Ethics for the Pediatrician: Genetic Testing and Newborn Screening
Janis L. Gonzales
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Genetic Testing and Newborn Screening

Janis L. Gonzales, MD, MPH, FAAP*

Introduction
Recent technological advances have made genetic testing possible for an unprecedented number of disorders. However, this technology brings with it complicated ethical questions in which individual and societal rights frequently are in conflict. The practitioner caring for children cannot help but be affected by these issues because more than 98% of the 4.3 million babies born in the United States every year participate in newborn screening (NBS). Of these, approximately 5,000 infants annually are found to have one of the heritable conditions identified by the screening process. (1) Primary care clinicians are called on to counsel the families of these infants and to assist them through the process of diagnosis and treatment.

NBS is a public health success story that began with testing for phenylketonuria in the 1960s. Recently, testing has expanded due to the availability of multiplex and DNA technologies. In 2005, the American Academy of Pediatrics (AAP) and the Secretary of Health and Human Services’ Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (SACHDNC) endorsed a report from the American College of Medical Genetics recommending that all states screen newborns for 29 core conditions (with an additional 25 conditions as second-tier recommendations).

The purpose of NBS is to identify, as early as possible, those babies who are at a higher-than-normal risk for a condition to promote health and prevent disease and disability. For newborns who have potentially fatal conditions and are asymptomatic at birth, such early identification can be lifesaving. Ideally, an NBS program involves much more than just the screening itself; an integrated program should include testing, short- and long-term follow-up, diagnosis, consultation, quality assurance, and evaluation, all coordinated with appropriate specialists and the infant’s medical home.

Ethical Issues
The application of ethical principles does not always give definitive answers to difficult medical questions, but these principles may be helpful in providing guidelines for making decisions. Although many ethical principles could be applied to genetic testing, the most commonly cited are autonomy/individual rights, beneficence and nonmaleficence (to do good and avoid harm), privacy, and justice. NBS programs are run by state public health departments that focus on the health of a population as a whole. Public health ethics often come into conflict with autonomy and respect for individual rights, as when public health acts to minimize disease in a population, even if this action disadvantages some individual members of the population.

The concept of autonomy includes the freedom to choose for oneself as well as issues of informed consent. With NBS, the parents are granted the authority to make the choice for their child, either by con-
senting directly to the screening or by exercising the option of waiving a mandatory screening test. Although an AAP policy statement on genetic testing in pediatrics (issued in 2001 and reaffirmed in 2009) (2) recommended that parental informed consent be standard procedure for NBS, most states continue to have mandatory screening based on passive consent: parents can opt out of testing (usually by signing a waiver) but are not required to give written consent before testing.

The Newborn Screening Panel
Wilson and Jungner, in a 1968 report for the World Health Organization, defined 10 criteria for determining whether certain medical screening tests should be implemented. (3) Among these guidelines are: 1) the condition should be an important public health problem, 2) there should be an effective treatment for patients in whom the disease is diagnosed, and 3) an effective screening test should exist that is “acceptable to the population.” The SACHDNC has developed its own guidelines for evaluating disorders nominated for inclusion in the screening panel. The Committee considers factors such as the clinical utility (benefit and harm) associated with screening, diagnosis, and treatment; the cost effectiveness of screening, diagnosis, and treatment; and the clinical validity of the screening test.

There is good reason to be cautious about adding new conditions to the NBS panel. Identifying a baby as having a “disease” when none exists may lead to unnecessary parental anxiety and labeling of the child. For example, several programs in the 1970s began screening for histidinemia but soon realized that this was a normal variant that did not require treatment.

Since the current panel was recommended in 2005, new disorders have continued to be proposed by various researchers and parent advocates. Severe combined immunodeficiency was recommended by the Advisory Committee in May 2010 for inclusion on screening panels, and several other conditions are being evaluated for screening or are being piloted by a few states, including lysosomal storage disorders (eg, Krabbe or Pompe disease), fragile X syndrome, and Duchenne muscular dystrophy. In September 2010, the SACHDNC voted to recommend adding critical congenital cyanotic heart disease to the panel; in September 2011, Secretary Sebelius agreed, bringing the total number of disorders recommended for screening to 31. It is still unclear how states will implement the recommendations.

Screening is now being proposed for disorders in which treatment is still experimental or may not exist, such as lysosomal storage disorders and fragile X syndrome, as well as for conditions that have later onset (outside of the newborn period), such as Duchenne muscular dystrophy. In addition to not meeting the Wilson and Jungner criteria, such expansion of NBS raises questions about the benefit versus harm of providing a diagnosis if no good treatment is available, whether it is ethical to test babies for a condition that most likely will not develop or show symptoms for many years, and whether individuals should be allowed to make the testing decision for themselves when they are older.

Genetic Discrimination and Carrier Testing
Identification of carrier status can be justified when such status affects health or helps inform reproductive choices. Carriers for sickle cell trait (SCT), those who have one sickle hemoglobin gene and one normal hemoglobin gene, are routinely identified today on NBS. Ever since a 1970 New England Journal of Medicine article described four military recruits born with SCT who died during basic training, (4) there has been debate over whether the carrier status is benign or associated with potentially life-threatening medical problems. Recent case reports of football players who had SCT and suffered exercise-related deaths led the National Collegiate Athletic Association to require that collegiate athletes be tested to confirm their SCT status if it was not already known. Although the intent of this testing is good, privacy concerns and possible discrimination based on carrier status have yet to be addressed.

Discrimination based on genetic difference is not new, but in the past it was largely limited to conditions that were phenotypically evident, such as Down syndrome. Since the Human Genome Project was completed, it is now possible to test for minute genetic differences that may never have any significant effect on a person’s health but that, if made public, could lead to discrimination in insurance applications, employment, and other opportunities.

These genetic differences, if tested for prenatally, have the potential to be used for what some have termed “eugenics.” The average lifespan for people born with Down syndrome has increased from 25 years in 1983 to nearly 60 years today, (5) and children who have Down syndrome are achieving more than previously believed possible in inclusive classrooms. However, studies show that 92% of women who receive a prenatal diagnosis of Down syndrome choose to terminate their pregnancies. (6)
ing be accompanied by complete, unbiased information to allow thoughtful decisions. However, mothers of children who have Down syndrome report frequently that they felt pressured to make decisions quickly in response to the test results and that they were given incorrect information regarding their child’s potential and, most importantly, the joy the child could bring into their lives. (7) Pediatricians can assist expectant parents greatly by ensuring that the information they receive is complete and accurate.

Retention and Storage of Blood Spots
Retention and use of residual blood spots is another controversial topic that the SACHDNC examined recently in a briefing paper. (8) Because NBS programs are run by the states, retention and storage practices vary widely. However, in general, these policies tend to fall into one of two groups: short-term storage (<3 y) for screening and quality control only, and long-term storage (18 to 21 y or more), which allows for the possibility of using the stored cards for research purposes.

NBS cards have been called the “ultimate biobank” and are looked on by many as a valuable resource for studying genetic factors in populations. On the other hand, states that destroy the cards relatively quickly report having concerns about the cost of storage, the space required for storage, legal questions around ownership of the cards, and the possible effect on NBS rates if parents suspect that research could be performed on their baby’s blood in the future without consent. In both Minnesota and Texas, parents have sued the state health departments over use of stored blood samples for research, and a new Oklahoma law, passed in September 2010, prohibits storage of infant DNA without parental consent.

Health Disparities and Treatment of Ethnic Minorities
The principle of justice requires that people receive fair and equal treatment. With regard to genetic testing, that principle means, at a minimum, equal access to genetic testing and counseling services. A 2006 study of predictive genetic testing showed that differential access to testing and counseling services “has led to growing health care disparities in clinical cancer genetics.” (9) Equality of access is complicated by the lack of universal medical coverage in the United States and by the fact that the prevalence of certain genetic mutations varies by ethnicity.

Minorities tend to be more concerned about privacy of genetic information, which can lead to resistance to genetic testing among certain populations. African Americans have been shown to be less likely to believe that their privacy is well protected and to have less confidence in the ability of doctors and institutions to keep their information private. (10) The Havasupai tribe recently won a legal battle with Arizona State University over DNA samples first given to researchers in 1990. (11) The blood samples were taken originally to study diabetes, but tribe members say they discovered later that the samples had been used for other purposes without their consent.

Role of the Primary Care Clinician
It is important for primary care clinicians to be aware of which conditions are screened for on an individual state’s panel and to remember that NBS is not diagnostic by itself. To minimize missed cases, false-positive results occur as a result of certain genetic conditions may be delayed when physicians feel reassured by a negative screening test result.

With each new condition added to the screening panel, the likelihood increases that an individual physician will be called with a positive result. The pediatrician should continue to be a primary source of education for parents and a valuable guide for them as they move through the NBS system. Likely there will not be enough genetic counselors to meet demand,
Summary

- Technology has allowed mapping of the human genome and screening for multiple genetic conditions with small drops of blood. Genetic tests are being marketed directly to consumers, bypassing the traditional role of the physician in determining which tests are appropriate for an individual patient.
- As genetic testing becomes even more widely available and NBS continues to expand, ethical issues must continue to be discussed and debated, including risks of discrimination and stigmatization, respect for autonomy of individuals, privacy rights, and anxiety associated with testing.
- The increase in direct-to-consumer marketing of genetic tests and the huge amount of genetic knowledge currently available make genetic counseling a vital resource that will become increasingly in demand. Primary care physicians will be called to coordinate care of patients who have genetic conditions as well as to counsel families and assist them in the decision-making process.
- Counseling should be nondirective, open-minded, and respectful of the individual’s autonomy and cultural values.

and knowledgeable, empathic communication from the pediatrician will be crucial. As with any genetic testing, the patients’ or parents’ values (including cultural values) need to be considered to assist families in making decisions.

References


Parent Resources From the AAP at HealthyChildren.org

The reader is likely to find material to share with parents that is relevant to this article by visiting this link: http://www.healthychildren.org/English/ages-stages/baby/pages/newborn-screening-tests.aspx.
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