetic information is much less diverse than written personal diaries and that "the secrets that our future diaries are supposed to hold, like our family histories, speak only to probabilities." Acknowledging that genetic exceptionalism is psychologically compelling, Ginsburg concludes that "the questions that genetic information raises are not sufficiently different from those raised before—either qualitatively or as a matter of degree—to justify the creation of unique legal solutions – solutions likely to serve only to press the popular debate ever more toward the reductionist forms of genetic exceptionalism."<sup>42</sup> Thomas Murray also challenges the basis of genetic exceptionalism as an "overly dramatic view of the significance of genetic information in our lives" and argues that "the more we repeat that genetic information is fundamentally unlike other kinds of medical information, the more support we implicitly provide for genetic determinism, for the notion that genetics exerts special power over our lives."<sup>43</sup>

Burris, Gostin, and Tress suggest that genetic information "is more like, than different from, other health information," and that genetic illnesses may even require less legal protection than sexually transmitted diseases, which often carry a stigma because of their transmission through voluntary risky behavior.<sup>44</sup> They raise arguments similar to those used against HIV exceptionalism:

*On a practical level, we must be cautious that the very people whom policymakers hope to encourage to take advantage of genetic testing may become more reluctant because of the heightened focus on its exceptional nature. Treating genetics as distinct from the rest of medicine may enhance the stigma of genetics testing, even as legislators attempt to remove its stigmatizing effects. This can create public fears and misapprehensions about genetics that could discourage individuals from seeking testing and treatment and thwart future scientific progress.*<sup>45</sup>

Another related normative issue is whether decisions about whether or not to integrate genetic advances into public health practice should focus primarily on their potential long-term benefits for population health, or instead on the potential social harms for individuals and groups. While both harms and benefits are assessed in all ethical analyses, approaches vary in their emphasis, particularly in situations of scientific uncertainty. A decision about whether to incorporate genetic information into existing surveillance systems on infectious disease and cancer illustrates the complexity of such an analysis, since both the benefits and harms are uncertain and difficult to quantify. Given the lack of empirical data, the critical question becomes which side bears the burden of justifying public health action or non-action.

Those who support the collection of additional surveillance data on genetics cite the potential (though unknown) opportunity costs of not acting and emphasize the population health benefits and prevention programs that would be possible with new knowledge about gene-environment interactions. Others believe that the potential harms for individuals are so great that clinical trials and empirical studies must first be conducted to evaluate and eliminate any social harms that might arise with the collection of genetic data. Disagreement focuses, in part, on the extent to which genetic information in public health data banks can be protected from breaches of confidentiality and misuse.

Different frameworks for balancing benefits and harms have been put forward. On one hand, Lori Andrews describes a fundamental rights approach to genetic policymaking, in large part to protect against harm. She explains that the fundamental rights model is appropriate for health care services, such as reproductive services, “that are central to our notions of ourselves” and that have “an impact on how the individual is viewed and treated by social institutions.”<sup>46</sup> Andrews suggests that genetic testing currently is being made available and used without appropriate understanding of and protections against potential negative psychological and social impacts, such as discrimination against individuals and minority groups. The fundamental rights approach, emphasizing individual rights and the need to protect individual freedom, thus gives great weight to individual decisions to voluntarily choose or reject genetic health services and to individuals’ access to extensive information about genetic services.<sup>47</sup>

Andrews raises special concerns about the potential negative impact of genetic services on women and vulnerable populations, such as people of color and individuals with disabilities, and calls for careful examination of the differential impact of genetic interventions on particular groups. Citing empirical research on differential medical treatment of women and minorities, and the history of the eugenics movement, Andrews maintains that individuals in disadvantaged groups “are most likely to have their individual decisions overridden, sometimes on the patronizing grounds that it is for their own good, other times for the supposed good of society.” She argues that “allowing individuals in disadvantaged groups to make informed, more autonomous choices could reduce the resulting stigmatization and inequalities.”<sup>48</sup>

Another ethical perspective focuses more on equal opportunity, maximizing the benefits from genetic science, and recognizing society’s obligations, grounded in requirements of distributive justice, to provide access to genetic services. This approach emphasizes the significant impact of access to genetic services on an individual’s fair access to equal opportunity (which can be severely limited by pain and disability), the potential to prevent grave harm, and the recognition that genetic technology has been created in part with public investment and financial resources from the population as a whole. Buchanan, Brock, Daniels and Wikler urge “maximum progress in developing the genetic techniques and safeguards against exclusion” and propose that “public policy should try to ensure that the benefits of genetic therapy and (particularly) enhancement are not distributed along class lines or selectively to those who already enjoy greater opportunity.”<sup>49</sup>

While acknowledging the concerns of disability rights groups that genetic interventions could further disadvantage those with genetically related disabilities, Buchanan *et al.* contend that this is not an inevitable consequence of genetic progress. They write:

*The problem lies not in our genes, but in their interpretation on a social level. One way we can resist the genetic determinism that constitutes part of the threat of greater discrimination is to demonstrate that we can, as a society, accommodate genetic advances while integrating, rather than marginalizing, people with disabilities.*<sup>50</sup>

These philosophers describe a potential role for the state (to balance market-based inequities) in providing access to genetic services with public funds. They argue that recognition of this role for the state “is not incompatible with a proper respect for reproductive freedom in particular and for liberty generally,”<sup>51</sup> and suggest that future public policy should focus on ameliorating the conditions of those

with disabilities and enacting protective safeguards. Several commentators point to the positive effects of federal protections, such as the 1990 Americans with Disabilities Act (ADA) that protects against employment discrimination for disabled workers who are otherwise qualified to do a job. Policies continue to evolve regarding the extent to which genetic conditions or genetic predispositions without any symptoms are considered disabilities under the ADA, but the law demonstrates society's ability to mandate the inclusion of and reasonable accommodation for those with particular needs or vulnerabilities.

Another set of background normative issues focuses on concerns about genetic reductionism and the identification of families, groups, subpopulations, or communities for public health targeting based on a genetic condition or genetic risk. Targeting particular subgroups with an elevated genetic risk is arguably justified because of the costs of universal screening for genetic conditions that have a very low incidence in the general population. However, concerns arise that increased use of genetic data and targeting will lead to victim-blaming and a public perception that health and illness are individual concerns.<sup>52</sup>

Clayton describes the risks and limitations of targeted public health interventions in general (especially for vulnerable subgroups at risk for stigmatization and discrimination) and the challenges of targeting subpopulations when genetic risk factors may have some correlation with race. Even though she points out that "genetic variation and community, population, and even race do not correlate very well," Clayton nonetheless proposes consulting communities to address the possibility of group harms and to acknowledge the significance of group identities and interests for some members of society. Community consultation, she says, "will provide several important benefits: (1) to understand the group's concerns and to develop responses; (2) to help investigators focus on the consequences of their research for the subjects; and (3) to capitalize upon the teachable moment of research to educate the group about genetics, perhaps mobilizing them to participate in a more informed manner in political debates about the appropriate use of genetic information."<sup>53</sup>

Others, in contrast, note the wide variation of beliefs and experiences within communities and reject the notion of community consent or a strong role for group involvement, proposing instead that *individuals* take into account the risks and benefits of genetic research and testing for their families and communities. Dena Davis, for instance, points out that "even within the most traditional and isolated of communities, a person still has multiple identities based on, for example, age, gender, and profession." She concludes that "(o)nly the individual can decide how her values will adjudicate among the many communities to which she belongs."<sup>54</sup> Others, however, focus on the family unit as having a more significant role regarding genetic information. For example, Doukas and Berg explore the creation of a family covenant for genetics that defines expectations among family members regarding autonomy and benefit and promotes discussion within families about the competing ethical claims and conflicts that arise over genetic testing and information.<sup>55</sup>

These different positions highlight the fact that genetic testing and screening provide information that may have significant implications for family members and particular communities. Courts have begun to address the issue of a physician's duty to warn their patient's family members (who are not their patients) about increased risk of genetic disease. In *Safer v. Pack*,<sup>56</sup> for instance, a New Jersey court focused on the foreseeability of the risk of avoidable harm; the fact that individuals or groups at risk can be easily identified; and that the harm can be averted or minimized by warnings. As genetics continues to be further integrated into public health practice, policies must address the claims of family members

and groups for access to shared genetic information; for warnings about genetic conditions that become known to professionals based on collected genetic data; and for protections from potential social harms. The degree of risk and the severity of the potential harm that can be averted will be significant factors in developing policies.

## Fact Sheet on Genetics/Gene Testing and Screening

*Excerpts adapted from the New York State Department of Health Task Force on Life & the Law Report, "Genetic Testing and Screening in the Age of Genomic Medicine," Executive Summary, pp.1-3 (<http://www.health.state.ny.us/nysdoh/taskfcr/screening.htm>)*

### Genes and Chromosomes

- Genes are the blueprints of heredity. Genes are made of hundreds to thousands of DNA bases. The human genome consists of tens of thousands of pairs of genes. Each person inherits one copy of each gene from each parent.
- Genes are organized along string-like structures called chromosomes. Each individual inherits two sets of twenty-three chromosomes, one from each parent: two sets of twenty-two autosomes and one set of sex chromosomes (X, X or X, Y).

### Genetic Variations, Mutations, and Human Disease

- The DNA base sequence of human genes is about 99.9 percent identical among individuals. About 1 of every 1,000 DNA bases varies among individuals, accounting for inherited differences in traits and disease susceptibility.
- Changes in a DNA base sequence, called mutations, account for inherited gene variations. Mutations may be harmful if they prevent a gene from making a normal copy of its specific protein. These mutations can cause, or increase susceptibility to, specific diseases.
- Single-gene diseases are relatively rare diseases that result when a person inherits one gene with a harmful mutation or a pair of genes in which each has a harmful mutation. Inheritance of these mutated genes generally results in a 100 percent chance of developing a specific disease. Single-gene diseases include autosomal dominant diseases (e.g., Huntington disease), autosomal recessive diseases (e.g., sickle cell disease), and X-linked diseases (e.g., Duchenne muscular dystrophy).
- Most diseases result from a complex set of both genetic and environmental causes. Inheritance of some harmful gene mutations increases the chance, although it does not ensure, that a person will develop a specific disease. These mutations are called inherited susceptibility mutations.

### Genetic Testing

- Genetic testing for inherited genetic variants is performed for several purposes: diagnosis of individuals with symptoms, determination of future disease risks in asymptomatic individuals, determination of genetic risks for progeny, guidance of medical treatment, research, and individual identification.
- Genetic testing for inherited genetic disease risks is an analysis of DNA, chromosomes, or gene products to provide specific information about variations in the number or form of genes or chromosomes in an individual or his or her progeny.

- Genetic information is information about specific variations in genes or chromosomes learned by genetic testing or by other means.
- *DNA-based testing* directly analyzes the DNA base sequence of a gene.
- *Phenotypic testing* identifies specific inherited gene variations indirectly, by detecting specific variations in the structure of a protein encoded by a gene or variations in a protein's enzyme activity.
- *Karyotype* analysis and fluorescent in situ hybridization analysis detect variation in form or number of chromosomes.
- New testing technologies that will promote genetic testing in health care include DNA chip technology and tandem mass spectrometry.

### Assessing the Accuracy and Usefulness of Genetic Tests

- Analytical validity of a genetic laboratory test is a measure of how well the test detects what it is designed to detect. It encompasses analytical sensitivity (the probability that the test will detect a gene variant it is designed to detect when present in a sample) and analytical specificity (the probability that the test will be negative when a specific variant tested for is not present in a sample).
- Clinical validity measures the extent to which an analytically valid test result can diagnose a disease or predict future disease. For predictive genetic tests, it includes positive predictive value (the ability to predict that an individual will develop a disease) and negative predictive value (the ability to predict that an individual will not develop a disease).
- For DNA-based testing, clinical validity is limited by genetic heterogeneity and incomplete penetrance. *Genetic heterogeneity* means that different mutations in a specific gene, or mutations in different genes, are associated with the same disease. *Incomplete penetrance* means that within a population, not everyone who tests positive for a specific gene mutation will develop the associated disorder.
- Utility of a test is a measure of how useful test results are to the person tested. Clinical utility is a measure of how a test may guide clinical decisions. In some circumstances, predictive genetic testing may not provide medical preventive or treatment options but may help reduce anxiety and/or aid planning for the future.

### Predictive Genetic Testing to Assess Reproductive Risks

- Reproductive genetic tests detect heritable genetic variations that are associated with disease. This type of testing includes carrier testing, prenatal testing of fetal cells, and pre-implantation testing of embryos formed by in vitro fertilization.

- Reproductive genetic tests generally are offered to individuals and couples who are at increased genetic risk for a specific disorder based on family history or membership in a racial or ethnic group that has identified genetic variants that increase risk for a specific disease.
- Carrier testing generally is performed to determine the risk of a healthy individual or couple of having a child with a recessive disorder. It may be performed before or after conception.
- Prenatal testing of fetal cells includes amniocentesis and chorionic villus sampling.
- Pre-implantation testing of embryos formed by in vitro fertilization is performed using single cells removed from individual embryos to detect specific gene mutations or chromosomal anomalies.

### **Predictive Genetic Testing to Assess Future Disease Risks in Healthy Adults**

- Presymptomatic genetic testing is predictive testing of apparently healthy adults to determine whether they are at risk for a single-gene disorder. These disorders occur with virtually 100 percent incidence in persons who have inherited a specific gene mutation.
- Susceptibility (predispositional) testing is predictive genetic testing of apparently healthy adults to determine whether they are at increased risk, relative to the general population, for a specific future disease. A positive test result (finding a mutation) does not necessarily mean that a person will develop a future disease.
- Pharmacogenetic testing is genetic testing of individuals to guide their pharmaceutical or other medical treatment. Pharmacogenetic testing seeks to promote a favorable response and to prevent an adverse response to a drug or other treatment based on genetic predisposition.

## Case Study 1: Cystic Fibrosis Carrier Screening

You are the nurse practitioner who directs one of the health department's largest prenatal clinics serving a diverse urban population, and you have received the following memo. What would be your position on cystic fibrosis carrier screening and why?

To: Senior Health Care Professional Staff  
From: Director, Division of Maternal and Child Health, State Health Department

*The state health department has become aware of new guidance from the American College of Obstetricians and Gynecologists, calling for widespread cystic fibrosis (CF) carrier screening. In light of the new recommendations, the state health department must consider whether to revise its screening policies for pregnant women who receive care in health department prenatal clinics.*

*The current department policy is that high-risk families (those with a family history or child with CF) are referred to a genetics clinic for genetic counseling and testing for CF, if indicated. (The prenatal clinics routinely screen all obstetrical patients for a number of conditions that include rubella, syphilis, and hepatitis B. Targeted sickle cell testing is done for African American patients and others in high risk groups, with follow-up referrals to private genetic clinics funded by the health department, when needed.)*

*Newborn screening for cystic fibrosis currently is not included in the state newborn screening program. Participants in the 1997 Centers for Disease Control and Prevention workshop, "Newborn Screening for Cystic Fibrosis: A Paradigm for Public Health Genetics Policy Development," recommended that several states conduct research/pilot studies to assess the benefits of newborn screening for CF, but evidence is still inconclusive.*

*About 15,000 maternity patients receive care in the state health department clinics each year. About 9,000 (60%) of the patients are Caucasian or another race or ethnicity considered at higher risk for carrying the CF gene. The cost of a test for CF carrier status is about \$250.00. If both parents test positive, a follow-up genetic consultation would cost about \$1,200. At this time, the only targeted testing routinely done in the health department prenatal clinics is for sickle cell anemia. About 6,000 (40%) of the obstetrical patients in the health department prenatal clinics are African American and they routinely receive the targeted sickle cell test, which costs about \$4.00 per test. (Sickle cell has a prevalence rate of about 1 in 600 in the African American population and a carrier rate of about 1 in 12.) The benefit of carrier testing for both sickle cell and cystic fibrosis is the provision of increased information to pregnant couples so that they have the opportunity to learn all they can before their delivery dates in order to make informed decisions and plans.*

*The maternal and child division is calling a meeting of senior health professionals in the division to discuss whether CF carrier screening should be provided. Please review the following material and prepare a brief statement of your perspective on the issue, particularly focusing on the ethical issues.*

## I. Recommendations from the American College of Obstetricians and Gynecologists

### *"Ob-Gyns Offering Large-Scale Cystic Fibrosis Screening"*

([http://www.acog.org/from\\_home/publications/press\\_releases/nr12-12-01-2.cfm](http://www.acog.org/from_home/publications/press_releases/nr12-12-01-2.cfm))

*Washington, DC* --The nation's obstetrician-gynecologists have initiated one of the first clinical changes in the US arising from discoveries of the human genome project. In recent weeks, ob-gyns began to greatly expand the number of couples offered genetic screening for cystic fibrosis (CF) during preconception or prenatal care, thanks to tests made possible by genetic research.

"The genetic revolution has begun," announced Michael T. Mennuti, MD, of The American College of Obstetricians and Gynecologists (ACOG), speaking today at an ACOG press briefing in New York City. "The advances of the human genome project have moved from the laboratory to the obstetrician's office. With these changes come new options and new decisions for expectant couples."

ACOG now recommends that ob-gyns make DNA screening for cystic fibrosis available to all couples seeking preconception or prenatal care -- not just those with a personal or family history of carrying the CF gene, as previously recommended. ACOG has distributed physician and patient education materials to its 40,000 members to help implement this major screening change.

Couples who learn they both carry the CF gene would have a 1 in 4 chance of delivering a child with cystic fibrosis. CF can bring pulmonary and gastrointestinal symptoms of varying severity, but most CF cases are associated with substantial illness and shortened lifespan and require lifelong medical care. Since the discovery in 1989 of the gene, called CFTR, that causes the autosomal recessive genetic disorder of CF, more than 900 mutations of the gene have been identified. Screening is now available for the most frequent CF mutations.

Among ACOG's new recommendations:

- Testing will be made available to all couples, whatever their risk for carrying the CF gene, through information brochures on CF given to couples seeking preconception or prenatal care. These materials explain the relative risks for carrying CF, screening options, and what steps are next should a couple learn that they carry the CF gene.
- For couples in ethnic or racial groups considered at higher risk for carrying the CF gene -- Caucasians, particularly those of European or Ashkenazi Jewish descent -- physicians will specifically offer screening and will follow up with inquiries about the couple's decision on whether to be screened.

"Our approach may become the prototype for future screenings for other genetic diseases," notes Dr. Mennuti, the secretary of ACOG who co-chaired a steering committee on the project.

CF is one of the most common genetic disorders in Caucasian populations, carried by about 1 in 29 Caucasians. CFTR is much less frequent in Asian Americans (carried by 1 in 90), in African Americans (1 in 65), and in Hispanic Americans (1 in 46).

Physicians and patients will need to discuss whether it is worthwhile for a couple to be screened. "Should a couple learn that they both carry the CF gene -- which gives them 1 in 4 odds of having a child with CF -- they must make the personal decision whether to continue or terminate the pregnancy," says Dr. Mennuti. He notes that some couples will want to continue the pregnancy and learn all they can about the health needs and treatments for children with CF. "Testing provides the opportunity for such couples to learn all they can before their delivery due date," notes Dr. Mennuti.

To help physicians and patients with these decisions, ACOG and the American College of Medical Genetics (ACMG) issued a guideline publication for physicians, *Preconception and Prenatal Carrier Screening for Cystic Fibrosis*. A companion brochure for patients, [\*Cystic Fibrosis Carrier Testing: The Decision is Yours\*](#), uses a question-and-answer format to help patients sift through information about their chances for carrying the disease and whether they should have testing. [\*Cystic Fibrosis Testing: What Happens If Both My Partner and I Are Carriers?\*](#) uses a similar format to explain the implications of test results and direct patients to appropriate counseling experts.

Francis S. Collins, MD, PhD, director of the National Human Genome Research Institute, told ACOG members at their 50th anniversary meeting in April that the human genome era in medicine "will have profound implications for all branches of medicine, but perhaps particularly so for obstetrics and gynecology." "It's not surprising that the impact of the human genome project will first hit home during prenatal care visits across the United States," adds Dr. Mennuti. "As we increase our ability to screen for more and more genetic diseases, the obstetrician's office becomes the first arena where individuals confront the new dilemmas presented by 21st century science."

ACOG's initiative is the final phase of a three-year project with ACMG and the National Human Genome Research Institute.

**2. Excerpt from "Access to Genetic Services in the United States: A Challenge to Genetics in Public Health,"** by Jane S. Lin-Fu, M.D. and Michele Lloyd-Puryear, M.D., Ph.D., in *Genetics and Public Health in the 21<sup>st</sup> Century*, ed. Muin J, Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, pp. 286-287.

### **Race and ethnicity in public health genetic programs**

In the United States, although racial designation in census data is based on self-identification, racial classification in the social context has no biological basis. Despite this illogical and offensive approach, the U.S. census and other governmental data sources continue to tabulate data according to race and ethnicity as defined by the 1977 U.S. Office of Management and Budget Directive No. 15.

The incidence of diseases often varies among different racial and ethnic populations, and it is common for public health programs to target high-risk groups who often are minorities. Although the method of reaching out to each community should be culturally appropriate, the actual test and treatment or prevention measures used are generally the same for all racial and

ethnic groups. This one-size-fits-all approach, however, may present a problem in public health genetic programs.

In planning for public health genetics programs, not only must one bear in mind that the frequency of genetic disorders is often very different in different populations and the genotype-phenotype correlation may vary from group to group, but common mutations for the same genetic disease often differ among racial and ethnic populations. A single public health policy on a genetic disease for all racial and ethnic groups may be neither prudent nor ethical. The 1997 National Institutes of Health Consensus Development Statement on Genetic Testing for Cystic Fibrosis [CF] (23) is a clear example.

The Statement recommended that genetic testing for CF should be offered to adults with a positive family history of CF, to partners of people with CF, to those seeking prenatal care and to couples planning a pregnancy. It did not recommend offering the CF test to the general population. The Statement acknowledged the wide range of test sensitivity in different population groups using current technology, nonetheless made no special recommendation for groups for whom the current CF test is of extremely low sensitivity. In the United States, the incidence of cystic fibrosis is much higher among European Americans (1/3,300) than among African Americans (1/15,300) or Asian Americans (1/32,100). Because of differences in mutation, the sensitivities of current cystic fibrosis tests vary widely, ranging from 90-95% among U.S. European Americans to 30% among Asian Americans. Thus offering CF testing to couples planning for a pregnancy or women seeking prenatal care, regardless of race or ethnicity, utilizing tests for the predominant mutations in U.S. European Americans would have an extremely low cost-benefit ratio in certain minority populations such as Asian American and Hispanic (24). More important, offering a genetic test of extremely low sensitivity to certain racial and ethnic populations raises the ethical issue of equity and questions the wisdom of such across-the-board one-size-fits-all genetics public policy for all U.S. populations. In CF testing, assuring true informed decision through effective counseling is a particular challenge for the Hispanic and Asian American populations. These two minority groups have the lowest test sensitivity (57% in Hispanics and 30% in Asian Americans) yet both have a very high proportion of immigrants who face severe linguistic and cultural barriers in accessing any service. Since offering a genetic test of 30-50% or even 75% sensitivity in a broad-based program should have been unacceptable to most public policy-makers, one must question what is an acceptable sensitivity level when genetic testing is recommended without regards to race and ethnicity? If one truly considers all human beings as equal, regardless of race and ethnicity, then shouldn't public health policies and programs on genetic testing seek a test sensitivity of 90-95% for all racial and ethnic groups and not just for the majority population? If this is deemed impractical, and public health programs decide to offer a test with less than 90% sensitivity to certain minority populations, is this ethical and how should people in these communities be counseled? Is equity in fact achievable in one-size-fits-all genetics public policies?

### **3. Recent Research: Cystic Fibrosis Carriers Unlikely to Inform Many Family Members of their Genetic Risk (<http://www.cdc.gov/genomics/update/text/gin1.htm>)**

WASHINGTON, D.C., Nov. 6, 2001 – On the heels of new guidelines from three major medical groups calling for widespread cystic fibrosis (CF) carrier screening, new research suggests that

individuals found to be CF carriers are unlikely to inform many at-risk family members of their status. Several CF papers are being presented here today at the 20th Annual Education Conference of the National Society of Genetic Counselors (NSGC). A report on the largest ethnicity-based prenatal screening program in an HMO setting also is being given today at the meeting.

Just a few weeks ago, the National Institutes of Health, American College of Medical Genetics and the American College of Obstetricians and Gynecologists issued joint guidelines calling for CF carrier screening to be offered to every Caucasian who is pregnant or considering having a baby.

CF is a chronic, progressive illness that causes serious breathing and digestive problems resulting from build-up of sticky mucus in the lungs, pancreas and other organs. The average life expectancy for a person with CF is 32 years. About 1 in 25 Caucasians are carriers of CF, the most common severe recessive condition in individuals of Northern European ancestry. Approximately 1 in 2,500 babies born in this country each year will have CF, which can occur only when both parents are carriers. Genetic testing can identify carriers and determine how likely a couple is to give birth to a child who has CF or will be a CF carrier.

***Carriers Should Be Educated about CF Risk, Importance of Notifying Family Members***

“Many people have never heard of CF and mistakenly believe that if it’s not present in their immediate family they are not at risk,” said Kelly E. Ormond, genetic counselor and director of the graduate program in genetic counseling at Northwestern University Medical School, Chicago.

Ormond conducted a study to determine how likely CF carriers were to inform immediate and extended family members of their carrier status and whether the presence of a family history of CF affects the likelihood that a carrier will notify at-risk relatives.

“It’s important not only to inform relatives if you discover you’re a CF carrier, but to explain the implications as well,” Ormond said. “Individuals with a first-degree relative who is a CF carrier have a 1 in 2 risk of being a CF carrier themselves. If a second-degree relative is a CF carrier, the risk is 1 in 4; and if a third-degree relative is a carrier, the risk is about 1 in 8.”

The Northwestern University study sought to determine the notification attitudes and practices of 48 CF carriers with 871 first-, second- and third-degree relatives. CF carriers who had a family member affected with CF informed 100 percent of their living first-degree relatives (parents, children, siblings and half-siblings); whereas, CF carriers without a family history only informed 84 percent of living parents and 56 percent of siblings.

The most common reasons for sharing CF carrier status with parents and siblings were closeness of social relationship and the birth of an affected child with CF, according to Ormond. Two-thirds of children at risk for being carriers had not yet been informed of carrier status, primarily because they were too young.

CF carriers with a family history of CF informed 68 percent of second-degree relatives (uncles, aunts, nieces and nephews) and 50 percent of third-degree relatives (first cousins). Carriers

without a family history of CF only informed 21 percent of second-degree relatives and 3 percent of third-degree relatives.

***Largest Prenatal CF Carrier Screening Program Finds Pre-Test Education is Essential***

During the NSGC meeting, Sharon Ungerleider, genetic counselor with Kaiser Permanente of Northern California, reported on the nation's largest ethnicity-based prenatal CF carrier screening in an HMO setting.

Since 1999, Kaiser Permanente Northern California Region has offered CF genetic screening to all pregnant women who identify either themselves or their partners as having Caucasian ancestry. A woman is tested first and when a mutated, or damaged, CF gene is found, the male partner is offered CF screening to help determine the likelihood that the fetus will be affected. Kaiser tests for 37 CF mutations; current guidelines recommend screening for 25 mutations. Of the 27,507 Kaiser members who have been screened to date, 952 female carriers and 27 male carriers were identified. All 27 high-risk couples were offered genetic counseling and prenatal testing.

"It takes two mutations to have a child affected with CF, but just because you're both carriers doesn't mean you will definitely have a baby with CF," Ungerleider said. "There is a 1 in 4 chance that the child will have CF. There is a 1 in 2 chance that the child will be a carrier, just like both parents, and there is a 1 in 4 chance that the baby won't have CF or be a carrier."

Pre-test education is extremely important when helping couples understand their CF risk and the significance of their genetic test results, according to David R. Witt, M.D., medical geneticist and director of Kaiser's regional CF screening program in Northern California.

"There is a spectrum of CF in terms of the severity of the disease that is influenced by the particular mutations that are present," Dr. Witt said. "Severe mutations represent about 90 percent of all mutations, and mild mutations represent about 10 percent. If a couple has one mild and one severe mutation, the mild mutation gives some protection with the gastrointestinal aspects of CF, but the lung aspects of the disease can still go either way in terms of severity. Explaining the expected impact of the mutation findings in terms of the future child's clinical course is a difficult but critical part of genetic counseling."

Knowing whether you're a carrier gives you options you wouldn't otherwise have had, Ormond said. "Your partner can be tested. You can have prenatal diagnosis if you're expecting a child. If both partners are CF carriers, couples planning a pregnancy can consider alternate methods for getting pregnant, including egg or sperm donation or pre-implantation diagnosis."

*(Co-authors on the paper on the topic being presented by Ormond are P.L. Mills, L. Lester and L. Ross. Co-authors on the paper on the topic being presented by Ungerleider are Dr. Witt and J. Coppinger.)*

## **Case Study 2: Ethical Implications of a Decision on MCADD Screening of Newborns**

As Director of the State Health Department, John Jamison has responsibility for the state's Newborn Screening Program, which currently screens every infant born in the state for six disorders, including phenylketonuria, hypothyroidism, and hemoglobinopathies. The state's newborn screening program has had a quiet and respected history in the state up until now, unlike some other health department programs, such as the state cancer registry that was a recent focus of legislative hearings and a public outcry over privacy concerns.

The nurse practitioner who directs the newborn screening program, Sally Scott, has just reported that pressure is building for the addition of new testing for genetic disorders to the battery of required state screenings for newborns. Sally says pressure is coming from many sources, including individual parents, powerful advocacy groups within the state, and even some physicians. A coalition of these interested parties has just met with her and requested the state health department's support for a bill to add a test for one particular disorder this legislative session – the test for Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD). The group intends to issue a press release within two or three days and plans to publicize whether the state health department is supportive of the test.

Sally believes the test for MCADD is likely to garner more attention and support from the public and the press than other newborn screening tests, because MCADD increasingly has been mentioned as a potential cause of Sudden Infant Death Syndrome (SIDS).

Sally met with Jamison yesterday for guidance. She warned him that MCADD is just the latest, in what she believes is becoming a continuing and growing problem for the state health department regarding genetic screening for newborns. As director of newborn screening for the last five years, she has been receiving frequent inquiries about the possibility of expanded newborn genetic screening, both for particular disorders and for predisposing conditions.

Jamison asked Sally to get back to him today with as much relevant material as she can quickly find, so that they can review the data and discuss the options with the department's epidemiologist, health policy analyst, and the Director of the Division of Maternal and Child Health.

At the meeting Sally presents the following information.

The State legislature, with guidance from the health department when appropriate, has the authority to establish newborn screening policies, including deciding which disorders should be included among the battery of newborn screening tests.

Currently parental consent is not required for the newborn screening tests in the state. All newborn screening tests are conducted by the state lab, which reportedly discards newborn blood samples after the initial testing.

The state newborn screening program provides follow-up notification of positive tests, counseling, and in some cases, state-provided treatment when newborn conditions are identified. These costs generally are not covered by health insurance.

The annual cost of the newborn screening program in the state is now \$2.5 million.

MCADD is a type of fatty oxidation disorder where an enzyme defect in the fatty acid metabolic pathway inhibits the body's ability to utilize stored fat. Initial clinical presentation occurs from two months of age to two years, and has not been found in children post-adolescence. An initial event of MCADD is usually triggered by prolonged fasting, which can lead to vomiting, lethargy, coma, apnea, cardiopulmonary arrest, and sudden death. Up to 30 percent of initial events result in death and lead to a misdiagnosis of SIDS in up to 5 percent of cases. One recent publication suggested that up to 50% of infants with MCADD died as a result of their first acute episode and in these cases, MCADD was diagnosed postmortem.

Current data suggest that the incidence of MCADD varies in the U.S. between a homozygous prevalence (individuals presenting with MCADD) of between 1 in 6,400 to 1 in 20,000 and a heterozygous prevalence (asymptomatic carriers of MCADD) of 1 in 6,900. The newborn screening data from three other states that currently test for MCADD show a per year incidence that ranges from 0.0001 in one state to 0.00003 in another state. A routine blood sample drawn at time of birth and processed via a Tandem Mass Spectrometer (TMS) can reveal MCADD gene involvement. Follow-up testing can confirm diagnosis. The state laboratory, however, currently does not have equipment to conduct these tests.

*Treatment:* Some studies suggest that early detection and follow-up treatment that could be as simple as eliminating prolonged periods of infant fasting could be life saving. Recent studies suggest that intravenous infusion with 10% dextrose will generally cause rapid improvement after an acute event. Other treatment options such as 150 mg per day of L-carnitine or cornstarch mixed with liquid at bedtime could prevent acute events leading to hospitalization or death. L-carnitine treatment has been recommended for the first three years of life for MCADD patients with confirmed diagnoses.

*Expected Outcome of the Newborn Screening Test:* Given current estimates of incidence rates, screening all infants in the state could result in approximately 8-10 confirmed cases/year. An estimated 30-50% of patients with MCADD die within their first two years; so about 4 lives are projected to be saved per year in the state.

### **Approximate Costs of MCADD Screening**

Given the state's annual birth rate of over 100,000, two tandem mass spectrometers will need to be purchased for the state lab at a total cost of about \$700,000. Annual operating costs for the systems would be about \$50,000. Two additional lab specialists would cost about \$80,000. Additional nursing time for assessment of laboratory results, follow-up, and outreach programs would cost between \$75,000, which would not be covered by insurance.

A fee of \$4.00/test would be added to the total cost of the current set of newborn screening tests, and would be billed to insurance carriers (this covers machine use cost, allowing for machine depreciation), for an additional annual screening cost of about \$500,000. (This raises the annual cost of the state program to \$3 million.)

Follow up confirmation testing for identified newborns will cost about \$6,000 a year. Treatment for MCADD for the 8-10 patients a year would cost about \$2,500 total, much of which would be covered by insurance.

Without early detection of newborn screening and preventive treatment, approximately four MCADD patients in the state each year will be expected to experience acute episodes of undiagnosed MCADD resulting in hospitalization. Based on cost analysis from another state, the average acute episode results in a seven-day NICU stay and a seven-day pediatric ward stay, with a total cost of about \$33,000 per episode. From a pure dollar outlay, adding this test will cost more to the state than the cost of treating those children with MCADD when they have acute events. This concludes Sally's report.

Jamison thanks Sally, and turns to the other three professionals at the meeting for their reactions. The health policy analyst quickly responds, "Sally's cautious approach to this question is well-founded because the issue of newborn genetic screening is potentially explosive. We cannot be in a position to go against the tide of these powerful advocacy groups, because they could create a media circus and undermine our position and support in the legislature on a number of important public health initiatives. This could result in cuts to our budget on critical issues -- on teen education for sexually transmitted diseases, for instance, and other public health programs that operate just below the public radar screen. As long as the newborn test is valid and preventive treatment is available, the health department must support the test and I think..."

The Director of the Division of Maternal and Child Health interrupts, "I disagree. My programs are significantly underfunded, and my staff overworked. I would like to initiate numerous new programs, some requiring far less money than this screening program. This new test will mean that I will have to reassign one or two of my staff nurses to run this program, which will require assessing the laboratory test results and following up with patients and physicians. Better funding of current programs or new programs we are planning for would result in saving the lives of many more than four newborns a year and additionally would result in a significant reduction in child and mother morbidity. I believe the health department should not be pressured into supporting particular programs without careful analysis of other potential uses of the funds."

The epidemiologist concurred, "I believe we should do a study about this screening program, including assessing other uses for health department funds and also our own study of the intervention's effectiveness, which is not clear to me. We might undertake a pilot test of the MCADD test and the preventive interventions. We could randomly screen a group of newborns in the state by sending their newborn blood samples to outside labs, and then divide positive babies into one of two groups: a treatment group who are given the L-carnitine for three years and a control group. This seems to me the only way to justify the program – with good science." The health policy analyst shakes his head, "Would you tell the parents of the control group babies that their children might be at increased risk for a disease that kills? Would you get informed consent from parents in the pilot screening program?"

Jamison holds up his hand. "There seem to be numerous ethical questions arising in our discussion. Let's explicitly address them. What are the ethical issues in this case as you see them and what are your positions?"

## Considering the Ethical Issues Involved in MCADD Screening

### *Assessing the Public Health Problem*

- What is at stake in the current situation? Is public health department missing SIDS cases? How should the health department make decisions about the use of limited resources to benefit the public? Are there other concerns?
- What role does the public have to play in this issue? Should there be public discussion? How could that discussion be elicited?
- Are commercial interests at stake? Has the company that manufactures the TMS machine been involved in discussions to date? Should it be?
- Who are *all* the stakeholders in this decision? Do any of the stakeholders have conflicts of interest? What are these? Do any have conflicts of obligation?
- Are there issues of power involved in the ongoing debate? Where is the interface between public health and politics in this situation?
- Is there money available to do the testing? What are the alternative uses to which it might be put? Are the MCADD advocates aware of those facts?

### *Advocacy*

- Do the roles and duties of advocates of MCADD testing differ from the roles of health department staff? Should they be different?

### *Ethical Issues*

- What specific ethical issues are involved in a decision to test (or not test) for MCADD? Specifically, what harms, risks and benefits may be involved for individual children, parents, other individuals and for the population at large?
- If money is diverted from other possible lifesaving uses to MCADD testing, should the harms, risks and benefits of the other intervention *not selected* be taken into account?
- What are the moral claims of the various stakeholders?
- Are there any other ethical issues that might be involved?
- Have any discussion of screening ethics occurred in the other states where MCADD testing is done? What were the considerations in those settings?

## Case Study 2: Discussion

### Ethical Problems

This case study presents John Jamison, Director of the State Health Department and Sally Scott, who directs that state's Newborn Screening program, with several dilemmas about how to respond to requests to take a position on the inclusion of an additional test in the state's current newborn screening program.

Each is aware that three other states currently include MCADD screening for newborns, making the option of adding it a technically feasible one. They are aware of the test's potential for saving the lives of several newborns in the state each year through use of the test. However, both are aware of other possible policy and ethical dilemmas.

First, although data are available from which to conduct a cost-benefit analysis, available data do not include any information on false negative or false positive screening tests. What information about false positive and false negative MCADD screening tests should be included in the direct cost-benefit figures?

Second, the source of funding for adding any new screening test is not obvious. While the actual costs of the laboratory tests will be covered by private insurance for those who have coverage, there still remains the significant costs for the health department to pay a staff nurse to interpret all of the laboratory results and do the followup, which insurance does not pay for. In addition, the state health department is responsible for the costs of the laboratory tests for the state's uninsured population. If adding a new test required diversion of resources from other current state programs, resulting in fewer children benefiting from those other programs, should that lost benefit be included in the cost-benefit analysis?

Third, state employees are being pressed to support legislation to further the goals of one advocacy group, the MCADD screening lobby. How should Jamison and Scott decide what position to take with the MCADD test?

### Relevant Values and Key Stakeholders in the Decision

In addressing this issue, Jamison must address the concerns of multiple stakeholders. Jamison is aware that different values lie behind the positions taken by various stakeholders, including his own staff. Advocates for MCADD screening, including perhaps parents of affected children, would like to totally eliminate morbidity and mortality related to MCADD. Advocates' position seems to give priority to *beneficence*. In the name of *autonomy*, some persons would like to limit newborn screening programs to tests done with parental consent. Manufacturers of testing equipment would like to increase the market for their product(s).

Jamison is also aware that roles and duties of health department staff differ from the roles of MCADD advocates. State health department staff must be concerned with values of *efficiency*, e.g., cost per MCADD case detected, and *utility*. Health department staff, including Sally Scott, must also be concerned with *non-maleficence* and *justice*, since they have to balance the value of a new screening test with the opportunity costs of other programs that might have to be cut to allow inclusion of the MCADD test. Specifically, health department staff would appear to have a *conflict of obligation*

between children/parents who might benefit from MCADD testing and children/parents who are beneficiaries of current programs that might have to be cut to allow MCADD screening.

Director Jamison has to include the concept of planning for an orderly decision process for this and future decisions. Finally, it is not yet clear what values might inform the responses of the state legislature, which will have to ultimately decide, based on Jamison's recommendation and on lobbying pressure, whether the MCADD test should be included (and perhaps whether new funds to pay for it should be added.)

### **Necessary Information**

In considering his decision, Jamison clearly needs objective information beyond the list of stakeholders and their values. The costs of MCADD screening (in equipment, staffing, etc.) and the benefits in terms of cases detected and lives saved are a starting point. In addition to the information already available, these data should include the frequency of false positive and false negative MCADD screening results. State health department staff is the best initial source for such information although information from manufacturers and from the coalition could also be reviewed. Similarly, if funds to pay for MCADD screening are not currently available, the *opportunity costs* of other programs to be cut must be included in the information. Specifically, what are the options for internal redirection of funds are what would be the program impacts of such redirection? Should the impact on other public health programs be made public, so that other stakeholders who may be adversely affected can take a position?

Jamison is also interested in knowing the position of the American Academy of Pediatrics (and its state affiliate chapter) on MCADD screening. He would also like to know more about how MCADD decisions were made in the states where its use has been discussed. (These states include not only the three states where MCADD testing was included but also any states where decision were made to *not* include MCADD testing.)

Finally, Jamison could consider discussing the MCADD screening issue with members of the legislature who ultimately would be making the key decisions about the testing program.

### **Available Options**

In considering any recommendation to the legislature, Jamison must consider each of the several options available:

- Do not add MCADD screening at this moment. Cost-benefit analysis may support this position in that costs for treating children with MCADD may be less than screening costs. (Note: This does not take into account the deaths.)
- Defer a decision while collecting additional information through additional study of MCADD testing.
- Add MCADD screening using current resources (Some other activity or program has to be cut to cover the health department's costs of nursing staff assigned to this program.)
- Add MCADD screening once new resources can be identified. This approach could perhaps include a form of partnership with the coalition.

- Consider a more comprehensive review of the state's approach to newborn screening: Because of Sally Scott's sense that more new screening tests and more advocacy will be coming in the near future, Jamison and Scott could also consider an option of asking for a review of state newborn screening policy. Outside experts in various fields could inform both the MCADD decision as well as provide recommendations for how the state should approach the issue of considering other new newborn screening tests as they come along.

### **Process for Arriving at a Decision**

In addition to discussions with his own staff, Jamison should be sure that he and his staff have heard from as many of the stakeholders as possible. Specifically, meeting with representative of the advocacy coalition can help inform his position. That discussion could include the issues and values at stake as well as options for moving toward consensus on an approach to adding a new test. During this meeting, in addition to hearing the coalition's perspective, a process of compromise could be discussed.

Jamison might also consider holding a public hearing on the MCADD issue either through the state health department or jointly with the state legislature.

### **Questions about options**

- What ethical justifications support each of the options, i.e.,
  - to support MCADD now?
  - to not support MCADD but use funds elsewhere?
  - to study the issue further?
  - to partner with advocacy group to raise external funds for MCADD testing?
- What is the appropriate role for the State Health Department in resolution of this issue?
- What roles could the State Health Director play in the resolution of this issue?
- Would a legal opinion from the department's legal counsel be helpful in resolving this issue?
- Would having the State Health Department proactively bring this issue to the legislature be helpful?
- Would an external ethics consultation be helpful?

### **Case Study 3: PKU and Follow-Up**

Dr. Susan McManus, director of the Adamsville Tri-County Health Region, asked to make a presentation at the monthly meeting of the state health department executive committee, which includes Dr. John Jenkins, the commissioner of the state health department, and the directors of the major state health divisions, including epidemiology and surveillance, maternal and child health, laboratory services, public clinics, and health policy.

Dr. McManus, herself a pediatrician by training, had been frustrated for a number of years about the continual cutback in preventive services available for maternal-child health care and had just become aware of yet another case of an infant born in her district with an easily preventable birth defect. The infant was born with microcephaly because her mother did not follow a special diet for Phenylketonuria (PKU) during pregnancy. This was the fourth such PKU-related case in her region in the past five years. Having done some research, Dr. McManus knew that her health district population could have an elevated risk for PKU because of the high population with Scot-Irish family backgrounds, and she was concerned that the state health professionals may not consider this problem significant from a state perspective.

Recent national attention about the problem of dietary control among pregnant women with PKU published by the Centers for Disease Control and Prevention, however, gave her the courage to institute a new policy in her health district, and she wanted both to notify the state health department heads and to enlist their support for her project.

As head of the one of the largest health districts in the state for ten years, Dr. McManus enjoyed a good personal relationship with many leaders in the state health department and felt comfortable beginning her presentation with the story about the infant recently born with microcephaly.

It was a heart-wrenching case. The mother was 21 years old, unmarried, and had discontinued formula use for PKU in early adulthood because of limited financial resources. She reported that she had not fully understood the importance to her infant's health of following the PKU diet, and was devastated when she found out that she could have easily prevented her infant's condition. While she expressed a strong willingness to adhere to the diet during pregnancy, her lack of transportation, financial constraints, and inability to take time off from work prohibited her from accessing care at the nearest metabolic clinic, which was 3 hours away. She did meet with local health department staff several months into the pregnancy to acquire formula, but it was too late. PKU was included in her prenatal medical records, and she was referred to a maternal-fetal specialist; however, her blood phe (phenylalanine) levels were not monitored and she was not referred to a metabolic clinic.

Dr. McManus looked her colleagues in the eye and said, "I am determined to prevent future cases like this one and I have an idea. I have decided to begin an on-going tracking system of these young women until they reach child-bearing age in order to provide special education to them about the importance of maintaining a special diet during their pregnancies. One way is to have a nurse visit with the child and her family each year. Another way is to maintain a record of the child's physicians or clinic, and send advisory letters to physicians to be included in the child's health records. In addition, for those infants/children who do not remain in contact with the health agency, the program will begin an

aggressive outreach to locate the young women when they turn 16 in order to provide them with the educational information about their condition and an appropriate diet during pregnancy.”

Dr. McManus looked at her colleagues: “Before you respond, I want to assure you that because I am initiating this program in my health district, the state will not be under pressure to adopt such a policy for all regions, since the population in my district is at greater risk of PKU because of their genetic backgrounds.

I’m sure you all have some concerns about my program, such as questions about targeting the young women in my health region and about the confidentiality and consent for the use of newborn genetic information. I am essentially creating a PKU registry, based on the newborn screening data, and I understand the public’s great sensitivity to public health registries. But I believe for my county the registry is justified by the increased risk and gravity of the harm that can be prevented. I would like to end my presentation by summarizing a recent report from the Centers for Disease Control and Prevention.” She then summarized the following report.

**Excerpts from “Barriers to Dietary Control Among Pregnant Women with Phenylketonuria – United States, 1998-2000” MMWR 2/15/2002/51(06);117-120.**

“Newborns in the United States are screened for phenylketonuria (PKU), a metabolic disorder that when left untreated is characterized by elevated blood phenylalanine (phe) levels and severe mental retardation (MR). An estimated 3,000--4,000 U.S.-born women of reproductive age with PKU have not gotten severe MR because as newborns their diets were severely restricted in the intake of protein-containing foods and were supplemented with medical foods (e.g., amino acid-modified formula and modified low-protein foods) (1--4).

When women with PKU do not adhere to their diet before and during pregnancy, infants born to them have a 93% risk for MR and a 72% risk for microcephaly (5--6). These risks result from the toxic effects of high maternal blood phe levels during pregnancy, not because the infant has PKU (5--6). The restricted diet, which should be maintained for life, often is discontinued during adolescence (5--10).

This report describes the pregnancies of three women with PKU and underscores the importance of overcoming the barriers to maintaining the recommended dietary control of blood phe levels before and during pregnancy. For maternal PKU-associated MR to be prevented, studies are needed to determine effective approaches to overcoming barriers to dietary control.

During the fall of 2000, CDC conducted an interview-based study of women with PKU who were aged >18 years and pregnant during 1998--2000 (index pregnancy), regardless of dietary management or pregnancy outcome. Women were recruited from three metabolic clinics that provided services funded by state and private sources and were interviewed using a structured questionnaire that was completed in person or by telephone. Medical records were requested to document timing of diet initiation, control of blood phe levels (defined as 2--6 mg/dL), and pregnancy outcome. The study protocol was approved by CDC's Institutional Review Board, and informed consent was obtained from each respondent.

A total of 30 women met the interview criteria; two could not be contacted. Of the 28 remaining women, 24 were interviewed (17 in person and seven by telephone). The median age was 28 years (range: 22--38 years); 75% were married, 96% were white, and 50% had a high school education or less. A total of 51 pregnancies had occurred among 24 women. Among the 24 index pregnancies, 18 (75%) resulted in live-born infants; 11 (46%) pregnancies were intended.

The use of formula-based medical foods before conception was reported more often among the 11 women who were trying to conceive than among those who were not (risk ratio=3.5; 95% confidence interval=1.6--10.2). Use of modified, low-protein medical foods to diversify the diet was reported only among women trying to conceive. No difference was reported in avoiding high-protein foods between women who were and who were not trying to conceive. One woman remained on the restricted diet throughout adulthood; 23 women had been off the diet for 6--24 years (average: 16 years). At the time of the interview, 17 (71%) women were not using medical foods (65% because of the unpleasant taste). A total of 22 women had resumed the diet before or during their index pregnancy, eight (33%) women had contacted the metabolic clinic before conception, and 11 (46%) had contacted the metabolic clinic after conception but by week 10 of gestation. Of the 22 medical records available, 12 (55%) records indicated controlled blood phe levels before 10 weeks of gestation.

All of the women expressed confidence in their metabolic clinic staff's knowledge of a phe-restricted diet and maternal PKU; eight (33%) perceived that their obstetricians were knowledgeable about maternal PKU. Approximately equal numbers of women used public assistance and private insurance to cover the costs associated with clinic visits (Table 1). Costs of medical foods were more often covered by public assistance than by private insurance (Table 1). Among the 13 women who used public assistance, nine (69%) reported that proof of pregnancy was required to receive services. When the data were stratified by state of residence, women in state C had the lowest rate of live births resulting from their pregnancies, lowest use of formula before pregnancy, fewest women achieving metabolic control before 10 weeks' gestation, and longest commutes to a metabolic clinic (Table 2). These differences were not significant by Fisher exact test."

Dr. McManus looked around the table of state health professionals, and smiled. "What do you think of my idea?" she asked. The room was quiet.

Dr. Jenkins shook his head, "Your idea raises many questions we have been struggling over and, quite frankly, avoiding. Should we keep identifiable genetic data from the newborn screening tests, or alternately, keep the blood samples as we do now in case they would be useful for surveillance in the future? And, as your program idea brings up: Should we allow, or perhaps are we ethically obligated to, follow-up on the test results years later, when the infants are able to understand the medical information themselves? Do we have a duty to these infants?"

Dr. Jenkins looked around the room at his staff. "What do you each think? What are the ethical issues here?" Should we allow this program in one region, targeted at this one particular group, to go forward?

## Case Study 3: Discussion

### Ethical Concerns

Dr. McManus is clearly aware of the various ethical issues at play.

First, acquiring and keeping information on individuals without their explicit consent could be perceived as a privacy (autonomy) threat to those persons. Part of this concern is the issue of contacting these phenylketonuria (PKU)-affected people who may be unaware that they have PKU and, more important, that their children are at grave risk.

A different perspective on the same issue is whether the state has an obligation to be sure that PKU-affected persons, detected in a state-supported screening program as children, are aware of their condition as they enter adulthood and their childbearing years. This obligation could be construed as an obligation to the children of persons with PKU as much as to those identified persons themselves.

One large generic ethical issue is regarding ownership of the information on individual citizens collected in a state-run or state-supported screening program.

Another practical consideration is that of reliably identifying “at risk” pregnancies prior to the actual risk period. Some at risk women are likely to have changed their names when married and thus undetectable by name based screening during pregnancies.

Another ethical issue involves the strength of the requirement to assure access to appropriate interventions once “at-risk” pregnancies have been identified.

Another issue is that of justice. This program is to be implemented in only one part of a state. Although the program suggested by Dr. McManus for her health region could be viewed as a pilot program for the state that could be extended if judged successful in an evaluation, it is worth considering the justice issues of a limited access program.

A final issue with ethical dimensions is that of the age for aggressive outreach (16 years). Is that age adequate to reach all females at risk before they become pregnant? What are the issues involved with choosing a younger age?

### Relevant Values and Stakeholders

Dr. McManus and the various program directors have a number of values to incorporate into whatever decision they make. One issue is *beneficence*, in terms of the need to protect children from untreated PKU. Identifying high-risk pregnancies and preventing disease among children “at risk” is a socially useful goal that could also benefit individual children and parents.

Another issue is that of risk to the affected women’s other relationships in various ways. For example, is there a risk involved in spouses or prospective spouses becoming aware that a woman has PKU? Is there a risk of discrimination from an insurance company’s becoming aware of PKU in a prospective customer?

Another issue is the state's obligation to assure freedom from future PKU, having identified it in the maternal generation. Is the state permitted to retain these records and conduct follow-up activities? Is, in fact, the state not only permitted but *obligated* to carry out follow-up in order to provide education and warnings?

From a societal standpoint, which health care professional or person should have a duty to warn? Who is in the best position to prevent harm?

### **Necessary Information**

Having information about existing PKU follow-up programs or similar follow-up programs from other states could provide both a framework for discussion in this state as well as experience in dealing with ethical concerns raised.

In addition, it could also be helpful to obtain new information as it becomes available from this state or elsewhere on adverse outcomes of potentially detectable but undetected PKU cases. Any new evaluations similar to that published by CDC would also be useful.

One additional piece of information includes the numbers of affected children born each year and the length of time needed to reliably determine benefits, costs, and any other adverse effects from the program.

Finally, a very clear description of the system used to protect the privacy and confidentiality of persons whose name is in this registry would be helpful. This should include information on confidentiality agreements signed by employees with access to the data as well as plans for follow-up of persons who move to known addresses in other health regions or states.

What would be the response if the mother of an affected child refused follow-up? Would the girl herself be contacted at some point? At what age?

### **Available Options**

In considering next steps, there may be several options:

- Allow Dr. McManus to do exactly what she has suggested, testing the effectiveness of several ways to stay in touch with affected girls and their families. This could be done as a formal research study.
- Conduct the program as suggested but have it done as a pilot program of the State Health Department.
- Carry out the program state-wide. This step would considerably shorten the time required to know whether the program is effective at ensuring follow-up.
- Tell Dr. McManus not to do the program.
- Defer a decision until an external Committee can discuss and provide guidance.

### **Process for Arriving at a Decision**

Dr. McManus and the State Health Director were clearly hoping for a discussion by senior state health officials present at this meeting. Although necessary, is that discussion sufficient? Could there be any value in having a broader public discussion of this issue among health officials (e.g., professional groups) and among the public? Would that answer differ as a function of whether this program is conducted in a region vs. the entire State? What might be the issues raised by those particularly concerned with privacy and confidentiality issues? What information would be needed to reassure them? Is the successful implementation of confidentiality protections for other public health registries in the state evidence that supports this proposal?

## **Case Study 4: State Genetics Commission: Ethical Implications of Informed Consent in the State Newborn Screening Program**

As the health commissioner of the largest city (population 5 million) in the state, you have been appointed by the Governor to a Blue Ribbon Commission on Ethics and Human Genetic Technologies to study and report on genetics issues in state health policy, as well as related issues in genetic reproductive technologies. The 15-member Commission includes representatives from a range of governmental, for-profit, and public interest groups, a number of whom you are developing collaborative partnerships with, such as the state hospital association and the largest health insurer in the state.

The Governor has asked the commission to explore the ethical issues and make recommendations on the major issue currently pending in the state legislature: should parental informed consent be required for the state newborn screening program?

Given that the legislature is expected to hold hearings within the month, each member of the Commission was asked to bring a statement of ethical concerns and a short position statement to the first commission meeting.

You have consulted the director of the city's department of maternal and child health and your health policy analyst and learned the following:

The current state law authorizes the state department of health to establish, maintain and carry out a newborn screening program to detect hypothyroidism, PKU, hemoglobinopathy, congenital adrenal hyperplasia (CAH), and maple syrup urine disease; and additionally to provide each infant determined to be at risk with a screening test for sickle cell diseases. The state legislature currently determines which tests will be administered under the newborn screening program, with consultation from an advisory board of the state health department.

The newborn screening requirements do not apply to infants whose parents object for religious or personal reasons. However, parental consent for newborn screening currently is not required, and even though newborn testing may not be conducted over parental objection, virtually no parents raise the issue or object to testing.

Currently only a few states require informed consent (that is, parental permission) for newborn screening, while about a dozen other states require that before testing is done, parents must be explicitly informed about newborn screening.

Your health policy analyst provided the following background information about informed consent.

- Analysis of informed consent generally focuses on five elements: competence, disclosure, understanding, voluntariness, and consent. Beauchamp and Childress include these elements, when they write: "One gives an informed consent to an intervention if (and perhaps only if) one is competent to act, receives a thorough disclosure, comprehends the disclosure, acts voluntarily, and consents to the intervention." They also acknowledge that in some circumstances obtaining consent that satisfies these rigorous standards may be

excessive or impossible to implement and that an alternate framework based on social or institutional rules of consent may be appropriate. They explain: "We should evaluate institutional rules not only in terms of respect for autonomy but also in terms of the probable consequences of imposing burdensome requirements on institutions and on professionals. Policies may legitimately account for what is fair and reasonable to require of health care professionals and researchers, the effect of alternative consent requirements on efficiency and effectiveness in delivering health care and advancing science, and the effect of consent requirements on the welfare of patients." \* In some circumstances, patients do not expect to be asked for or to give full and rigorous informed consent, for example, as with a routine battery of blood tests; consent in these circumstances is presumed or implied because testing is routine.

- In the context of screening, Gostin describes five forms of screening and consent:\*\*
  1. Compulsory Screening (with no informed consent), authorized by state legislation under its police powers, for specific circumstances, such as when a person is exposed to blood borne infections, or for certain class of persons, such as newborns, inmates or prostitutes.
  2. Conditional Screening, which make benefits contingent upon screening, as in the case of requirements for a PPD tuberculin test in order to work in a school or nursing home.
  3. Routine Screening with Advance Notification (Opt-In), which involves offering screening tests to a population, with patients not given the test until they have consented or "opted in."
  4. Routine Screening without Advance Notification (Opt-Out), which involves routinely or automatically screening individuals in a population (who may not be aware of or understand the purposes of the screening tests), unless patients explicitly refuse to have the test.
  5. Voluntary Screening, which requires full and rigorous informed consent.
- Regarding parental consent for newborn screening in particular, some commentators raise ethical arguments that focus on the role of the state to protect children from harm and suggest there are compelling arguments against a policy requiring parental consent or honoring parental refusals of screening for some conditions; others focus on the important role of parents as caretakers and highlight the clinical value of involving parents in newborn screening decision making; and still others focus on the potential value of more public participation in the policy-making process for newborn screening programs so that questions about parental consent will be addressed by parents and consumers in a public policy-making body.

What position would you take on the issue now pending in the legislature? Why?

---

\* Beauchamp, T. and Childress, J., *Principles of Biomedical Ethics* (5th Ed.), (Oxford and New York: Oxford University Press, 2001) p.78-79.

\*\* Gostin, L, *Public Health Law*, (Berkeley and Los Angeles: University of California Press, 2000) pp.193-195.

## **Case Study 4: Discussion**

### **Ethical Concerns**

This case study presents you, as a health commissioner and as a member of the Governor's Blue Ribbon Commission, with an opportunity to elicit and express opinions about the informed consent process in the state's current newborn screening program. You are aware that the focus in this case is on currently available and validated newborn screening tests rather than new or still experimental tests.

You are aware of at least two large and partially overlapping ethical concerns in this situation.

The first concern addresses balancing the autonomy or respect for autonomy of those involved as participants in the screening process with the obligation of the State (i.e., the government) to reduce preventable morbidity, i.e., society's disease burden, by identifying disease risk among those not yet affected.

A second ethical concern involves clarifying the potential beneficiary or beneficiaries of the newborn screening process and being sure that whatever consent process that is put in place protects the interest of all parties, including the pregnant woman or new mother, the fetus or infant, the father and the society at large.

### **Relevant Values and Stakeholders**

In addressing this informed consent issue, the Commission must identify various stakeholders and address their concerns and interests. Advocates for women who are either tested themselves or whose newborns are being tested are appropriately concerned with respecting the autonomy of those women to consent to or refuse the screening process. They point out that the State's interest in reducing disease among its citizens may not automatically override maternal autonomy. Advocates may be concerned about a coercive nature to the screening process, especially when children of ethnic minority or poor women are being tested.

Others may raise opposite issues, concerned that the interests of children may not always be best represented by decisions of their mothers, especially when the information transmitted as part of the informed consent process is uncertain.

A related value raised could be that of competence of women to give what is essentially surrogate consent for their children. For example, what are the issues involved in having a new mother who is herself a minor give or refuse consent for screening for her newborn child. Is a woman giving or refusing consent in this setting also consenting or refusing on behalf of the child's father? Does the answer to that question vary when the parents are not married? Can a child damaged by a disease which might have been detected except for refused consent by his/her mother have a valid claim against her mother once the child becomes an adult. In a related question, what is the state's obligation to provide support to a child or family if a child becomes ill in a setting of refused consent?

### **Necessary Information**

In considering this issue, you, as a health director and as a member of the Blue Ribbon Commission, can be informed by several kinds of information.

In terms of objective information, information on the frequency and severity of conditions being screened for can help provide a context for consent discussions. Such information should include not only assessment of medical consequences but also information on treatment cost of disease in unscreened persons as well as costs among persons whose disease was detected earlier by screening.

Information from your state and from other states on the frequency of refusal of consent—as well as the consequences of refusal—can provide additional perspective on the magnitude of the problem.

Information from the State's attorney general or other legal counsel can be helpful in understanding the boundaries of the Commission's – or the State's - decision-making ability. The State Constitution may provide guidance about the limitations of unconsented testing as well as guidance on the State government's responsibility and authority to act on behalf of the community. That official can also provide opinions about options for considering justifications for religious or other refusals should mandated testing be recommended.

Finally, opinions on informed consent can be solicited from parents providing - or refusing -- consent as well as from persons affected by disease that might have been prevented had newborn screening been done.

Arguments generally raised in public AGAINST requiring consent from parents focus on the fact that the benefits of screening are obvious and substantial, relative to potential harms; that no “reasonable” parent would refuse screening (perhaps raising questions of child neglect); that obtaining consent from each parent is difficult, costly and an unwarranted expenditure of time and money; and that the history of newborn screening has led to the current expectation that newborn screening is routine and that parental consent is appropriately “presumed.” Some of the arguments raised in public FOR requiring parental consent include: parental consent is necessary because refusal to newborn screening is not unreasonable, given that many conditions for which newborn testing is done are rare and that newborn screening does have adverse consequences, particularly psychological harms associated with false positive tests; that long-term parental care taking is enhanced when parents are included in all clinical decisions about their children; and that the process of obtaining consent does not have to be time-consuming or burdensome for health care professionals but rather can be part of an educational process that enhances the health professional-patient relationship.

### **Available Options**

In considering consented screening recommendations to the governor, you and the Commission must consider each of the options available, which include:

- Mandatory screening without consent. This process could still allow for a refusal of conscience for religious or other reasons.
- Presumed consent, which includes public awareness of the screening program and testing unless objection is raised.
- Explicit consent, including a counseling and consent process with each new mother.

Within each of these options, a second set of options must be prepared to address procedures should there be a difference of consent opinion between the two parents.

### Process for Arriving at a Set of Recommendations

In addition to collecting and discussing the objective information described earlier, you could encourage the Commission to hold open hearings where various opinions can be solicited and heard.

The state's legal counsel can be helpful in clarifying within the recommendations a set of procedures for deciding on the competence for consent of underage persons as well as options for including fathers in the consent process.

---

<sup>1</sup> Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, "Genetics and public health: A framework for the integration of human genetics into public health practice," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p. 5.

<sup>2</sup> James F. Childress, Ruth R. Faden, and Ruth D. Gaare, *et al.*, "Public Health Ethics: Mapping the Terrain," Journal of Law, Medicine, & Ethics, 30, no. 2 (Summer, 2002), p. 173.

<sup>3</sup> "Out of Eugenics," in The Code of Codes, ed., Daniel J. Kevles and Leroy Hood, Massachusetts, Harvard University Press, 1992, p. 9.

<sup>4</sup> *Buck v. Bell*, 274 U.S. 200 (1927)

<sup>5</sup> Association of State and Territorial Health Officers (ASTHO), "Public Health Genetics Policy Statement," PHG-I.4.6, p. 49, ratified October, 2001, [http://www.astho.org/pubs/consolidatedpolicy.html#PHG-I\\_PubHealthGenetics](http://www.astho.org/pubs/consolidatedpolicy.html#PHG-I_PubHealthGenetics).

<sup>6</sup> Celeste M. Condit, Roxanne L. Parrott, and Beth O'Grady, "Principles and practices of communication processes for genetics in public health," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p. 550.

<sup>7</sup> *Ibid.* 555.

<sup>8</sup> Childress, Faden, and Gaare *et al.*, p. 174

<sup>9</sup> Norman Daniels, "Accountability for Reasonableness," British Medical Journal, 321 (2000), p.1301.

<sup>10</sup> Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, "Genetics and public health," p. 9.

<sup>11</sup> Lorenzo D. Botto and Pierpaolo Mastroiaco, "Surveillance for birth defects and genetic diseases," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p. 125-126.

<sup>12</sup> Steven S. Coughlin and Wylie Burke, "Public health assessment of genetic predisposition to cancer," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, pp. 151-165

<sup>13</sup> Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, "Genetics and public health," p. 7.

<sup>14</sup> Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, "Genetics and public health," p. 7, citing Rothman, KJ. Modern epidemiology. Boston: Little, Brown, 1986, p. 14.

<sup>15</sup> MJ Khoury, JF Thrasher, W Burke, EA Gettig, F Fridinger, R. Jackson, "Challenges in Communicating Genetics: A Public Health Approach. p.3. Centers for Disease Control and Prevention website. <http://www.cdc.gov/genomics/info/reports/program/communicate.htm>

<sup>16</sup> Scott Burris, Lawrence O. Gostin, and Deborah Tress, "Public health surveillance of genetic information: Ethical and legal responses to social risk" in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p 539.

<sup>17</sup> Neil A. Holtzman and Michael S. Watson, eds., "Promoting Safe and Effective Genetic Testing in the United States: Final Report of the Task Force on Genetic Testing" (ELSI, September 1997). P. 6. [http://www.nhgri.nih.gov/ELSI/TFGT\\_final/](http://www.nhgri.nih.gov/ELSI/TFGT_final/).

<sup>18</sup> *Ibid.*, pp. 8-9.

<sup>19</sup> Tom L. Beauchamp and James F. Childress, Principles of Biomedical Ethics (Fifth Edition), New York, Oxford University Press, 2001, p.301.

<sup>20</sup> American Academy of Pediatrics Newborn Screening Task Force, "Newborn Screening: A Blueprint for the Future,"

---

Pediatrics 106, No. 2, August, 2000, p. 389-390. See also, Diane B. Paul, The Politics of Heredity, New York, State University of New York Press, 1998, pp.173-186

<sup>21</sup> Michael A. Stoto, Donna A. Almario, and Marie C. McCormick, editors, Reducing the Odds, Washington, D.C., National Academy Press, 1999, pp. 27-29.

<sup>22</sup> *Ibid.*, p. 29.

<sup>23</sup> Holtzman and Watson, eds., "Promoting Safe and Effective Genetic Testing" p. 27-28.

<sup>24</sup> National Research Council, "Committee for the Study of Inborn Errors of Metabolism," Genetic Screening: Programs, Principles and Research, Washington, D.C., National Academy of Sciences, 1975.

<sup>25</sup> L.B. Andrews, J.E. Fullarton, N.A. Holtzman, and A.G. Motulsky, eds., "Assessing Genetic Risks. Implications for Health and Social Policy," Washington, D.C., National Academy of Sciences, 1994, cited in American Academy of Pediatrics Newborn Screening Task Force, "Newborn Screening: A Blueprint for the Future," Pediatrics 106, No. 2, August, 2000, p.391.

<sup>26</sup> American Academy of Pediatrics Newborn Screening Task Force, "Newborn Screening: A Blueprint for the Future. Executive Summary: Newborn Screening Task Force Report," Pediatrics 106, No. 2, August, 2000, p. 387.

<sup>27</sup> Committee on Bioethics, American Academy of Pediatrics, "Ethical Issues with Genetic Testing in Pediatrics," Pediatrics, 107, No. 6, June, 2001, pp. 1451-1455, (Website, <http://www.aap.org/policy/re9924.html> )

<sup>28</sup> *Ibid.*, p.1453

<sup>29</sup> Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, "Genetics and public health," p. 9

<sup>30</sup> Arno Motulsky and Ernest Beutler, "Population Screening in Hereditary Hemochromatosis," Annual Review of Public Health, 2000. 21 (1): 65-79

<sup>31</sup> *Ibid.*, p. 79.

<sup>32</sup> Michele Reyes and Muin Khoury, "Screening for Iron Overload due to Hereditary Hemochromatosis," Centers for Disease Control and Prevention Website, <http://www.cdc.gov/genomics/info/factshts/hemoscreen.htm> , 4/13/02

<sup>33</sup> Lori B. Andrews, Future Perfect, New York, Columbia University Press, 2001, p. 42.

<sup>34</sup> Committee on Bioethics, American Academy of Pediatrics, "Ethical Issues with Genetic Testing in Pediatrics," Pediatrics, 107, No. 6, June, 2001, p.1451-1455, website citation, <http://www.aap.org/policy/re9924.html>, p. 6

<sup>35</sup> Judith Benkendorf, Beth Peshkin, Caryn Lerman, "Impact of genetic information and genetic counseling on public health," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p 365.

<sup>36</sup> Diane B. Paul, The Politics of Heredity, New York, State University of New York Press, 1998, p.149.

<sup>37</sup> Allen Buchanan, Dan W. Brock, Norman Daniels, and Daniel Wikler, From Chance to Choice, Genetics & Justice, Cambridge (UK), Cambridge University Press, 2000, p. 325.

<sup>38</sup> Jane S. Lin-Fu and Michele Lloyd-Puryear, "Access to genetic services in the United States: A challenge to genetics in public health," in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p.286.

<sup>39</sup> Ronald N. Green & Matthew Thomas, "DNA: Five Distinguishing Features for Policy Analysis, II Harvard J. L. & Tech. 571 (1998) in Lori B. Andrews, Maxwell J. Mehlman and Mark A. Rothstein, Genetics: Ethics, Law and Policy, St. Paul, Minn., West Group, 2002, p. 608 (note)

<sup>40</sup> George J. Annas, "The Limits of State Laws to Protect Genetic Information," New England Journal of Medicine, Vol. 345, No. 5, August 2, 2001, p. 385

<sup>41</sup> George J. Annas, "Genetic Privacy: There Ought to be a Law," 4 Tex. Rev. L. & Politics 9, 9-13 (1999) in Lori B. Andrews, Maxwell J. Mehlman and Mark A. Rothstein, Genetics: Ethics, Law and Policy, St. Paul, Minn., West Group, 2002, p. 604, 606.

<sup>42</sup> Douglas H. Ginsburg, "Genetics and Privacy," 4 Tex. Rev. L. & Politics 17, 22-23 (1999) in Lori B. Andrews, Maxwell J. Mehlman and Mark A. Rothstein, Genetics: Ethics, Law and Policy, St. Paul, Minn., West Group, 2002, pp. 606-607.

<sup>43</sup> Thomas H. Murray, "Genetic Exceptionalism and "Future Diaries": Is Genetic Information Different from Other Medical Information?" in Mark A. Rothstein, ed. 1997, Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era, 1997, in Lori B. Andrews, Maxwell J. Mehlman and Mark A. Rothstein, Genetics: Ethics, Law and Policy, St. Paul, Minn., West Group, 2002, p. 608.

<sup>44</sup> Scott Burris, Lawrence O. Gostin, and Deborah Tress, "Public health surveillance of genetic information: Ethical and legal responses to social risk" in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J.

---

Thomson, New York, Oxford University Press, 2000, p. 538.

<sup>45</sup> Ibid.

<sup>46</sup> Lori B. Andrews, Future Perfect, New York, Columbia University Press, 2001, p. 27, 29.

<sup>47</sup> Ibid., at pp.176-177.

<sup>48</sup> Ibid., at p. 106.

<sup>49</sup> Allen Buchanan, Dan W. Brock, Norman Daniels, and Daniel Wikler, From Chance to Choice, Genetics & Justice, Cambridge (UK), Cambridge University Press, 2000, p.332.

<sup>50</sup> Ibid., pp. 332-333.

<sup>51</sup> Ibid., pp. 342

<sup>52</sup> Scott Burris, Lawrence O. Gostin, and Deborah Tress, "Public health surveillance of genetic information: Ethical and legal responses to social risk" in Genetics and Public Health in the 21<sup>st</sup> Century, ed. Muin J. Khoury, Wylie Burke, and Elizabeth J. Thomson, New York, Oxford University Press, 2000, p.540.

<sup>53</sup> Ellen Wright Clayton, "The Complex Relationship of Genetics, Groups, and Health: What It Means for Public Health," The Journal of Law, Medicine & Ethics, 30:2, pp. 297, Summer, 2002.

<sup>54</sup> Dena S. Davis, "Groups, Communities, and Contested Identities in Genetic Research," Hastings Center Report 30, no. 6 (2000), p. 38-45

<sup>55</sup> David J. Doukas and Jessica W. Berg, "The Family Covenant and Genetic Testing," American Journal of Bioethics 1, no. 3 (2001), p. 2.

<sup>56</sup> Safer v. Pack, Superior Court of New Jersey, Appellate Division, 677 A.2d 1188, (N.J.Super.Ct.App.Div.1996)